Core Concepts in Cardiac Surgery
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Edited by

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and

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Contents

List of abbreviations  vii
List of contributors  ix

1 CABG conduits and graft configuration  1
   David Glineur

2 Off-pump versus on-pump coronary artery bypass grafting  33
   Michael E. Halkos, Emmanuel Moss, and John D. Puskas

3 Current status of minimally invasive, robotic and hybrid coronary artery bypass surgery  53
   Stephanie Mick, Suresh Keshavamurthy, and Johannes Bonatti

4 Aortic valve repair  73
   Munir Boodhwani and Gebrine El Khoury

5 Aortic valve: Conventional valve replacement and transcatheter valve implantation  97
   Jörg Kempfert and Thomas Walther

6 Open and endovascular treatment options in thoracic aortic surgery  111
   Ourania Preventza and Joseph S. Coselli

7 Mitral valve repair: Conventional open techniques  135
   A. Marc Gillinov and Tomislav Mihaljevic

8 Minimally invasive mitral valve repair  145
   Evelio Rodriguez and W. Randolph Chitwood, Jr

9 Surgical therapy for heart failure  157
   Stephen Westaby

10 Surgery for atrial fibrillation  175
    Jason O. Robertson, Lindsey L. Saint, and Ralph J. Damiano, Jr

11 Mechanical circulatory support  197
    William E. Stansfield, Antigone Koliopoulou, Stephen H. McKellar, and Craig H. Selzman

12 Current status of heart transplantation  223
    Ayyaz Ali and Robert L. Kormos

13 Current status of lung transplantation  241
    Varun Puri and G. Alexander Patterson

Index  263
### List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACAB</td>
<td>atraumatic coronary artery bypass</td>
</tr>
<tr>
<td>ACE</td>
<td>angiotensin-converting-enzyme</td>
</tr>
<tr>
<td>ACT</td>
<td>activated clotting time</td>
</tr>
<tr>
<td>AF</td>
<td>atrial fibrillation</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>AI</td>
<td>aortic insufficiency</td>
</tr>
<tr>
<td>AR</td>
<td>aortic regurgitation</td>
</tr>
<tr>
<td>AS</td>
<td>aortic valve stenosis</td>
</tr>
<tr>
<td>AV</td>
<td>aortic valve</td>
</tr>
<tr>
<td>AVJ</td>
<td>aorto-ventricular junction</td>
</tr>
<tr>
<td>AVN</td>
<td>atroventricular node</td>
</tr>
<tr>
<td>AVR</td>
<td>aortic valve replacement</td>
</tr>
<tr>
<td>BAV</td>
<td>bicuspid aortic valve</td>
</tr>
<tr>
<td>BH-TECAB</td>
<td>beating heart total endoscopic coronary bypass grafting</td>
</tr>
<tr>
<td>BIMA</td>
<td>bilateral internal mammary artery</td>
</tr>
<tr>
<td>BITA</td>
<td>bilateral internal thoracic artery</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
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<td>BOS</td>
<td>bronchiolitis obliterans syndrome</td>
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<tr>
<td>CABG</td>
<td>coronary artery bypass graft</td>
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<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
<tr>
<td>CF</td>
<td>continuous flow</td>
</tr>
<tr>
<td>CP</td>
<td>chordal procedure</td>
</tr>
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<td>CPB</td>
<td>cardiopulmonary bypass</td>
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<td>cardiopulmonary resuscitation</td>
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<td>computed tomography</td>
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<td>dual antiplatelet therapy</td>
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<td>DCD</td>
<td>donation after cardiac death</td>
</tr>
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<td>DDAVP</td>
<td>desmopressin acetate</td>
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<td>DES</td>
<td>drug-eluting stent</td>
</tr>
<tr>
<td>DHCA</td>
<td>deep hypothermic circulatory arrest</td>
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<tr>
<td>DLCO</td>
<td>diffusing capacity of the lungs for carbon monoxide</td>
</tr>
<tr>
<td>DT</td>
<td>destination therapy</td>
</tr>
<tr>
<td>EACTS</td>
<td>European Association for Cardio-Thoracic Surgery</td>
</tr>
<tr>
<td>ECGI</td>
<td>electrocardiographic imaging</td>
</tr>
<tr>
<td>ECMO</td>
<td>extracorporeal membrane oxygenation</td>
</tr>
<tr>
<td>EDHF</td>
<td>endothelium-derived hyperpolarizing factor</td>
</tr>
<tr>
<td>ERP</td>
<td>effective refractory period</td>
</tr>
<tr>
<td>FAA</td>
<td>functional aortic annulus</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FFR</td>
<td>fractional flow reserve</td>
</tr>
<tr>
<td>GEA</td>
<td>gastro-epiploic artery</td>
</tr>
<tr>
<td>HF</td>
<td>heart failure</td>
</tr>
<tr>
<td>HIFU</td>
<td>high-intensity focused ultrasound</td>
</tr>
<tr>
<td>IABP</td>
<td>intra-aortic balloon pump</td>
</tr>
<tr>
<td>ICU</td>
<td>intensive care unit</td>
</tr>
<tr>
<td>IEA</td>
<td>inferior epigastric artery</td>
</tr>
<tr>
<td>IEOA</td>
<td>indexed effective orifice area</td>
</tr>
<tr>
<td>IMA</td>
<td>internal mammary artery</td>
</tr>
<tr>
<td>IRAD</td>
<td>International Registry of Acute Aortic Dissection</td>
</tr>
<tr>
<td>ISDN</td>
<td>isosorbide dinitrate</td>
</tr>
<tr>
<td>ITA</td>
<td>internal thoracic artery</td>
</tr>
<tr>
<td>IVC</td>
<td>inferior vena cava</td>
</tr>
<tr>
<td>LA</td>
<td>left atrium</td>
</tr>
<tr>
<td>LAA</td>
<td>left atrial appendage</td>
</tr>
<tr>
<td>LAD</td>
<td>left anterior descending artery</td>
</tr>
<tr>
<td>LCC</td>
<td>left coronary cusp</td>
</tr>
<tr>
<td>LHB</td>
<td>left-sided descending artery</td>
</tr>
<tr>
<td>LIMA</td>
<td>left internal mammary artery</td>
</tr>
<tr>
<td>LITA</td>
<td>left internal thoracic artery</td>
</tr>
<tr>
<td>LRA</td>
<td>leaflet resection with an annuloplasty</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricular</td>
</tr>
<tr>
<td>LVAD</td>
<td>left ventricular assist devices</td>
</tr>
<tr>
<td>LVEDP</td>
<td>left ventricular end diastolic pressure</td>
</tr>
<tr>
<td>LVEF</td>
<td>left ventricular ejection fraction</td>
</tr>
<tr>
<td>MACCE</td>
<td>major adverse cardiac and cerebrovascular events</td>
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<td>MCS</td>
<td>mechanical circulatory support</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarcion</td>
</tr>
<tr>
<td>MIDCAB</td>
<td>minimally invasive direct coronary bypass</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------</td>
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<tr>
<td>MIMVS</td>
<td>minimally invasive mitral valve surgery</td>
</tr>
<tr>
<td>MLD</td>
<td>minimal lumen diameter</td>
</tr>
<tr>
<td>MR</td>
<td>mitral regurgitation</td>
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<tr>
<td>MRA</td>
<td>magnetic resonance angiography</td>
</tr>
<tr>
<td>MV</td>
<td>mitral valve</td>
</tr>
<tr>
<td>MVST</td>
<td>multivessel small thoracotomy</td>
</tr>
<tr>
<td>NC</td>
<td>non-coronary</td>
</tr>
<tr>
<td>NCC</td>
<td>non-compaction cardiomyopathy</td>
</tr>
<tr>
<td>NIRS</td>
<td>near-infrared spectroscopy</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
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<tr>
<td>ONCAB</td>
<td>on-pump coronary artery bypass</td>
</tr>
<tr>
<td>OPCAB</td>
<td>off-pump coronary artery bypass</td>
</tr>
<tr>
<td>OR</td>
<td>operative room</td>
</tr>
<tr>
<td>PA</td>
<td>pulmonary artery</td>
</tr>
<tr>
<td>PAU</td>
<td>penetrating atherosclerotic ulcer</td>
</tr>
<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
</tr>
<tr>
<td>PDA</td>
<td>patent ductus arteriosus</td>
</tr>
<tr>
<td>PGD</td>
<td>primary graft dysfunction</td>
</tr>
<tr>
<td>PLA</td>
<td>posterolateral artery</td>
</tr>
<tr>
<td>PPM</td>
<td>patient–prosthesis mismatch</td>
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<tr>
<td>PTCA</td>
<td>percutaneous transluminal coronary angioplasty</td>
</tr>
<tr>
<td>PTFE</td>
<td>polytetrafluoroethylene</td>
</tr>
<tr>
<td>PTLD</td>
<td>post-transplantation lymphoproliferative disease</td>
</tr>
<tr>
<td>PV</td>
<td>pulmonary vein</td>
</tr>
<tr>
<td>PVI</td>
<td>pulmonary vein isolation</td>
</tr>
<tr>
<td>PVR</td>
<td>pulmonary vascular resistance</td>
</tr>
<tr>
<td>QoL</td>
<td>quality of life</td>
</tr>
<tr>
<td>RA</td>
<td>radial artery</td>
</tr>
<tr>
<td>RAA</td>
<td>right atrial appendage</td>
</tr>
<tr>
<td>RCA</td>
<td>right coronary artery</td>
</tr>
<tr>
<td>RCC</td>
<td>right coronary cusp</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>RFA</td>
<td>radiofrequency ablation</td>
</tr>
<tr>
<td>RGEA</td>
<td>right gastroepiploic artery</td>
</tr>
<tr>
<td>RIMA</td>
<td>right internal mammary artery</td>
</tr>
<tr>
<td>RITA</td>
<td>right internal thoracic artery</td>
</tr>
<tr>
<td>RV</td>
<td>right ventricular</td>
</tr>
<tr>
<td>RVAD</td>
<td>right ventricular assist device</td>
</tr>
<tr>
<td>SAM</td>
<td>systolic anterior motion</td>
</tr>
<tr>
<td>SAN</td>
<td>sinoatrial node</td>
</tr>
<tr>
<td>SAVR</td>
<td>surgical aortic valve replacement</td>
</tr>
<tr>
<td>SCA</td>
<td>sudden cardiac arrest</td>
</tr>
<tr>
<td>STJ</td>
<td>sinotubular junction</td>
</tr>
<tr>
<td>STS</td>
<td>Society of Thoracic Surgeons</td>
</tr>
<tr>
<td>SV</td>
<td>stroke volume</td>
</tr>
<tr>
<td>SVC</td>
<td>superior vena cava</td>
</tr>
<tr>
<td>SVG</td>
<td>saphenous vein graft</td>
</tr>
<tr>
<td>SVST</td>
<td>single-vessel small thoracotomy direct-vision bypass grafting</td>
</tr>
<tr>
<td>TAAA</td>
<td>thoracoabdominal aortic aneurysm</td>
</tr>
<tr>
<td>TAVI</td>
<td>transcatheter aortic valve implantation</td>
</tr>
<tr>
<td>TECAB</td>
<td>totally endoscopic coronary artery bypass</td>
</tr>
<tr>
<td>TEE</td>
<td>transesophageal echocardiography</td>
</tr>
<tr>
<td>VAD</td>
<td>ventricular assist device</td>
</tr>
<tr>
<td>VAJ</td>
<td>ventriculo-aortic junction</td>
</tr>
<tr>
<td>VAS</td>
<td>ventricular assist system</td>
</tr>
</tbody>
</table>
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Chapter 1

CABG conduits and graft configuration

David Glineur

Coronary artery bypass graft (CABG) conduits

Left internal thoracic artery (LITA)

Anatomy

The internal thoracic artery (ITA) supplies the anterior chest wall; it arises from the subclavian artery near its origin and travels downward inside the chest wall, approximately one centimeter from the edges of the sternum. It runs posterior to the internal intercostal muscles, but anterior to the transverse muscles. The ITA divides into the musculophrenic artery and the superior epigastric artery around the sixth intercostal space.

Histology

The major characteristic of the LITA is the presence of more elastic laminae compared to gastro-epiploic artery (GEA), inferior epigastric artery (IEA), or radial artery (RA), which contain more smooth muscle cells in their walls and are therefore less elastic.¹

Intima  Both connective tissue and smooth muscle are present in the intima, the border of which is delineated by the internal elastic membrane. The internal elastic membrane may not be conspicuous due to the abundance of elastic material in the tunica media.

Media  This is the thickest of the three layers. Smooth muscle cells are arranged in a spiral around the long axis of the vessel, and secrete elastin in the form of lamellae, which are fenestrated to facilitate diffusion. These lamellae, and the large size of the media, are the most striking histological features of elastic arteries. In addition to elastin, the smooth muscle cells of the media secrete reticular and fine collagen fibers and proteoglycans. No fibroblasts are present.

Adventitia  This is a relatively thin connective tissue layer. Fibroblasts are the predominant cell type, and many macrophages are also present. Collagen fibers predominate and elastic fibers (not lamellae) are also present. The collagen in the adventitia prevents elastic arteries from stretching beyond their physiological limits during systole. Blood vessels supplying the adventitia and outer media, known as the vasa vasorum, are also present.
Endothelium function

Endothelium acts as an antithrombotic barrier as well as a modulator of vascular tone and growth. For these reasons, it is believed to be the milestone of the graft long-term patency. In response to a variety of agonists, endothelial cells generate three major autacoids that regulate vascular relaxation and other endothelium-dependent vascular functions: nitric oxide (NO), prostacyclin (PGI2), and endothelium-derived hyperpolarizing factor (EDHF).

Lüscher and colleagues studied endothelium-dependent relaxation in internal mammary arteries, internal mammary veins, and saphenous veins. Vascular rings with and without endothelium were suspended in organ chambers, and isometric tension was recorded. Acetylcholine, thrombin, and adenosine diphosphate evoked potent endothelium-dependent relaxation in the mammary artery but weak responses in the saphenous vein. In the mammary artery, relaxation was greatest in response to acetylcholine, followed by thrombin and adenosine diphosphate. In the saphenous and mammary veins, relaxation was less than 25%. Relaxation was unaffected by indomethacin but was inhibited by methylene blue and hemoglobin, suggesting that endothelium-derived relaxing factor was the mediator. Endothelium-independent relaxation in response to sodium nitroprusside was similar in arteries and veins. Lüscher concluded that endothelium-dependent relaxation was greater in the mammary artery than in the saphenous vein.

The specificity of the ITA explains why it is less damaged by arteriosclerosis compared to other arteries, a phenomenon that has been studied with an ultrasonic system. This study revealed that the intima-media complex of the ITA is protected from the influence of arteriosclerosis, in comparison with the morphological changes found in the intima-media thickness of the common carotid artery. This demonstrated protective mechanism underlines the widespread use of the ITA as a CABG conduit.

In addition, β-adrenoceptor agonists do not induce a significant relaxation of the ITA, and the use of β-adrenoceptor antagonists do not lead to IMA vasospasm.

Patency

Long-term LITA to the left anterior descending artery (LAD) patency is usually greater than 90% (range 83–98% in historical studies) (Table 1.1). Factors known to potentially influence patency include the degree of preoperative proximal coronary stenosis, the time from CABG in non-LAD arteries, sex, date of surgery, target other than LAD, and smoking status.

Degree of coronary stenosis ITA graft patency decreased as proximal coronary stenosis decreased. These findings are consistent with the physiology of arterial grafts. ITAs are able to autoregulate size and blood flow in response to demand. As proximal coronary stenosis decreases, competitive flow increases, and demand for ITA graft flow falls. This cascade of events results in ITA constriction and, over time, increased risk of atrophy and occlusion.

Kawasuji and colleagues performed angiography one month after CABG in 100 patients with ITA to LAD grafts; all grafts were patent, but 15% (2/13) of those performed to coronary arteries with 50% or less stenosis were severely constricted. Seki and colleagues observed either severe constriction or occlusion in 9.5% (14/147) of ITA grafts.
### Table 1.1 Summary of different studies on LITA patency

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Studied/ Operated</th>
<th>Percent studied</th>
<th>Interval</th>
<th>Graft patency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green⁶</td>
<td>1972</td>
<td>70/165</td>
<td>42</td>
<td>2 wk–3 y</td>
<td>97</td>
</tr>
<tr>
<td>Kay⁷</td>
<td>1974</td>
<td>91/628</td>
<td>14</td>
<td>19.5 mo</td>
<td>98</td>
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<tr>
<td>Barner⁸</td>
<td>1976</td>
<td>139/307</td>
<td>45</td>
<td>20 days</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td></td>
<td>139/307</td>
<td>45</td>
<td>13 mo</td>
<td>90</td>
</tr>
<tr>
<td>Tector⁹</td>
<td>1976</td>
<td>43/275</td>
<td>15</td>
<td>9–24 mo</td>
<td>95</td>
</tr>
<tr>
<td>Geha¹⁰</td>
<td>1979</td>
<td>175/208</td>
<td>82</td>
<td>2 wk</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td></td>
<td>?/208</td>
<td>49</td>
<td>6 mo–5 y</td>
<td>97</td>
</tr>
<tr>
<td>Tyras¹¹</td>
<td>1980</td>
<td>527/765</td>
<td>69</td>
<td>1 mo</td>
<td>95</td>
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<tr>
<td></td>
<td></td>
<td>?/765</td>
<td>65</td>
<td>1 y</td>
<td>93</td>
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<tr>
<td>Lytle¹²</td>
<td>1980</td>
<td>46/100</td>
<td>46</td>
<td>20 mo</td>
<td>91</td>
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<tr>
<td>Tector¹³</td>
<td>1981</td>
<td>88/298</td>
<td>29</td>
<td>60–108 mo</td>
<td>94.40</td>
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<td>Singh¹⁴</td>
<td>1983</td>
<td>34/</td>
<td>NA</td>
<td>3–12 y</td>
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<tr>
<td>Grondin¹⁵</td>
<td>1984</td>
<td>37/40</td>
<td>92</td>
<td>1 mo</td>
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<td>1 y</td>
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<td></td>
<td></td>
<td>20/40</td>
<td>50</td>
<td>10 y</td>
<td>84</td>
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<tr>
<td>Okies¹⁶</td>
<td>1984</td>
<td>259/4183</td>
<td>6</td>
<td>5 y, 10 y</td>
<td>83, 70</td>
</tr>
<tr>
<td>Lytle¹⁷</td>
<td>1985</td>
<td>140/</td>
<td>NA</td>
<td>5 y</td>
<td>97</td>
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<tr>
<td>Loop¹⁸</td>
<td>1986</td>
<td>855/2306</td>
<td>37</td>
<td>8.7 y</td>
<td>96</td>
</tr>
<tr>
<td>Zeff¹⁹</td>
<td>1988</td>
<td>37/39</td>
<td>92</td>
<td>8.9 y</td>
<td>95</td>
</tr>
<tr>
<td>Ivert²⁰</td>
<td>1988</td>
<td>91/99</td>
<td>92</td>
<td>2 wk</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>84/99</td>
<td>85</td>
<td>1 y</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66/99</td>
<td>67</td>
<td>5 y</td>
<td>89</td>
</tr>
<tr>
<td>Goldman²¹</td>
<td>1990</td>
<td>237/670</td>
<td>23</td>
<td>1 y</td>
<td>93</td>
</tr>
<tr>
<td>Fiore²²</td>
<td>1990</td>
<td>182/200</td>
<td>91</td>
<td>13 y</td>
<td>82</td>
</tr>
<tr>
<td>Galbut²³</td>
<td>1990</td>
<td>53/947</td>
<td>6</td>
<td>2 mo–15 y</td>
<td>92</td>
</tr>
<tr>
<td>Boylan²⁴</td>
<td>1994</td>
<td>57/100</td>
<td>57</td>
<td>&lt;10 y, &gt;10 y</td>
<td>93, 90</td>
</tr>
<tr>
<td>Goldman²⁵</td>
<td>1994</td>
<td>167/1,031</td>
<td>25</td>
<td>3 y</td>
<td>90</td>
</tr>
<tr>
<td>FitzGibbon²⁶</td>
<td>1996</td>
<td>456/476</td>
<td>96</td>
<td>6 mo</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td></td>
<td>123/476</td>
<td>26</td>
<td>5 y</td>
<td>80</td>
</tr>
<tr>
<td>Gill²⁷</td>
<td>1997</td>
<td>25/25</td>
<td>100</td>
<td>4–6 h</td>
<td>96</td>
</tr>
</tbody>
</table>
studied 16 days to 62 months after CABG. Two (14%) of these failed ITA grafts bypassed LADs with more than 50% stenosis, whereas 12 (86%) bypassed LADs with 50% or less proximal stenosis.

**Target** ITA patency is the most durable of grafts performed to the LAD, possibly because of the ease of anterior coronary arteries grafting, but also because the amount of myocardium supplied by the LAD is greater than that supplied by other coronary arteries, resulting in a larger blood flow demand. ITA grafts with greater blood flow demand are less likely to fail.\(^{34}\) In contrast, Glineur et al.\(^{35}\) could not find any significantly difference at 6 months between the right internal thoracic artery (RITA) directed to the lateral wall of the heart versus the LITA to the LAD territory (Table 1.2).

**Gender** Because of their smaller size, women have smaller coronary arteries than men. Technical difficulties associated with grafting small arteries are one possible cause of the higher operative risk observed in women, and may also be responsible for lower graft patency.\(^{28}\)

**Risk factors** Smoking is strongly associated with progression of coronary artery disease (CAD), and patients who continue to smoke after CABG have a higher risk of return of angina, myocardial infarction, and coronary reintervention.\(^{28}\) In addition, multivariable analysis revealed that a history of smoking decreased ITA graft diameter.\(^{6}\) These effects on both coronary arteries and ITA grafts probably account for the lower graft patency we observed in smokers.\(^{36}\)

**Right internal thoracic artery (RITA)**

**Anatomy, histology, endothelium function**

There are no significant differences between the left ITA and right ITA in terms of anatomy, histology, and endothelial function.\(^{37}\) There were also no statistical differences between LITA and RITA concerning mean intimal diameter (1.52 ± 0.24 vs. 1.58 ± 0.28 mm, \(P < 0.06\)), medial diameter (2.21 ± 0.27 vs. 2.52 ± 0.28 mm, \(P < 0.15\)), or wall thickness (0.39 ± 0.12 vs. 0.41 ± 0.16 mm, \(P < 0.47\)). The intimal diameters diminished significantly from the origins (1.69 ± 0.34 and 1.86 ± 0.41 mm, respectively) to the terminations (1.25 ± 0.26 and 1.14 ± 0.25 mm, respectively) of both vessels.

In order to determine whether endothelial function differs between left and right ITA segments in a Y-graft configuration, Glineur et al. studied 11 patients 3 years after surgery.\(^{18}\) The endothelium-dependent vasodilator substance P was selectively infused (1.4 up to 22.4 pmol/min in doubling dose increments) in the ostium of ITA Y-grafts. A maximal endothelium-independent vasodilatory response was then obtained by intragraft infusion of 2 mg isosorbide dinitrate (ISDN).

A similar dose-dependent vasodilatory response to substance P was observed in the left and in the right ITA (Figure 1.1). No difference in maximal endothelium-dependent response to substance P (7.4 ± 4.3% in left ITA and 8.1 ± 5.3% in right ITA) or in maximal endothelium-independent response to ISDN (12.2 ± 4.4% in left ITA and 10.6 ± 8.1% in right ITA) was observed. The endothelium-dependent and the endothelium-independent
## Table 1.2 RITA patency results

<table>
<thead>
<tr>
<th>Studies cited within Glineur et al. (2008)</th>
<th>Year</th>
<th>n</th>
<th>Methodology</th>
<th>Angiography no.</th>
<th>Mean follow-up</th>
<th>Angiographic patency rate (%)</th>
<th>Actuarial angiographic patency rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dion (49)</td>
<td>1989</td>
<td>231</td>
<td>Retro Seque IMA grafts</td>
<td>157</td>
<td>6 mo</td>
<td>Overall IMA patency of 95%</td>
<td>Overall IMA patency of 95%</td>
</tr>
<tr>
<td>Galbut (50)</td>
<td>1990</td>
<td>1,087</td>
<td>Retro</td>
<td>53</td>
<td>53 mo</td>
<td>92.1</td>
<td>84.9</td>
</tr>
<tr>
<td>Fiore (51)</td>
<td>1990</td>
<td>200</td>
<td>Retro</td>
<td></td>
<td>13 y</td>
<td>82</td>
<td>85</td>
</tr>
<tr>
<td>Chocron (52)</td>
<td>1994</td>
<td>80</td>
<td>Retro BIMA Y, Retro BIMA T</td>
<td>62</td>
<td>6-25 mo</td>
<td>97</td>
<td>63</td>
</tr>
<tr>
<td>Tector (53)</td>
<td>1994</td>
<td>486</td>
<td>Perioperative</td>
<td></td>
<td></td>
<td>98.3</td>
<td>86.5</td>
</tr>
<tr>
<td>Barra (54)</td>
<td>1995</td>
<td>80</td>
<td>Retro BIMA Y</td>
<td>80</td>
<td>16 mo</td>
<td>93.4</td>
<td>85.2</td>
</tr>
<tr>
<td>Gerola (55)</td>
<td>1996</td>
<td>201</td>
<td>Retro RIMA TS</td>
<td>36</td>
<td>51.6 mo</td>
<td>94.4</td>
<td>91.6</td>
</tr>
<tr>
<td>Pick (56)</td>
<td>1997</td>
<td>320</td>
<td>Retro</td>
<td>84</td>
<td>6.9 y</td>
<td>88</td>
<td>75</td>
</tr>
<tr>
<td>Tatoulis (57)</td>
<td>1997</td>
<td>1,454</td>
<td>Retro free RIMA</td>
<td>71</td>
<td>41.5 mo</td>
<td>94.5</td>
<td></td>
</tr>
<tr>
<td>Ura (58)</td>
<td>1998</td>
<td>115</td>
<td>Retro RIMA TS</td>
<td>73</td>
<td>59 mo</td>
<td>92.3</td>
<td>89.9</td>
</tr>
<tr>
<td>Dion (59)</td>
<td>1999</td>
<td>500</td>
<td>Retro Seque IMA grafts</td>
<td>161</td>
<td>7.4 y</td>
<td>94.3% seque IMA anast patent</td>
<td>94.3% seque IMA anast patent</td>
</tr>
</tbody>
</table>
vasodilator capacity of the two branches of a Y-graft ITA configuration appear similar 3 years after bypass surgery, suggesting that the preservation of the ITA pedicle did not significantly affect basal vasomotor tone, long-term endothelial function, or vasodilator reserve.

**Patency** The widely accepted success of the LITA has led to the use of both ITAs, although the RITA, used as an *in situ* or free graft, has never become as popular as the LITA. The apparent difference in the clinical and angiographic performance between the two ITAs was thought to be more related to the technical and flow-dynamic mechanisms than to their intrinsic characteristics.  

The overall patency of the RITA grafts to the left system is almost identical with that of LITA grafts (Table 1.3). This observation is not surprising, considering that both ITAs have identical histopathology.

The target artery grafted affected patency of both ITA, with maximum patency when grafted to the LAD. Grafts to the non-LAD arteries were at higher risk with the worst patency seen in the right coronary artery (RCA) territory.

In a recent angiographic study, Glineur et al. observed an excellent patency rate with no significant difference between the *in situ* or Y-shape use of the RITA. However, there was a significant difference with a larger number of arterial anastomosis allowed by the bilateral internal thoracic artery (BITA) Y-configuration. Long-term follow-up will help determine whether the larger number of ITA distal anastomosis allowed by the use of the Y-graft configuration translates into a superior late clinical outcome.

In a secondary analysis of this population, Glineur et al. evaluated the angiographic parameters influencing the function of the RITA used in a Y-graft configuration. In multivariate analysis, the function of the RITA was positively influenced by the number of anastomoses (OR = 0.5, 95% CI: 0.4–0.7), and a severely narrowed first circumflex...
(OR = 39.1, CI: 8.1–189.2) and negatively by the presence of a grafted intermediate coronary artery (OR = 0.01, CI: 0.003–0.06), and of a grafted RCA (OR = 0.08, CI: 0.02–0.35). The size of targeted vessel, history of infarction, and regional myocardial function did not influence RITA function.

In a recently published meta-analysis, Yi et al. confirmed that use of both mammary arteries in coronary revascularization already allowed survival benefit after 10 years of follow-up. Despite those long-term reported data, RITA remains widely underused.

**Right gastroepiploic artery (RGEA)**

**Anatomy**

The RGEA is a branch of the gastro-duodenal artery, which in turn diverges from the common hepatic artery, and thus is the fourth branch of the abdominal aorta. The RGEA runs from right to left along the greater curvature of the stomach, between the layers of the greater omentum, anastomosing with the left gastroepiploic branch of the splenic artery. This vessel gives off numerous branches: the gastric branches that ascend to supply both surfaces of the stomach, and the omental branches that descend to supply the greater omentum and anastomose with branches of the middle colic. This anatomical fact is

---

**Table 1.3** Six-month systematic angiographic control

<table>
<thead>
<tr>
<th></th>
<th>BITA Y n = 146</th>
<th>BITA in situ n = 126</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITA anastomosis angiographic patency control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LIMA</td>
<td>190/197 (96%)</td>
<td>166/169 (98%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Diagonal</td>
<td>49/51</td>
<td>43/43</td>
<td>0.55</td>
</tr>
<tr>
<td>LAD</td>
<td>141/146</td>
<td>123/126</td>
<td>0.88</td>
</tr>
<tr>
<td>RIMA</td>
<td>260/267 (97%)</td>
<td>121/126 (96%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Intermediate</td>
<td>10/10</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>OM1</td>
<td>135/137</td>
<td>120/125</td>
<td>0.37</td>
</tr>
<tr>
<td>OM2</td>
<td>81/84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLA</td>
<td>17/19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDA</td>
<td>17/17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>450/464 (97%)</td>
<td>287/295 (97%)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

crucial because coronary blood supply is determined by a pressure gradient between the aorta and the left ventricle; thus, the driving pressure of the RGEA could be lower than other graft (in situ ITA or free aorto-coronary graft).

**Histology**
The RGEA is a more muscular artery than the internal mammary artery (IMA). Smooth muscle fibers are plentiful in the media of the GEA but rare in the IMA, and elastic fibers are more plentiful in the media of the IMA than the GEA. Suma and associates reported that the RGEA has slightly more intimal thickening than the ITA, but significant luminal narrowing caused by arteriosclerosis is rare; however, one RGEA out of 35 (3%) showed overt arteriosclerosis in a patient with associated aortoiliac occlusive disease.

**Endothelium function**
Experimental data obtained in vivo has demonstrated similarities in endothelial function between rings of GEAs and IMAs, suggesting that this concept of a protective role of the endothelium contributing to the greater long-term patency rate of mammary arteries may also be applicable to GEAs. Globally similar endothelium-independent and endothelium-dependent relaxation phenomena were observed in response to several substances such as acetylcholine, metacholine, substance P, and histamine, but a much more pronounced contractility was observed in response to norepinephrine or potassium chloride in gastroepiploic than in mammary arteries, which may explain its propensity to spasm.

Cremer et al. evaluated endothelium-dependent relaxation in vivo by measuring intraoperatively the intraluminal graft pressure at mechanically controlled constant flow rates. They observed a favorable vasodilatory response to acetylcholine in IMAs, but no reaction in GEAs. Hanet et al. observed vasoconstriction in GEA grafts in contrast to no vasoconstriction in ITAs in response to methylergometrine.

**Patency**
The early graft patency rate of the GEA is comparable to that of the ITA, whereas the 10-year patency rate of the GEA is inferior to that of the ITA (Table 1.4). Flow competition between the GEA and the coronary artery could be one of the major factors affecting graft patency. The patency rates of the RGEA and the RA are highly dependent on the degree of stenosis of the native vessel, and RGEA use remains limited due to its association with a high risk of graft failure from competitive flow. The flow capacity of the RGEA under maximal stress conditions has also been questioned. For these reasons, the GEA gives an excellent clinical performance when implanted for severe coronary artery stenosis.

Glineur et al. reported similar results. Minimal lumen diameter (MLD) values for RCA stenosis of 0.77–1.4 mm and percent stenosis approximately 48–64% appear to discriminate between functional and non-functional RGEA.

**Radial artery (RA)**

**Anatomy**
The radial artery arises from the bifurcation of the brachial artery in the cubital fossa, running distally on the anterior part of the forearm. There, it marks the division between
the anterior and posterior compartments of the forearm, with the posterior compartment beginning just lateral to the artery. The artery winds laterally around the wrist, passing through the anatomical snuffbox and between the heads of the first dorsal interosseous muscle. It passes anteriorly between the heads of the adductor pollicis and becomes the deep palmar arch, which joins with the deep branch of the ulnar artery. Along its course, the RA is accompanied by the radial vein.

The most frequently encountered distal anatomical variation of the RA is a rather sizable palmar branch located in a more superficial plane than the tendon of the flexor carpi radialis muscle, situated on its radial side before turning to the dorsum of the hand at the distal extremity of the radius. Their incidence has been reported at between 1% and 15%, depending on their location in the upper or lower forearm, respectively.

**Histology**

On microscopic analysis, the wall of the RA is significantly thicker than the wall of the ITA, due to an increased thickness of the three layers (intima, media, adventitia).

**Intima**

The intima of the RA is constituted of one layer of endothelial cells above multiple layers of subendothelial cells. The internal elastic lamina is well-individualized, presenting multiple fenestrations.
Media

The elements found in the media are the same in the RA and ITA: leiomyocytes, elastic fibers, collagen fibers, and few fibroblasts and fibroblast-derived cells. However, architectural differences exist between the media of both arteries; in the RA, the myocytes are organized in multiple tight layers. Due to this dense myocyte architecture, the connective tissue seems rarefied. In the ITA, myocytes are larger and irregular in shape, and are less organized with a loose structure, making the elastic fibers and ground substance appear more abundant. Interestingly, the ratio of the thickness of media/intima is higher in the mammary artery compared to the RA (4 and 3, respectively). The external elastic lamina is identical in both arteries, is less individualized than the internal elastic lamina, and presents large fenestrations.

Adventitia

The adventitia is constituted of connective tissue containing fibroblasts and macrophages. The vasa vasorum accompanied by nerves and lymphatic vessels are exclusively located in the adventitia. This layer is thicker in the RA.

Endothelial function

As a muscular artery, the RA graft is susceptible to vasospasm, which was thought to be the principal cause of early graft failure. Numerous studies have revealed that the RA has a higher receptor-mediated contractility compared with the IMA, and human RA is an α-adrenoceptor dominant artery with weak β-adrenoceptor function. In addition, the RA exhibits greater contraction in response to potassium chloride, serotonin, and norepinephrine than the IMA. These aspects of the RA may contribute to its vasospastic characteristics. When a comparison was made of nitric oxide (NO) release and EDHF-mediated hyperpolarization for IMA and RA, the basal and stimulated releases of NO and EDHF-mediated hyperpolarization in the IMA were significantly greater than those in the RA. The lower level of NO basal release, the reduced and shorter period of stimulated NO release, and the lower EDHF-mediated hyperpolarization in the RA may account for the predisposition of RA graft to the perioperative vasospasm, and may have an impact on the early and long-term results of the graft patency.

Patency

Initially described in 1973, RA grafting was soon abandoned because reports documented dismal early angiographic outcomes. However, improvements in graft harvesting techniques, avoidance of mechanical dilation, new preservation methods, and the use of postoperative calcium channel blocker therapy to prevent early vasospasm led to improvements in RA graft patency and resurgence in the use of the RA as a bypass graft in the 1990s.

Prospective randomized control trials and meta-analyses comparing radial and saphenous vein graft (SVG) patency reached the following conclusions: RA patency is comparable to SVG patency in the short term, but is superior over both the medium and long term (Table 1.5). This was most recently demonstrated by Gaudino and the RADIAL Investigators (2018), in their landmark patient-level meta-analysis of over 1000 patients. They found that the RA graft occlusion rate of 8.1% was significantly decreased compared to the SVG graft occlusion rate of 19.9% (HR 0.44; 95% CI 0.28–0.70; P < 0.001). Finally, a prospective study
with 20-year follow-up by Gaudino and colleagues found a long-term patency of 84.8% with superior patency compared to SVG grafting.

Several factors affect the RA graft patency:

a) The severity of the target coronary artery lesion is a major predictor of RA patency because of its effect on competitive flow. RA patency decreases in correlation with the decrease of the target coronary stenosis. The less stenosed the less patent. The cut off for RA use has been placed above 85% of stenosis.

b) Skeletonization may improve patency at up to 1-year follow-up (96.5–100% vs. 77.5–86.7%). However, this improvement may result from using an ultrasonic scalpel, which has been associated with significantly increased RA blood flow.

### Table 1.5 Results of major studies on radial artery patency

<table>
<thead>
<tr>
<th>Randomized control trial</th>
<th>&lt;1 year</th>
<th>&lt;5 year</th>
<th>&gt;5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desai (2004) RAPS</td>
<td>Occlusion: RA 8.2%, SVG 13.6% (P = 0.009)</td>
<td>Patency: RA 98.3%, SVG 86.4% (P = 0.04)</td>
<td>Patency: RA 90.0%, SVG 87.0% (P = 0.29)</td>
</tr>
<tr>
<td>Collins (2008) RSVP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hayward (2010) RAPCO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goldman (2011)</td>
<td>Patency: RA 89.0%, SVG 89.0% (P = 0.98)</td>
<td>Complete occlusion: RA 8.9%, SVG 18.6% (P = 0.002)</td>
<td></td>
</tr>
<tr>
<td>Deb (2012) RAPS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Meta-analysis

<table>
<thead>
<tr>
<th>Benedetto (2010)</th>
<th>Failure: RA 14.1%, SVG 14.6% (P = 0.372)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hu (2011)</td>
<td>Occlusion: RA vs. SVG: RR 0.507 (95% CI 0.41–0.63, P &lt; 0.05)</td>
</tr>
<tr>
<td>Athanasiou (2011)</td>
<td>Patency: RA vs. SVG: OR 1.04 (95% CI 0.68–1.61, P = 0.84)</td>
</tr>
<tr>
<td></td>
<td>Patency: RA vs. SVG: OR 2.06 (95% CI 1.29–3.29, P = 0.002)</td>
</tr>
<tr>
<td></td>
<td>Patency: RA vs. SVG: OR 2.28 (95% CI 1.32–3.94, P = 0.003)</td>
</tr>
<tr>
<td>Deb (2012)</td>
<td>Occlusion: RA vs. SVG: OR, 0.52 (95% CI, 0.34–0.79; P = 0.002)</td>
</tr>
<tr>
<td>Cao (2012)</td>
<td>Complete patency: RA 79.2%, SVG 82.5% (OR 0.79, P = 0.33)</td>
</tr>
<tr>
<td></td>
<td>Complete patency: RA 89.9%, SVG 63.1% (OR 5.19, P &lt; 0.0001)</td>
</tr>
<tr>
<td>Gaudino (2018)</td>
<td>Occlusion: RA 8.1%, SVG 19.9% (P &lt; 0.001)</td>
</tr>
</tbody>
</table>

c) The proximal site of anastomosis influences the patency of the RA graft. The RA can be anastomosed as an aortocoronary graft or as a composite graft from the LITA. Jung and colleagues\(^92\) stated that increased drive pressure from a direct aortic anastomosis would improve flow through the RA when compared with anastomosis to the left internal mammary artery (LIMA). Gaudino and colleagues\(^93\) studied the same phenomenon. They concluded that ITA-anastomosed RA grafts seem to be more vulnerable to the detrimental effect of chronic native competitive flow than aorta-anastomosed conduits; Y-grafts should then probably be reserved to target vessels with subocclusive stenosis (Figure 1.2).

d) Sequential grafting improves the RA patency,\(^94–95\) especially in coronary targets of less than 1.5 mm diameter and with poor distal runoff.

**Saphenous vein graft (SVG)**

Since the late 1960s,\(^96\) CABG using saphenous vein conduits has been championed as the solution to CAD. However, it was soon evident that CABG provides only palliation to an ongoing process that is further complicated by the rapid development of vein graft atherosclerosis.

Early thrombosis and neointimal hyperplasia with subsequent atherosclerosis are thought to be the primary causes of graft failure. The cause of this failure may stem from thrombosis within the vein graft, caused by a combination of structural and physiological alterations in the vessel wall.

Neointimal hyperplasia, defined as the accumulation of smooth muscle cells and extracellular matrix in the intimal compartment of the vein, is the major disease process in
venous grafts within the first year. Nearly all veins implanted into the arterial circulation develop intimal wall thickening within 4–6 weeks, thereby reducing the lumen size. Smooth muscle cells in the media of normal adult arteries proliferate at a very low rate (<0.1%/day) but can switch very rapidly from quiescence to a proliferative state in response to appropriate stimuli.97

Injury to the intima results in migration and proliferation of smooth muscle cells from the media to the intima. The resulting luminal narrowing of the vein graft is not usually flow-limiting in itself. However, over time the area of neointimal hyperplasia may become an atherosclerosis-prone region that may lead to subsequent stenosis (Box 1.1).98

Anatomy

The SVG is the large (subcutaneous) superficial vein of the leg and thigh. The SVG originates from the joining of the dorsal vein of the first digit and the dorsal venous arch of the foot. After passing anterior to the medial malleolus (where it often can be visualized and palpated), it runs up the medial side of the leg. At the knee, it runs over the posterior border of the medial epicondyle of the femur bone. The SVG then courses laterally to lie on the anterior surface of the thigh before entering the saphenous opening in the fascia lata. It joins with the femoral vein in the region of the femoral triangle at the saphenofemoral junction.

Histology

Intima This intima consists of the endothelium and a thin subendothelial layer with smooth muscle cells among the connective tissue elements. A thin internal elastic membrane may or may not be present; if present, it is not nearly as prominent as in arteries.

Media This media is much thinner relative to that of an artery, and consists mostly of circularly arranged smooth muscle and collagen fibers. The tunica intima and media therefore tend to be less distinct from one another than is the case in arteries.

Adventitia The adventitia is usually thicker than the media and is made up mostly of collagen fibers. It may contain longitudinally oriented smooth muscle bundles.

Box 1.1 Pathogenesis of venous coronary artery bypass graft (CABG)

<table>
<thead>
<tr>
<th>Phase I: Acute thrombotic phase (&lt;1 month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II: Intimal hyperplasia (1–12 months)</td>
</tr>
<tr>
<td>♦ Hyperplasia of smooth muscle cells in the media</td>
</tr>
<tr>
<td>♦ Smooth muscle cell migration from the media to the intima</td>
</tr>
<tr>
<td>♦ Smooth muscle cell proliferation and extracellular matrix production</td>
</tr>
<tr>
<td>Phase III: Atherosclerosis (&gt;3 years)</td>
</tr>
</tbody>
</table>
**Endothelial function** The superiority of the IMA over the SVG is thought to result from favorable biological properties of the endothelium to protect this vessel against vasospasm, thrombus formation, and atherosclerosis.

Unlike ITA grafts, SVGs constrict in response to ergotamine (ERGO) and do not dilate in response to ISDN. These differences in vasomotor response could reflect heterogeneity in the sensitivity of vascular smooth muscle to these agents or differences in the basal level of vasomotor tone.

**Patency** It is estimated that during the first year after coronary bypass surgery, 10–15% of venous grafts occlude. The graft attrition rate has been estimated at 1–2% per year between 1 and 6 years, and at 4% per year between 6 and 10 years after surgery. By 10 years after surgery, approximately 60% of the vein grafts are patent; only 50% of these patent vein grafts remain free of significant stenosis.

The following list describes the relationship of patient variables to graft patency:

1. Younger age and left ventricular ejection fraction <30% significantly reduced graft patency. A possible explanation is that younger patients have a higher prevalence of risk factors (such as smoking and cholesterol) and more severe coronary disease. Reduced ejection fraction may indicate large areas of infarcted myocardium with poor distal runoff.

2. Year of operation significantly affected graft patency. For any given angiogram interval, more recently performed operations were associated with better graft patency. This observation could be due to routine use of aspirin, vigorous treatment with cholesterol-lowering agents, and the improved harvesting, preparation, and storage techniques that have evolved over the last three decades. Aspirin (325 mg/d) is associated with improved SVG patency during the first year after surgery.

3. The interval from operation to angiogram significantly affected graft patency. Graft patency of angiograms studied at less than 1 year, 1–4 years, 5–9 years, 10–14 years, and >15 years was 78%, 78%, 60%, 50%, and 50%, respectively.

Operative variables were related to graft patency as follows:

1. The target coronary artery grafted significantly affected graft patency. Grafts to the RCA had the worst patency, and those to the LAD had the best patency. The order of increasing patency was RCA > obtuse marginal artery > posterior descending artery > diagonal > LAD.

2. Target coronary artery diameter significantly affected graft patency with endarterectomy presenting the worst patency. The most likely reason is that a large-diameter vessel has a better runoff and, therefore, better graft patency.

3. Conduit diameter significantly affected graft patency. Large-diameter veins were associated with worse graft patency; better graft patency was associated with smaller conduit size.
4. Conduit wall thickness showed a trend toward affecting graft patency. The conduit wall thickness was graded as thick, normal, and thin. A thick wall was defined as >1.5 mm, normal as 1.0–1.5 mm, and thin as <1.0 mm. Thick-walled veins were associated with worst graft patency. Poor results that followed the use of large-diameter and thick-walled saphenous veins may stem from low-velocity flow within the conduit, leading to deposition of oxidized low-density lipoprotein in the graft wall.

5. Target coronary artery stenosis was not significantly associated with graft patency. Veinous grafts, as opposed to arterial grafts, are less susceptible to spasm and are less affected by competitive flow and autoregulation.

6. Distal anastomosis type, that is, end to side or side-to-side (sequential), was associated with better graft patency with the latter.

**Graft configuration**

**Strategies to revascularize the left coronary system**

BITAs have clearly demonstrated their superiority over all other types of grafts in terms of patency, freedom from arteriosclerosis, and survival benefit for revascularization of the left coronary system. Several meta-analyses have demonstrated the benefits of BITA vs. single ITA (SITA) grafting. Seven to ten years of follow-up were required before the advantages of BITA grafting were apparent, but from 10 to 20 years, the benefits of BITA are statistically and clinically significant (Figure 1.3). However, even if the ideal graft has clearly been demonstrated, the method of use is still controversial. Therefore, several configurations of BITA have been proposed to achieve complete left-sided myocardial revascularization.

There are two major BITA assembly strategies to revascularize the left coronary system with two ITA: *in situ* and free:

1a. *In situ* LITA to the LAD territory and *in situ* RITA to the circumflex territory through the transverse sinus (Figure 1.4a);

1b. *In situ* RITA to the LAD and *in situ* LITA to the circumflex territory (Figure 1.4b);

2a. *In situ* LITA to the LAD territory and free RITA implanted in a Y or T fashion into the LITA (Figure 1.4c);

2b. *In situ* LITA to the LAD territory and free RITA implanted in the aorta (Figure 1.4d).

Advantages:

a) Each ITA is used *in situ* and therefore is able to consistently provide sufficient blood flow to each target vessel;

b) The RITA does not cross the mid-line of the chest in front of the aorta in case of redo sternotomy or aortic valve surgery.
Disadvantages:

a) When using the RITA through the TS, the length used to cross the chest to reach the circumflex territory enables the grafting of medial or distal marginal branches;

b) In order to reach the proximal marginal or intermediate artery, the entire length of the RITA until its distal bifurcation is necessary. Therefore, the RITA anastomotic site is often small and very muscular, which has been identified as a factor leading to worse patency;

c) The possibilities of making sequential anastomosis is poor due to the short RITA length;

d) If multiple marginal branches have to be grafted, it is necessary to use another graft such as the radial graft or SVG. Glineur et al.\textsuperscript{37} compared \textit{in situ} RITA vs. free RITA found that the total number of graft anastomosis performed per patient was similar in both groups. However, the composite BITA Y-configuration allowed the right ITA

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\textbf{Figure 1.3} Kaplan–Meier survival curves comparing propensity-matched bilateral internal mammary artery (BIMA) and LIMA-SVG patients ($P < 0.0001$).

to reach more distal marginal branches and, in some cases, the posterolateral artery (PLA) or the patent ductus arteriosus (PDA); consequently, the number of graft anastomoses performed with ITA was significantly larger in the BITA Y group than in the BITA in situ group. Consequently, a larger number of complementary grafts were used in the BITA in situ group.

1b. *In situ* RITA to the LAD and *in situ* LITA to the circumflex territory

Advantages:

a) Each ITA is used *in situ* and therefore is able to consistently provide sufficient blood flow to each target vessel;

b) The LITA can revascularize several branches of the circumflex system, avoiding the need for an accessory graft for the circumflex system.

Figure 1.4 Different bilateral internal thoracic artery (BITA) assembling.

Image courtesy of the University of Ottawa Heart Institute
Disadvantages:

a) The RITA crosses the mid-line of the chest in front of the aorta, increasing the risk of graft injury during redo or aortic valve surgery;

b) If the LAD is very diseased and needs to be grafted distally, it is not always possible with the RITA;

c) It is very difficult to perform a sequential grafting of the diagonal and LAD with the RITA used in such configuration because of the shortage of length.

2a. *In situ* LITA to the LAD territory and free RITA implanted in a Y or T fashion into the LITA

Composite Y-graft configurations using the free RITA graft anastomosed proximally to the LITA have been widely used.\textsuperscript{116}

Advantages:

a) This assembly allows a complete myocardial revascularization with two ITAs without a complementary graft;

b) RITA does not cross the mid-line in case of redo sternotomy or aortic valve surgery;

c) There is often no need to completely harvest the RITA in this assembly, decreasing the risk of wound complications by keeping a substantial residual blood supply in the lower half of the right hemisternum.

Disadvantages:

a) The ability of this arrangement to completely revascularize the coronary system, including the RCA, has been controversial. It has been questioned whether a single ITA can consistently provide sufficient blood flow, especially in the composite Y-graft to three territories. Royse *et al.*\textsuperscript{117} reported that a composite Y-graft configuration led to a 75% increase in the free flow through a single ITA pedicle, and that the composite Y-graft had considerable potential for flow reserve.

b) There is a theoretical possibility of a “steal phenomenon” (the diversion of blood flow from a high resistance to a low resistance branch during hyperemia), resulting in a fall in the perfusion pressure in one branch of the Y assembly during periods of maximal myocardial blood flow demand.

Glineur *et al.* studied the “steal phenomenon” and completeness of revascularization with this configuration by measuring the fractional flow reserve (FFR) and the pressure drops in both branches of the composite configuration at rest and during maximal hyperemia.\textsuperscript{118} They demonstrated that a Y-graft arterial configuration with a free RITA attached to an *in situ* LITA allowed adequate revascularization of the entire left coronary system with an even distribution of perfusion pressure in both distal branches, with minimal resistance to maximal blood flow. The resulting gradual decrease in pressure along the graft was negligible under basal conditions, and remained small during maximal hyperemia induced by coronary arteriolar vasodilation. Not surprisingly, most of the pressure drop observed during hyperemia occurred across the common part of the Y-graft where the blood flow is maximal. In addition, the conductance of both branches of the Y-graft, as assessed by FFR, appeared identical, excluding the possibility of a steal phenomenon.
c) A third possible disadvantage of the BITA Y-configuration is the increased risk of competitive flow in the composite graft compared with the in situ graft. Indeed, in such assemblies the mechanism of competitive flow is more complex than in the individual graft, where the interaction is only between the proximal inflow and the distal anastomosis outflow. In this sequential composite bypass, the interaction is also between all the anastomosed branches within the composite graft, leading to a phasic delay between the pressure waves in the grafts and in the coronary arteries, especially in the more distant ones such as the RCA. Nakajima et al.\textsuperscript{119} found that the most significant predictor of competitive flow and graft occlusion was the presence of a moderately stenotic branch in the RCA territory. Glineur et al. analyzed the functioning of the right internal mammary artery (RIMA) in a Y-graft assembling, and found that the function of the RITA was significantly improved when used on several branches of the circumflex artery or on a severely narrowed (>70%) first circumflex and negatively by the presence of a grafted RCA.\textsuperscript{120}

d) The RITA arrangement for the intermediate branch grafting can be problematic when multiple grafting on the lateral wall of the heart is needed. Indeed, Glineur found that grafting a coronary branch in the intermediate region had a negative prognostic influence on RITA function.\textsuperscript{120} Some of these arrangements may cause kinking of the intermediate anastomosis, especially if the proximal Y anastomosis is performed near the pulmonary artery region or inside of the pericardium (Figure 1.5a). As a result of this finding, Glineur proposed several solutions to avoid kinking on the intermediate branch: (a) perform a proximal T anastomoses on the LITA (Figure 1.5b); (b) use a

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure15.png}
\caption{Different Y-graft composite assembling.}
\label{fig:figure15}
\end{figure}

Image courtesy of the University of Ottawa Heart Institute
second small Y-graft to prevent seagull kinking (Figure 1.5c); (c) perform the proximal composite anastomosis of a free RITA on the LITA very high on the LITA in order to obtain a smooth curve of the RITA to the intermediate branch (Figure 1.5d); and (d) perform an L/L anastomosis on the intermediate, and a T anastomosis on the circumflex artery (Figure 1.5e). It must be noted that, the latter three solutions decrease the available length of the RITA to the distal marginal branches or RCA branches.

2b. In situ LITA to the LAD territory and free RITA implanted in the aorta:

Advantages:

a) This configuration allows to do multiples anastomosis with the RITA on the lateral wall of the heart;

b) The RITA in this configuration is able to consistently provide sufficient blood flow to each target vessel;

C) The risk of competition flow is decreased in this configuration due to the high pulsatility wave generated by the direct reimplantation in the aorta.

Disadvantages:

a) The reimplantation of the RITA in the aorta requires aortic manipulation;

b) There is often a large discrepancy between the aorta and the RITA. For this reason, some authors have proposed the use of a vein or pericardial patch on the aorta to decrease this mismatch;

C) The patency of RITA reimplanted on the aorta is less than when used in situ.\textsuperscript{121}

**Strategies to revascularize the right coronary system**

Left and right coronary systems exhibit distinct physiological flow patterns and different patterns of atheromatous disease, which, for example, may account for poorer patency of an in situ RITA grafted to the RCA compared with a left-sided target. Therefore, selection of the optimal conduit for the RCA or its branches cannot simply be extrapolated from data arising from left-sided or mixed targets.

The conduits used for revascularization of the RCA system include the saphenous vein, the RITA in situ, or in a Y-composite arrangement, the free RA reimplanted in the aorta or used as a composite graft, and the RGEA. The influence of clinical results on the choice of conduit type remains unclear, and the complementary conduit of choice to this system has yet to be determined. No superior patency rate for any one of these grafts to the RCA has been established.\textsuperscript{122–123} The use of the RA or RGEA as the conduit for moderate stenosis of the RCA is limited due to its association with a high risk of graft failure owing to competitive flow. Limited flow capacity of the RGEA has also been reported.\textsuperscript{124}

Hadinata and colleagues\textsuperscript{125} reported absolute patency rates of 83.6% for the RA and 76.5% for the stroke volume (SV) targeted on the RCA; these patencies are lower than the latest reported patency rates of “Radial Artery Patency and Clinical Outcomes” (RAPCO) patients (90% for RA and 82% for SVG) on a 5-year average follow-up.\textsuperscript{126} Possible explanations for these differences include: (a) longer mean duration of follow-up may lead to a
later drop off in patency; (b) the RCA is likely a smaller target artery and has a smaller territory of runoff than the majority of the RAPCO study grafts, most of which were directed to the left side (indicating that the RCA was thought by the surgeon to be a lower-order target); (c) competitive flow in native vessel stenosis of at least 80% is a significant risk factor in RA graft failure on the right side; (d) Tatoulis and colleagues demonstrated that competitive flow in native vessel stenosis of at least 80% is a significant risk factor in RA graft failure on the right side, which may be more frequent a problem than on the left side, thereby reducing mean RA patency to the RCA territory; (e) with regards to reporting of results, symptom-directed studies may underestimate overall patency rates compare to protocol-directed angiography.

An important factor in the choice of graft conduit is the analysis of the coronary lesion. In addition to maximal percent stenosis, we use minimum lumen diameter as a surrogate for competitive flow. Maximum percent stenosis is not as good a measure of competitive flow as minimum lumen diameter; competitive flow through a 50% stenosed, 5-mm RCA must be greater than through a similarly stenosed 2-mm artery. Using only maximal coronary artery stenosis does not adjust for coronary artery size, whereas minimum lumen diameter does.

Glineur et al. enrolled 172 consecutive patients for coronary revascularization. Revascularization of the RCA was randomly performed with SVG in 82 patients and RGEA in 90 patients. All patients underwent a systematic angiographic control six months after surgery. They found that a measure above a third quartile (0.77–1.4 mm) or a stenosis of less than 55% predicted an unfavorable flow pattern in RGEA but not in SVG at six-month follow-up. In these stenosis of intermediate severity, the SVG is preferred to the RGEA or the RITA (Figure 1.6).

**Figure 1.6** In these stenosis of intermediate severity, the saphenous vein graft (SVG, shown in blue) is preferred to the right gastroepiploic artery (RGEA, shown in green) or the right internal thoracic artery (RITA).

Adapted from Glineur et al. (2011) Angiographic predictors of 3-year patency of bypass grafts implanted on the right coronary artery system: A prospective randomized comparison of gastroepiploic artery, saphenous vein, and right internal thoracic artery grafts *J Thorac Cardiovasc Surg*. 142(5):980–8 with permission from Elsevier
Figure 1.7 Decision tree for patients less than 75 years old with a three-vessels disease.
Figure 1.8 Decision tree for patients more than 75 years old with a three-vessels disease. Reproduced from Glineur D. (2013) Importance of the third arterial graft in multiple arterial grafting strategies, Annals of Cardiothoracic Surgery 2(4):475–480 with permission from the AME publishing company.
Summary

This literature review should guide surgeons in their strategies of coronary artery grafting and the manner in which they approach a patient with coronary artery disease. Accurate assessment of the severity of the coronary lesion is paramount. If the severity of the lesion is questionable, then further assessment with FFR is necessary.

Glineur proposed a decisional tree for patients younger than 75 years old (Figure 1.7). They currently use BITAs to revascularize the left coronary system in patients with no contraindications for harvesting of both ITAs. The LITA is systematically used to revascularize the LAD territory. If there is a need to revascularize a diagonal branch, a sequential jump diagonal LAD is then performed. For the lateral wall of the heart, the RITA is used in situ or in a composite fashion. If grafting of several marginals is required, the RITA is used in a composite fashion.

If the use of both ITAs is contraindicated, the RA is used for the lateral wall of the heart. Because the RA is much more sensitive to the competition flow than the ITAs, the RA is reimplanted in the aorta if the targeted coronary exhibits less than 90% stenosis. If the stenosis is more than 90%, a composite assembly is performed in the same manner as with the RITA.

For the right coronary system, a RGEA or a RITA is used only if the MLD of the coronary lesion is less than 1 mm or if the stenosis is more than 55%. In all other cases a SVG is used.

For patients older than 75 years (Figure 1.8), the strategy for the LAD territory is the same as just described; for the circumflex territory, a SVG is used. When the quality of the SVG is poor or when there are no available SVGs, a RA is used in the same manner as just described. For the right coronary system, a SVG is systematically used. If there are no SVGs available, a RA is implanted on the aorta.

References


Chapter 2

Off-pump versus on-pump coronary artery bypass grafting

Michael E. Halkos, Emmanuel Moss, and John D. Puskas

Introduction

Coronary artery bypass grafting (CABG) remains the gold standard for multivessel coronary revascularization. Despite advances in percutaneous coronary intervention and medical therapy, CABG continues to play a key role in the treatment of patients with coronary disease. Although an abundance of literature comparing on-pump (ONCAB) versus off-pump (OPCAB) coronary artery bypass grafting exists, the optimal surgical strategy remains controversial. While many centers have adopted off-pump techniques, OPCAB surgery remains in the minority of CABG procedures performed in the United States. Proponents of ONCAB cite the lack of convincing data in randomized trials demonstrating a benefit for OPCAB. Proponents of OPCAB frequently cite large observational and registry data that suggest a reduction in-hospital mortality and morbidity with OPCAB. Even more controversial are the reports of graft patency, completeness of revascularization, and the need for repeat revascularization. Reports from both randomized and observational trials can be found which suggest either equivalent or inferior results with OPCAB. Some studies have suggested that certain high-risk patient subgroups are more likely to benefit from an OPCAB approach. These include patients with advanced ascending aortic atherosclerosis, renal insufficiency, advanced age, ventricular dysfunction, and chronic lung disease, all of which are more common in patients referred for CABG compared to the general population. In these high-risk patients, avoiding the deleterious effects of cardiopulmonary bypass and minimizing or eliminating aortic manipulation may lead to improved short-term outcomes. Thus, it is important for coronary surgeons to be facile with OPCAB techniques in order to be able to implement this strategy when warranted.

Outcomes

Operative mortality

Randomized controlled trials have consistently shown comparable in-hospital mortality rates between OPCAB and ONCAB.\(^1\)\(^{-17}\) In the ROOBY trial, the largest randomized trial at the time (2,203 patients), Shroyer and colleagues demonstrated excellent 30-day mortality
rates with OPCAB and ONCAB surgery (1.9% vs. 1.8%, P = 0.25).\textsuperscript{15} In a meta-analysis of 37 randomized trials (3,369 predominantly low-risk patients), no significant differences were found for 30-day mortality (odds ratio (OR), 1.02; 95% confidence interval (CI) 0.58–1.80).\textsuperscript{18} More recently, the 4,752-patient CORONARY trial compared OPCAB to ONCAB in patients at increased risk of complications following CABG surgery and also showed equivalent 30-day mortality rates (2.5%).\textsuperscript{16} OPCAB was, however, beneficial with regard to transfusion rates, reoperation for bleeding, respiratory complications, and acute kidney injury. Another recent randomized controlled trial (RCT) compared the two surgical strategies in patients greater than 75 years of age and found equivalent mortality at 30 days (2.6% vs. 2.8% for OPCAB and ONCAB, respectively).\textsuperscript{17} In randomized patients undergoing urgent/emergent surgery for ST-segment elevation myocardial infarction, Fattouch and associates demonstrated a reduction of in-hospital mortality with OPCAB compared to ONCAB.\textsuperscript{19}

One of the criticisms of earlier randomized trials was the relatively small sample sizes, which increased the probability of type I error, especially when trying to detect differences for an infrequent event (e.g., mortality). The recent RCTs are more robust and, although each has inherent limitations, would appear to more reliably compare rare complications such as mortality, stroke, and renal failure. Several registry studies have been published that are certainly adequately powered to detect differences in mortality outcomes; however, these retrospective studies have their own limitations. In a study by Hannan et al.,\textsuperscript{20} 49,830 patients from the New York State registry underwent risk-adjusted analysis comparing outcomes after OPCAB versus ONCAB. In this study, OPCAB patients had significantly lower 30-day mortality (adjusted OR 0.81, 95% CI 0.68–0.97, P = 0.0022). In a large registry study of California CABG outcomes, Li and colleagues also demonstrated a significant reduction in propensity-adjusted operative mortality with OPCAB compared to ONCAB (OR 2.59% 95% CI 2.52–2.67% vs. 3.22%, 95% CI 3.17–3.27%).\textsuperscript{21} An intention-to-treat retrospective analysis of 42,477 patients from the Society of Thoracic Surgeons National Database (STS) showed a reduction in risk-adjusted operative mortality (adjusted OR 0.83, P = 0.03).\textsuperscript{22–25} These studies have demonstrated that operative mortality may be reduced in patients undergoing OPCAB compared to ONCAB. The perceived benefits of OPCAB may become more apparent in high-risk patients, especially those with chronic obstructive pulmonary disease, renal insufficiency, and advanced aortic atheromatous disease where avoiding aortic clamping, as well as the systemic effects of cardiopulmonary bypass being more advantageous than in low-risk patients. In a large retrospective cohort, Puskas and colleagues reported that patients in the highest risk quartile had a significant reduction in-hospital mortality with OPCAB compared to ONCAB (3.2% vs. 6.7%, P < 0.0001, OR 0.45 95% CI 0.33–0.63, P < 0.0001) (Figure 2.1).\textsuperscript{26} This study provides further evidence that OPCAB may disproportionately benefit high-risk patients. Additional studies have also reported improved outcomes in high-risk patients such as those with dialysis-dependent renal failure,\textsuperscript{27} left ventricular dysfunction,\textsuperscript{28} previous sternotomy,\textsuperscript{29} advanced age,\textsuperscript{29–32} previous stroke,\textsuperscript{33} and female patients.\textsuperscript{24}

Other studies challenge the aforementioned large registry and STS National Database conclusions. In a study by Chu and associates of 63,000 patients, there was no difference
in-hospital mortality between OPCAB and ONCAB (3.0% vs. 3.2%, \(P = 0.14\))\textsuperscript{34}. In summary, randomized trials have shown comparable in-hospital mortality rates with either strategy, whereas most observational analyses suggest a reduction in-hospital mortality with OPCAB compared to ONCAB.

Emergent conversion from OPCAB to ONCAB has been associated with significantly increased hospital mortality. Patel and colleagues reported an in-hospital mortality rate of 12% in those converted urgently to ONCAB compared to 1.5% in those who did not require urgent conversion (\(P = 0.001\))\textsuperscript{35}. Similarly, Jin and associates reported results from a large registry of over 70,000 patients. In this cohort, 5.8% of attempted OPCAB patients were converted to ONCAB and hospital mortality was significantly higher in converted patients compared to OPCAB patients or patients initially operated by an on-pump technique (9.9% vs. 1.6% vs. 3.0%, respectively)\textsuperscript{36}. Importantly, there does not appear to be an increased risk of complications in patients who are electively converted to ONCAB. This occurs during a reversible period of hemodynamic instability, which initially manifests during cardiac positioning, displacement, or coronary stabilization. Once these maneuvers are reversed, the clinical condition stabilizes, and commencement of cardiopulmonary bypass can be done under controlled circumstances.
Mid- and long-term mortality

Mid- and long-term survival has been comparable between OPCAB and ONCAB patients. In an observational study by Hannan et al., 3-year survival was equivalent in OPCAB versus ONCAB patients (unadjusted 3-year survival 89.4% vs. 90.1%, log-rank test, \( P = 0.20 \)). Within our own institutional database, 10-year survival of over 12,000 patients was equivalent between OPCAB and ONCAB groups. In a long-term follow-up (6–8 years) study of two randomized trials, Angelini compared survival outcomes of OPCAB versus ONCAB and found no difference in long-term survival between the two groups (hazard ratio, 1.24; 95% CI 0.72–2.15, \( P = 0.44 \)). Long-term follow-up of a randomized trial by Puskas and colleagues similarly showed equivalent survival between the two groups at a mean of 7.5 years.

However, the 2009 RCT by Shroyer and colleagues reported a higher 1-year composite outcome of death, repeat revascularization, or non-fatal myocardial infarction for patients undergoing OPCAB compared to ONCAB (9.9% vs. 7.4%, \( P = 0.04 \)), although the individual endpoints were not statistically different. With sensitivity analysis, 1-year death from cardiac causes was slightly higher in the OPCAB group compared to the ONCAB group (2.7% vs. 1.3%, \( P = 0.03 \)). Therefore, the 1-year results from this multi-institutional randomized trial need to be compared with the aforementioned randomized and observational analyses that have longer follow-up and which have consistently shown comparable mid- and long-term mortality rates.

Neurologic outcomes

There are no prospective randomized trials that have shown a reduction in stroke with OPCAB compared to ONCAB. Large retrospective analyses have shown that OPCAB may be associated with a reduced incidence of stroke compared to ONCAB. Hannan et al. reported a risk-adjusted decrease in postoperative stroke with OPCAB compared to ONCAB (adjusted OR 0.70, 95% CI 0.57–0.86, \( P = 0.0006 \)). Nishiyama and colleagues reported that OPCAB was associated with a significant reduction in early stroke compared to ONCAB (0.1% vs. 1.1%, \( P = 0.0009 \)). Mishra and colleagues performed a propensity matched comparison of OPCAB versus ONCAB in 6,991 patients with atheromatous aortic disease and found a significant decrease in postoperative stroke, with OPCAB being the only independent predictor of a decreased stroke rate.

Conversely, postoperative stroke was not significantly reduced in two recent meta-analyses of off- versus on-pump CABG among relatively low-risk patients. Furthermore, Chu and colleagues did not find any differences in stroke between OPCAB and ONCAB. However, the mechanisms responsible for the observed reduction in postoperative stroke have not been well-defined in most of these studies. OPCAB eliminates the need for aortic cannulation, cardiopulmonary bypass, and application of a cross-clamp but does not eliminate the need for construction of aortocoronary proximal anastomoses. Furthermore, partial aortic clamping for construction of proximal anastomoses is still routinely performed in patients undergoing OPCAB. Thus, the benefits of OPCAB may be attenuated because of aortic manipulation and atheroembolic risk associated with
partial aortic clamping. Kim and associates reported a lower incidence of postoperative stroke in patients undergoing OPCAB without any manipulation of the aorta compared to patients undergoing OPCAB with partial clamping and patients undergoing ONCAB.\textsuperscript{43} Our group recently published similar findings, showing incremental rise in stroke risk with increased degree of aortic manipulation.\textsuperscript{34} Approaches utilized to decrease the incidence of atheroemboli associated with aortic manipulation include avoidance of aortic cannulation for cardiopulmonary bypass, avoidance of aortic clamping, and use of clampless anastomotic devices for proximal anastomoses.\textsuperscript{45–47} However, the impact of these different strategies on reducing postoperative stroke has not been investigated in large-scale, prospective trials.

**Graft patency and completeness of revascularization**

Completeness of revascularization has been critical for the success and durable benefit of coronary artery bypass surgery.\textsuperscript{48,49} Evidence from several randomized trials suggests equivalent revascularization with OPCAB compared to ONCAB techniques.\textsuperscript{10,11,17,50–51} However, a multicenter study from Veterans Affairs medical centers found that fewer grafts completed than originally planned occurred more frequently in the OPCAB group (17.8\% vs. 11.1\%). A meta-analysis of randomized trials has consistently shown a lower number of grafts per patient in OPCAB versus ONCAB (2.6 vs. 2.8, \(P < 0.0001\)).\textsuperscript{24} However, the terms for completeness of revascularization and number of grafts performed should be differentiated. A common formula has been to divide the number of grafts performed by the number of grafts needed (number of graftable vessels with angiographically significant stenosis) by preoperative assessment of the cardiac catheterization. This value gives an index of completeness of revascularization. In a study of the STS National Database by Puskas and colleagues, OPCAB patients had a slightly lower index of complete revascularization than ONCAB patients.\textsuperscript{22} In a study by Magee and coworkers, the number of grafts were fewer in the OPCAB group (2.75 ± 1.12) compared to the ONCAB group (3.36 ± 1.01).\textsuperscript{52} However, because the OPCAB group needed fewer grafts, the index of complete revascularization was comparable between OPCAB and ONCAB (1.03 and 1.07, respectively). Thus, it appears that selection bias may be partly responsible for this observation, since surgeons may choose to utilize on-pump techniques on patients requiring more than three grafts. Completeness of revascularization should not be compromised when deciding whether to use or avoid cardiopulmonary bypass unless the use of cardiopulmonary bypass poses obvious and significant risk for morbidity or mortality.

Graft patency has been evaluated in five randomized trials from in-hospital to 1 year postoperatively. Puskas demonstrated no difference in graft patency at discharge and at 1 year,\textsuperscript{21} whereas Khan showed a decreased graft patency in the off-pump group at 3 months.\textsuperscript{10} Similarly, Widimsky and associates demonstrated equivalent arterial but reduced vein graft patency in OPCAB patients compared to ONCAB patients.\textsuperscript{8} Shroyer \textit{et al.} found that the overall rate of graft patency (driven by vein graft patency) was lower in the OPCAB group compared to the ONCAB group (82.6\% vs. 87.8\%, \(P < 0.001\)).\textsuperscript{15} Lamy and colleagues found an increased incidence of repeat revascularization at 30 days (0.7 vs. 0.2\%,}
Although OPCAB was associated with lower in-hospital mortality and morbidity and equivalent long-term outcomes compared to ONCAB, the need for repeat revascularization was slightly greater in the OPCAB group (93.6% vs. 89.9%). Because this was a retrospective analysis, this study was unable to differentiate whether this difference was due to incomplete revascularization during OPCAB, reduced graft patency, or due to unrecognized confounding variables.

**OPCAB technique**

**Negotiating the learning curve**

Unlike ONCAB, where graft sequence and hemodynamic management are relatively straightforward, OPCAB requires careful consideration of coronary anatomy, confounding patient variables, and attention to hemodynamic fluctuations. Early in a surgeon’s experience, patients with difficult lateral wall targets, severe left ventricular dysfunction, left main disease, or other complex cases should be excluded from an OPCAB approach. Ideal early candidates for OPCAB include those undergoing elective primary coronary revascularization with good target anatomy, preserved ventricular function, and one to three grafts with easily accessible lateral wall targets. With increasing experience, OPCAB can be safely and effectively applied to most patients requiring CABG.

**Patient variables**

The preoperative evaluation of patients for OPCAB demands careful planning and consideration for certain risk factors. It is important to consider the presence of right ventricular dysfunction, valvular regurgitation, or pulmonary hypertension since cardiac positioning and displacement during OPCAB can result in dramatic changes in hemodynamics under these conditions. With lateral displacement and transient lateral wall ischemia, even patients with mild to moderate mitral regurgitation can develop severe mitral regurgitation and pulmonary hypertension, leading to cardiovascular deterioration. Overall, the clinical condition of the patient, the urgency of the operation, and ventricular function need to be carefully assessed to determine whether an off-pump approach is practical. Patients with left ventricular dysfunction from a recent infarct pose a more difficult challenge than those with chronic ventricular dysfunction, with the former being much more sensitive to cardiac manipulation and displacement and more likely to develop intraoperative arrhythmias during transient ischemia.

**Anesthesia**

As in other cardiac operations, all patients require invasive monitoring. We routinely utilize transesophageal echocardiography to provide valuable information about valvular
regurgitation, regional myocardial function, and pulmonary hypertension. Unlike with ONCAB, adequate perfusion pressures are not controlled with cardiopulmonary bypass, careful coordination and communication between the surgeon and anesthesiologist are imperative to avoid hemodynamic demise. Subtle changes in hemodynamic status, gradual elevation in pulmonary artery pressures, frequent boluses or increased requirement of inotropes and vasopressors to maintain hemodynamic stability, and rhythm changes can herald cardiovascular collapse. Therefore, adequate volume-loading and the judicious use of inotropes and vasopressors may be required to ensure stable hemodynamics during cardiac manipulation. To adjust loading conditions, the first maneuver is adjusting the position of the operating table. Autotransfusion of intravascular volume from the lower extremities by Trendelenberg positioning can provide a rapid increase in preload, while reverse Trendelenberg can have the opposite effect. We prefer to avoid giving large volumes of intravenous fluids, which can complicate the postoperative course. If preload conditions have been optimized, then vasopressor agents such as norepinephrine or neosynephrine may be utilized to assist with maintaining adequate blood pressure during distal anastomoses.

Maintaining normothermia is critically important and requires more effort during OPCAB procedures. This can usually be accomplished by infusing intravenous fluids through warmers, warming inhalational anesthetic agents, maintaining warm room temperatures before and during the procedure, and using convective forced-air warming systems.

**Anticoagulation**

In our practice, patients receive an aspirin rectal suppository (1,000 mg) after induction of anesthesia. Aspirin 81 mg and clopidogrel (150 mg postoperatively, then 75 mg/day) are routinely administered early in the postoperative period after mediastinal drainage decreases below 100 cc/hour for four hours. This has not been associated with an increased risk of mediastinal re-exploration. This regimen is followed due to concerns regarding a relative hypercoagulable state in the early postoperative period. Intraoperative anticoagulation regimens can vary since cardiopulmonary bypass is not required. We routinely administer 5,000 units of heparin prior to the skin incision primarily to prevent thrombus formation within saphenous veins during endoscopic harvest. Prior to coronary anastomosis, some surgeons implement a full dose of heparin with 400 international units/kg to maintain an activated clotting time (ACT) of >400 seconds; others use a half dose or 180 international units/kg while others start with 10,000 units and administer additional doses (3,000 international units every half-hour) to maintain an ACT of 275–300 seconds. Reversal of anticoagulation with protamine is usually administered to facilitate hemostasis.

**Exposure**

Although OPCAB allows for minimally invasive approaches, the most common approach is via median sternotomy. The pericardium is incised in an inverted T
configuration, and then incised laterally along the diaphragm to facilitate cardiac displacement. Unlike ONCAB, the heart is not decompressed and extra conduit length is often necessary to avoid tension on the anastomosis during rightward displacement for lateral wall grafting.

Several pericardial traction sutures are placed to assist with exposure and lateral displacement of the heart. To avoid compression on the right heart during lateral displacement, the right pericardium can be dissected along the diaphragm or the right pleural space opened to allow the heart to fall into the right chest during lateral displacement. Placing rolled towels under the right side of the retractor helps to elevate the right side of the sternum to allow the heart to be displaced into the right chest. An important traction suture is the “deep stitch,” which is placed approximately two-thirds of the way between the inferior vena cava and left pulmonary vein at the point where the pericardium reflects over the posterior left atrium (Figure 2.2). Care should be taken with placement of this suture to avoid the underlying descending thoracic aorta, esophagus, left lung, and adjacent inferior pulmonary vein. This suture should be covered with a soft rubber catheter to prevent laceration of the epicardium during retraction. A warm moist laparotomy pad can be placed between the heart and the “deep stitch” to assist with elevating the heart out of the pericardium. Alternatively, a warm laparotomy pad

![Figure 2.2](image_url) The “deep stitch,” which is placed two-thirds of the way between the inferior vena cava and inferior left pulmonary vein, allows anterior and lateral displacement with retraction.
can be used alone and the “deep stitch” can be avoided. Retracting on both the left and right sides of the pericardium should not be done simultaneously during cardiac positioning since retracting the right pericardium with lateral displacement of the heart will cause compression of caval inflow. Relaxing the right pericardial sutures while pulling the left-sided sutures and the “deep stitch” taught greatly enhances exposure of the anterior and lateral walls of the heart, while avoiding compression on the right heart. These maneuvers, along with table positioning, facilitate excellent exposure once the cardiac positioner is placed.

**Positioning and stabilization**

Cardiac positioners and stabilizers have greatly increased the ability to manipulate the heart with minimal hemodynamic compromise. Two such systems include the Medtronic Octopus Tissue Stabilizer and Starfish or Urchin Heart Positioner (Medtronic, Inc, Minneapolis, MN) and the Maquet ACROBAT stabilizer and XPOSE positioner (Maquet, GMBH & Co, Rastatt, Germany). Cardiac positioning devices are frequently placed at the apex or slightly off the apex. Because these suction-based cardiac positioning devices pull the heart in the appropriate direction rather than pushing it, the heart is not compressed, functional geometry is maintained, and hemodynamics remain stable. The current generation of coronary stabilizers relies on epicardial suction rather than compression to maintain epicardial tissue capture and a motionless field in the region of grafting. Aggressive myocardial compression with the stabilizer should be avoided, since this will compromise ventricular function and lead to a paradoxical increase in motion in the target region. Instead, gentle traction on the epicardium provides for an area of stabilization. The anterior wall vessels often require only the coronary stabilizer for adequate exposure (Figure 2.3). The stabilizer is positioned along the caudal aspect of the retractor toward the left, with the retractor arm placed out of the way to prevent interference during the anastomosis. For the lateral and inferior wall vessels, the cardiac positioner is usually placed on the surgeon’s side at the most cephalad location of the retractor. The coronary stabilizers can then be placed on either side (Figure 2.4). A general rule is to put the stabilizer in the assistant’s way instead of the surgeon’s, to prevent these devices from obstructing the surgeon’s view or interfering with hand positioning during suturing.

In preparation for distal anastomosis, a soft silastic retractor tape mounted on a blunt needle (Retract-o-tape, Quest Medical, Inc, Allen, TX) is placed widely around the proximal vessel for transient occlusion (Figure 2.5). For inferior wall vessels, this suture can be displaced posteriorly and caudally by tying a more posterior pericardial suture loosely around the Retract-o-tape. The pericardial retraction suture serves as a “pulley,” which not only enhances coronary exposure and the surgeon’s view but also keeps this retraction stitch from interfering with the sutures during the anastomosis (Figure 2.6). Similarly, this maneuver can be employed for lateral wall targets. If there are concerns about hemodynamic stability during regional ischemia, the proximal vessel can be test occluded for 2–5 minutes. This gives the surgeon some assurance before committing to
Coronary grafting

Careful attention must be paid to the sequence of grafting since regional myocardial perfusion is temporarily interrupted in the beating heart. As a general rule, the collateralized vessel is grafted first, and the collaterализing vessel grafted last. For example, in patients with an occluded right coronary artery with a posterior descending artery supplied by collaterals from the left anterior descending artery, grafting the left anterior
descending first would not only leave the anterior wall ischemic, but also disrupt flow to the septum, inferior wall, and right ventricle. Thus, a more reasonable approach would involve grafting the posterior descending artery first, then performing a proximal anastomosis to ensure adequate flow while the proximal left anterior descending is occluded during construction of the left anterior descending artery (LAD) anastomosis. Another scenario that may pose problems is a large moderately (60–70%) stenotic right coronary artery. Not uncommonly, temporary occlusion of this artery will result in profound bradycardia and hypotension. In these circumstances, the surgeon must be prepared to use an intracoronary shunt or provide temporary epicardial pacing. A “proximals first” approach has been advocated by some OPCAB surgeons to allow adequate regional perfusion following completion of each distal anastomosis. With this approach, the left internal mammary artery/left anterior descending artery (LIMA-LAD) anastomosis can...
be performed after the other territories have been revascularized which minimizes subsequent cardiac and LIMA pedicle manipulation after completion of this anastomosis. During the anastomosis, it is important for the surgeon and anesthesiologist to communicate any hemodynamic alterations that occur. If hemodynamics become compromised, gently relaxing the cardiac positioner or coronary stabilizer can often ameliorate the situation. Optimizing table positioning, fluid boluses, inotropes, vasopressors, or pacing, may also help. However, if it appears that hemodynamic conditions are deteriorating, then the safe next step is to place an intracoronary shunt, relax and release both the

Figure 2.5 With the cardiac positioner and coronary stabilizer, the obtuse marginal vessels can be exposed. The right pericardial sutures should be relaxed to allow the heart to rotate into the right chest. After positioning the coronary stabilizer, a Retract-o-tape is doubly-looped around the proximal coronary artery to allow transient occlusion during the anastomosis.
OPCAB technique

stabilizer and positioner, and allow the heart to recover. At this point a decision must be made to convert “electively” to an on-pump procedure or to complete the procedure off-pump.

**Proximal anastomoses**

Epiaortic ultrasonography is utilized in all our patients undergoing cardiac surgery. It adds only 2–3 minutes to the procedure and provides both the surgeon and the anesthesiologist a simple, non-invasive, and inexpensive tool for assessing the extent of atheromatous disease in the ascending aorta in preparation for aortic clamping or selection of an alternative clampless technique. The 8.5 MHz linear array probe is placed inside a sterile sleeve filled with sterile saline to act as a medium between the probe and the surface of the aorta (Figure 2.8). This information allows the surgeon to individualize placement of aortic clamps and proximal anastomotic devices to minimize the risk of atheroembolism.

Traditionally, proximal anastomoses during OPCAB have been performed with the use of an aortic partial-occluding clamp. Unlike on-pump coronary artery bypass,
Figure 2.7 The coronary vessel is exposed and occluded proximally using the Retract-o-tape. The humidified CO$_2$ blower is shown maintaining a blood-free field.

Figure 2.8 The epiaortic ultrasound probe can be seen in a sterile saline-filled bag, being positioned over the aorta. Ascending aortic atherosclerotic burden can be adequately assessed, allowing safety of partial aortic clamping, and optimal location of proximal anastomoses, to be determined.
OPCAB provides the opportunity to completely avoid manipulation of the aorta. Avoiding partial clamping during proximal anastomoses can be achieved by performing proximal anastomoses to *in situ* arterial grafts, or using proximal automated anastomotic connectors or facilitating devices.\(^{47,60–62}\) Commercially available devices available for clampless proximal anastomoses include the Heartstring III™ (Maquet Cardiovascular LLC, San Jose, CA) or the PAS-Port™ Proximal Anastomosis System (Cardica Inc, Redwood City, CA). The Heartstring device creates a hemostatic seal with the inner surface of the ascending aorta that allows the creation of a hand-sewn anastomosis with a relatively bloodless field. The PAS-Port Proximal Anastomosis System was specifically designed to create an automated anastomosis between a saphenous vein graft and the aorta.

**Conclusions**

In conclusion, OPCAB provides surgeons with a valuable tool to enable coronary revascularization without the use of cardiopulmonary bypass or aortic clamping. This technique requires a unique skill set that can be mastered with careful patient selection and experience. While it is readily apparent that either an on- or off-pump approach can yield excellent in-hospital outcomes, there is some data suggesting that OPCAB may be advantageous in certain high-risk subgroups. Although technically more demanding than ONCAB, OPCAB allows the surgeon to avoid the potentially deleterious consequences of extracorporeal circulation and aortic manipulation, which is clearly beneficial in select circumstances. Conversely, several reports about incomplete revascularization and inferior graft patency plague the otherwise comparable mid- and long-term outcomes seen with OPCAB. Regardless of the approach selected, patients referred for surgery should undergo complete revascularization, and the precision and quality of the anastomosis must not be compromised in an effort to avoid the pump. With modern cardiac stabilizers and positioners, and with the techniques described here, excellent surgical outcomes can be expected in patients undergoing off-pump coronary artery bypass surgery.

**Acknowledgments**

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Minimally invasive direct coronary bypass (MIDCAB)

MIDCAB surgery (also referred to as single-vessel small thoracotomy direct-vision bypass grafting, or SVST) uses an anterior, medially placed, mini-thoracotomy incision for both direct-vision left internal mammary (LIMA) harvest and creation of an anastomosis of the LIMA to a coronary artery in off-pump fashion.\(^1\) It requires the use of a stabilizer placed directly through the operative (or separate port) incision.

Due to limited access to the lateral and posterior surfaces of the heart, revascularization using MIDCAB is generally limited to the left anterior descending artery (LAD) or the diagonal vessels. Specially designed retractors are available for internal mammary artery (IMA) harvesting. Originally described in 1965 by Kolessov,\(^2\) the MIDCAB procedure was reintroduced in the mid-1990s and was adopted at many centers. In comparison to conventional coronary artery bypass grafting (CABG), its decreased utilization of resources, earlier return to full activity, reduced transfusion requirement, and initially acceptable graft patency were demonstrated in many early series.\(^3\) Studies have also suggested decrease in duration of ventilation and hospital stay.\(^4\)

Pain due to chest wall retraction may be experienced following MIDCAB\(^1\) and this may have contributed to the decreased popularity. Nevertheless, experienced centers continue to successfully perform large numbers of MIDCAB procedures.\(^5\) The significant learning curve\(^5,6\) and less than optimal graft patency at some centers are probable causes for the low general acceptance of MIDCAB.

Tech

Technical details

Preoperative considerations

As in standard CABG, all patients should undergo a complete preoperative work-up, and body mass index and body habitus are to be noted. Obesity is considered a relative contraindication for MIDCAB as it may predispose to wound infection; this concern is primarily due to tissue necrosis caused due to the pressure on the wound edges by the
retractor during LIMA harvest. For similar reasons, female patients with large breasts may be at increased risk for wound-related complications. With regard to preoperative imaging, taking note of the heart position relative to the interspaces on chest X-ray can be helpful in determining the optimal placement of the access incision.

**Conduct of operation**

The patient is positioned supine with the left side up. Optimally, single lung ventilation is employed, however this is not absolutely necessary (if not utilized, reduction in tidal volume and packing of the lung away from the field are helpful maneuvers). The incision is placed in the left submammary area approximately at the mid-clavicular line in either the fourth or fifth intercostal space (Figure 3.1). The level of incision constitutes the lower limit of LIMA harvesting as the chest wall caudal to the incision cannot be visualized. Some surgeons use the fifth interspace approach in order to obtain maximal conduit length. Extending the LIMA using a segment of an additional arterial conduit to reach distal LAD targets and to avoid graft tension have been described.

Retractors utilized for LIMA harvesting (e.g., Medtronic Inc, Minneapolis, MN) have an elongated superior blade designed to retract the upper ribs out of the line of vision, preventing them from acting as a shelf, thereby limiting exposure (Figure 3.2). The LIMA is preferably taken down in a skeletonized fashion or as a thin pedicle, and is divided.

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**Figure 3.1** The limited left anterolateral thoracotomy for minimally invasive direct coronary bypass (MIDCAB) is ~5–7 cm commencing in the mid-clavicular line in the fourth intercostal space. Also shown is the port placement for the endo stabilizer which can later be used for insertion of a chest tube.

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following systemic anticoagulation (to ACT levels of 300 s). The LIMA retractor is then replaced with a standard thoracotomy retractor. The pericardial fat pad is then resected.

Prior to incising the pericardium, the phrenic nerve should be identified. The pericardium is incised longitudinally anterior to the phrenic to the level of the base of the heart. Stay sutures are useful in positioning the heart. The apex is first identified and then the LAD, which is situated to its right and courses parallel to the sternum. A diagonal artery may be the first vessel visualized and it is important not to mistake this for the LAD. Once the LAD has been identified, a stabilizer is positioned (Figure 3.3). Silastic loops are placed proximally and distally if necessary (note that distal snares are preferably avoided as they may lead to scar lesions and impaired flow). Premedication with lidocaine or another antiarrhythmic should be employed prior to vessel occlusion. Should hemodynamic compromise be encountered following occlusion, the use of an intracoronary shunt may be employed with the vessel occluders released while performing the anastomosis. Whether shunted or not, the anastomosis is created with continuous 7-0 Prolene if the artery is fragile or small. Assessment of flow is recommended using transit time ultrasound.

After heparin reversal and confirmation of hemostasis, the pericardium is loosely reapproximated to prevent heart herniation and adherence of the apex to the intercostal
space (some authors recommend using a patch of bovine pericardium). It is important to ensure the LIMA does not kink, particularly as it passes through the pericardium. A nerve block may be achieved by direct infiltration of 0.25% bupivacaine into the posterior intercostal spaces from ribs four to six. A single chest tube is placed and the ribs, pectoral muscle, and skin closed in a standard fashion.

**Thoracoscopic MIDCAB**

The LIMA is harvested thoracoscopically via port access incisions and the LIMA to LAD anastomosis is created through a mini-thoracotomy with minimal rib spreading.

The largest series of thoracoscopic MIDCAB was reported by Vassiliades et al. in 2007 who termed this approach “endoscopic atraumatic coronary artery bypass” (endo-ACAB) and reported a 3.6% conversion to sternotomy/thoracotomy rate, a 1% postoperative mortality rate (compared to the Society of Thoracic Surgeons (STS) National Database-predicted 30-day mortality of 2.7%), and a 0.3% stroke rate. These authors report a 96% LIMA to LAD patency rate at a mean follow-up of 18 months. The mean length of stay in the intensive care unit was 11.2 ± 9.9 hours, and hospital stay an impressive 2.4 ± 1.3 days. With an estimated 50-case learning curve required for mastery of the technique, the thoracoscopic MIDCAB has not achieved widespread adoption at this time; however, centers with expertise in the technique have shown good results. Robotically assisted MIDCAB represents an alternative and will be discussed here in conjunction with other robotic techniques.
Technical details

Preoperative considerations

In general, patients with body mass index less than 30 are selected for surgeons early into their learning curve. Women with large breasts may be challenging as a larger submammary incision may be required or ports may need to pass through breast tissue. Thoracoscopic LIMA takedown requires hemithorax insufflation with CO₂ and the ability to tolerate single lung ventilation should be assessed preoperatively—FEV1 less than 1 L on spirometry is usually the cutoff value.

Conduct of operation

The patient is positioned supine as with MIDCAB. Using single lung ventilation, three ports are placed in the left mid-axillary line in the third, fifth, and seventh interspaces (some recommend the fifth interspace port be placed in the anterior axillary line). Standard thoracoscopic instruments are used. A 30-degree (either 5 mm or 10 mm) thoracoscope is placed via the fifth space and carbon dioxide insufflation is initiated to a target pressure of 8 mmHg. If hemodynamic compromise occurs, it may be due to hypertensive pneumothorax (especially in patients with compromised left ventricular function). Decreasing the rate of insufflation or evacuating some of the carbon dioxide from the thoracic space should rapidly improve the hemodynamics.

Next, a grasper and electrocautery or harmonic scalpel via the third and seventh interspaces are inserted. Gentle spatulation with the electrocautery or harmonic scalpel should be used to identify the side branches of the IMA. The entire IMA can be harvested from the subclavian vein to the level of the xiphoid process (clips are seldom used) in a pedicled fashion. Care should be taken to avoid damage to the phrenic nerve and subclavian vein.

Anastomosis creation proceeds in a manner similar to that described for MIDCAB.

Multivessel minimally invasive procedures

The benefits of the MIDCAB can be extended to those patients with multivessel disease by combining it with percutaneous coronary intervention (PCI) for lesions on the posterior and lateral surfaces of the heart in a hybrid approach when the non-LAD lesions are amenable to PCI.

The use of bilateral MIDCABs involving the use of bilateral anterior (medially placed) mini-thoracotomies and bilateral direct-vision internal mammary (as well as radial artery) conduits use has been reported. The use of bilateral thoracoscopic IMA harvesting followed by right anterior thoracotomy for the bypass of right coronary artery and LAD territories has also been described. However, bypassing the posterolateral surface requires bilateral thoracotomies.

One procedure, termed the “anterolateral thoracotomy/coronary artery bypass” (ALT-CAB) uses a larger left thoracotomy to harvest both the LIMA and right internal mammary artery (RIMA) under direct vision and all territories of the heart may be bypassed.
In a series of 255 patients, complete revascularization was achieved in all patients with no conversions to cardiopulmonary bypass (CPB). The mortality and stroke rate in this series was 1.2% and 0.8%, respectively, and 65.1% of patients were discharged within 48 hours.16

The most recent non-robotic minimally invasive option for multivessel disease (introduced in 2005) is termed “minimally invasive coronary artery bypass grafting” (MICS-CABG)15 (also referred to as “multivessel small thoracotomy,” MVST).17 The MICS-CABG technique uses a more laterally placed thoracotomy than open MIDCAB and employs a specialized pivoting retractor that allows harvesting of the full-length of the LIMA. Two additional port-site incisions allow for the use of an epicardial stabilizer and an apical positioner. MICS-CABG is performed off-pump and does not require the use of thoracoscopic or robotic equipment and essentially amounts to a multivessel off-pump coronary artery bypass (OPCAB) performed through small non-sternotomy incisions. One limitation of the MICS-CABG is that RIMA takedown is not possible without using a larger incision, thoracoscopic or robotic assistance18; however, this limitation is in part offset by the use of saphenous vein grafts with proximal anastomoses to the ascending aorta.15

A dual center series of 450 patients over 3.5 years was reported for the MICS-CABG technique and showed encouraging results. A 3.8% conversion to sternotomy was reported and conversion to on-pump procedure (via peripheral cannulation) was reported in 7.6%. Proponents of MICS-CABG assert that it has a greater potential for wider adoption as it does not require the costly infrastructure associated with robotic or thoracoscopic procedures.17

MICS-CABG was compared to standard OPCAB using case-matching of a single surgeon’s practice. There were no differences in mortality or rate of atrial fibrillation between groups, however a higher rate of pleural effusion in the MICS-CABG group was observed (15% vs. 4%, \( P = 0.002 \)).19 There is no long-term data available on graft patency, but early studies suggest acceptable short-term patency rates (92% for all grafts and 100% for LIMA grafts at 6 months).20

**Robotically assisted revascularization**

Robotic surgical systems are telemanipulators in which a surgeon controls microinstruments remotely from a console. The most widely used system is the da Vinci Si (Intuitive Surgical, Mountain View, CA). The system conveys high definition three-dimensional imaging to the surgeon at the console and sensors register finger and wrist movements and translate them, tremor-free, into the motion of the microinstruments in the operative field. Around 2,000 robotic cardiac operations are performed in the United States per year and the number is increasing modestly.21

There are several ways in which robots are used in CABG. These include robotically assisted MIDCAB (robotic IMA harvest with hand-sewn anastomosis via anterior thoracotomy) to totally intrathoracic revascularization performed solely through small
port-site incisions (totally endoscopic CABG, or totally endoscopic coronary artery bypass (TECAB)). TECAB can be performed with or without use of CPB and cardioplegic arrest. When cardioplegic arrest is used, the term arrested heart TECAB (AH-TECAB) is used. When the heart is not arrested, the procedure is referred to as beating-heart TECAB (BH-TECAB).

Robotically assisted IMA harvest is followed by single hand-sewn anterior anastomosis via a small thoracotomy in an off-pump fashion. When compared with a single-vessel OPCAB, robotically assisted MIDCAB has been shown to result in shorter hospital stay and quicker return to work. Robotically assisted MIDCAB has also been utilized as part of hybrid revascularization. TECAB may be used for single or multiple vessel bypasses (generally utilizing bilateral IMAs) and is the least physically invasive means of coronary revascularization. In contrast to other minimally invasive approaches, TECAB does not involve the use of incisions larger than port sites. First performed in 1998, proponents of TECAB cite minimal surgical trauma and rapid recovery as the major advantages to this procedure. As no rib spreading is involved, there is minimal intercostal nerve trauma and less postoperative pain.

A recent review on TECAB showed results that compare favorably with conventional approaches with the exception of reoperation for bleeding. The early patency rate was 96.4% (in the 253 patients who had some form of early imaging study). Five-year data on 62 single-vessel disease patients undergoing TECAB demonstrate 95.8% survival, 83.1% freedom from major adverse cardiac and cerebrovascular events (MACCE), and 91.1% freedom from angina. Long-term follow-up on graft patency comes from Currie et al., who reported a 92.7% overall patency rate at 8 years in a mixed on- and off-pump practice.

**Technical details**

**Preoperative evaluation**

We recommend preoperative computed tomography (CT) angiography of the chest, abdomen, and pelvis to assess for the size of the heart and its relation to the chest wall, size of the pericardial fatpad, and relation of the internal mammary arteries to the target vessels. In our experience, a distance of less than 25 mm from the left heart border to the chest wall can lead to significant technical challenges owing to insufficient working space. Additionally, the course (intramyocardial vs. epicardial) of the target vessels should be noted along with the ascending aortic diameter and grade of aortoiliac atherosclerosis. We also recommend pulmonary function testing in all patients being considered for TECAB with the FEV1 and diffusing capacity of the lungs for carbon monoxide (DLCO) values, which are important not only for determining the patient’s ability to tolerate single lung ventilation during IMA takedown but also to obtain a sense of intrathoracic volume. We have observed intraoperative technical difficulties (related to space limitations), and postoperative morbidity to increase in patients with an FEV1 of less than 2.5 L.
The role of cardiopulmonary bypass and cardioplegic arrest in TECAB

TECAB can be performed with or without the use of CPB. Endoscopic suturing is technically challenging and we strongly advise gaining experience with arrested heart TECAB prior to undertaking BH-TECABs. We recommend prophylactic peripheral cannulation under all circumstances, even if BH-TECAB is planned, to be prepared for “worst case scenarios” (e.g., ventricular fibrillation with the robot docked). Without prior cannulation and the ability to immediately initiate CPB, such situations can rapidly grow dire, with potential for great harm to the patient and the TECAB program at the surgeon’s institution. Therefore, we reiterate our recommendation to prophylactically cannulate all cases under controlled conditions. It is to be noted that going on bypass and deflating both lungs can also provide significant additional space inside the chest if needed in a BH-TECAB.

Arrested heart TECAB requires specific perfusion and cardioplegia skills. Surgeons are strongly advised to develop remote access perfusion techniques in other minimally invasive cardiac cases before attempting TECAB. Remote access CPB and the use of ascending aortic balloon occlusion is technically challenging and requires discipline in patient selection. Femoral cannulation and endoballoon should only be used in patients without aortoiliac atherosclerosis (~2/3 of patients in our experience). Axillary antegrade perfusion and femoral insertion of the endoballoon is the best option for patients with moderate grades of aortoiliac atherosclerosis. Transthoracic clamping and direct aortic root cannulation for cardioplegia is in its early stages of development; challenges associated with this technique include transthoracic puncture of the ascending aorta, as well endoscopic robotic control of bleeding after catheter removal.

Technical considerations in cannulation

If there is no aortoiliac atherosclerosis, femoro-femoral CPB and use of an endoaortic balloon is standard. It is possible for all cannulation maneuvers including exposure of femoral vessels to be performed by one team member as another harvests the IMA. We also recommend use of a distal perfusion cannula via superficial femoral artery in all cases to ensure adequate limb perfusion. The aortic endoballoon catheter is inserted into the sidearm of an arterial perfusion cannula and advanced into the aortic root over a guidewire. We recommend cardioplegia induction with 6 mg adenosine after cross-clamping to induce prompt arrest. Use of a percutaneous coronary sinus cannula allows a standard protocol of antegrade and retrograde cardioplegia administration.

If mild to moderate aortoiliac atherosclerosis is present, femoral arterial retroperfusion is avoided and perfusion through the left axillary (via an 8-mm Dacron sidearm) and a non-perfusing endoballoon is used. Axillary exposure and anastomosis of the sidearm should be completed before docking of the robot. In these cases, the aortic endoballoon is inserted through a separate 19 F cannula in the femoral artery.

In case preoperative CT shows significant aortoiliac atherosclerosis, we forgo endoballoon use and operate on the beating heart with prophylactic peripheral
cannulation. An ACT level of ≥300 sec is used for cannulation and before starting the anastomosis with cardioplegia, the ACT is increased to ≥480 s.

**Procedural details**

Single lung ventilation is mandatory as is transesophageal echo (TEE) monitoring throughout the entire procedure. R2 defibrillator patches are placed in positions that allow sternotomy. An endovent and/or percutaneous coronary sinus cannula are placed if arrested heart TECAB is planned.

The patient is placed on the operating table (Figure 3.4) in the supine position with arms tucked and left chest slightly elevated (Figure 3.5). The patient is prepped and draped as for open CABG and all equipment for conversion to full sternotomy should be immediately available.

Correct port insertion is a step that significantly influences the whole procedure and should be performed by the most experienced team member. First, a 12.5 mm camera port is inserted (gently and cautiously so as to avoid injury to the heart or mediastinum) into the fifth intercostal space in the anterior axillary line after deflation of the left lung. Carbon dioxide insufflation (at pressures of 8 mmHg) is then initiated and an angled camera inserted. Under direct videoscopic vision, the left and right instrument ports are then placed into the third and seventh intercostal spaces, slightly anterior to the camera port. During this phase, the surgical team should remain focused on the patient’s hemodynamics as increase in intrathoracic pressure may cause hemodynamic compromise. Communication with the anesthesia team is critical; if hypotension develops during insufflation, the first attempts at correction should be lowering the CO$_2$ pressure or evacuating intrathoracic CO$_2$ (via one of the ports) rather than fluid or inotrope administration.

Following port placement, the robotic system is docked and the internal mammary artery is harvested in skeletonized fashion with the angled camera view in the “up” position using the robotic electrocautery spatula (on low-power setting) and a DeBakey forceps. Most side branches can be cauterized and clips used only for larger branches. Dissection should proceed primarily via cautery tip spatulation of surrounding tissue (Figure 3.6). It should be noted that both the left and right IMA can be taken down using the aforementioned technique. To access the right IMA, the retrosternal tissue is divided and the right pleura is entered. When bilateral conduits are used, the right IMA is harvested prior to the left. Approximately midway through IMA takedown, we fully heparinize to allow bypass to be started expeditiously should technical difficulties occur as the case proceeds.

A 5 mm assistance port is placed after IMA harvesting in the left parasternal region. This port allows insertion of material needed throughout the procedure such as bulldogs, suture material, silastic tapes, and suction tubing.

The pericardial fatpad is removed and pericardiotomy performed with the angled camera view “down” using robotic longtip forceps and electrocautery at 30 Watts. The pericardium is opened slightly lateral to the right ventricular outflow tract and extended all the way down to its reflection and then taken laterally in the caudal and cranial part, so
that a pericardial flap is created which falls into the left pleural space. This step is significantly easier on CPB (especially in obese patients and those with cardiomegaly).

**Exposure of target vessels**

The LAD can be visualized and accessed without difficulties using the aforementioned port arrangement. In beating-heart TECAB and arrested heart cases with lateral target vessels, vessel exposure is facilitated with an endostabilizer (brought in through a
**Figure 3.5** Patient positioning for TECAB with port placement sites. Ports are placed four fingerbreadths apart.

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**Figure 3.6** Robotic internal mammary artery (IMA) take-down.

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subcostal port inserted two finger breaths left lateral to the xiphoid angle) docked to the fourth arm of the robotic system.

In using the endostabilizer to access obtuse marginal branches, the operator should steer the endostabilizer gently over the left ventricle and then lift the lateral wall. In beating-heart TECAB, this maneuver can lead to hemodynamic compromise and ischemic changes and CPB could be used to obviate this problem.

The right coronary artery system may also be accessed from the patient’s left side. In this case, the endostabilizer is inserted through the left instrument port (change to a 12-mm port is necessary) and the left robotic instrument is inserted through a subcostal port. The acute margin can be lifted so that the posterior descending artery and the posterolateral branch are easily visible and accessible for anastomosis, taking great care not to injure the right ventricular epimyocardium. It should be noted that we have only utilized this technique on the arrested heart.

Once the target coronary artery is properly located and exposed, a robotic DeBakey forceps and robotic Pott’s scissors are used to incise the epicardium. The target vessel is then incised using robotic lancet beaver knife. This can be challenging at first due to the lack of tactile feedback (Figures 3.7 and 3.8). For anastomosis creation, bilateral robotic black diamond microforceps are used as needle drivers of a 7 cm 7-0 double armed polypropylene suture. The first stitch is inside-to-out on the coronary artery, forming the first bite of the first stitch of the back wall of the anastomosis close to the toe. This needle is then “parked” at a distance from the anastomosis and the anastomosis is continued with the other arm of the stitch, suturing the whole back wall going inside-to-out on the graft and outside-in on the target vessel. The graft parachuted to the coronary artery wall following the first three bites and the operator gently pulls on both suture ends frequently to ensure adequate suture tension (Figure 3.9). Suturing then continues around the heel of the anastomosis, again suturing inside-to-out on the graft and outside-to-in on the
Figure 3.8 Preparation of the conduit for grafting.
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Figure 3.9 Technique of anastomosis starting at the “toe”: note “inside-out” bites on both the coronary artery and the conduit.
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target coronary artery (Figure 3.10). This needle is then “parked” and the previously used needle is used to suture the toe and rest of the anterior wall of the anastomosis (Figure 3.11).

**Tips on anastomotic creation in arrested heart TECAB**

The coronary artery should be incised during administration of antegrade cardioplegia to fill the vessel and reduce the risk of back wall injury. The use of silastic vessel occluding loops can be very helpful in cases of target vessel backflow. All foreign material should be removed from the chest before the aortic endoballoon is deflated. The heart may later on become hyperdynamic and these maneuvers will be difficult.

**Tips on anastomotic creation in beating-heart TECAB**

Silastic loops should be placed both proximally and distally to the anastomotic site (although usually only the proximal needs to be occluded) and suturing is carried out around an intraluminal shunt. All stitches require an extra degree of gentleness in order to avoid injury to vessel walls. The magnified bouncing operative field is challenging until experience has been gained.
Multivessel TECAB

Multivessel TECAB may be achieved using bilateral in situ mammary artery grafts, sequential grafting, or Y-grafts constructed with the contralateral IMA or radial artery. Use of a vein graft with proximal anastomosis creation to the left axillary artery is also possible.26

Post-anastomosis procedures

In the robotic setting with high magnification, any needed repair sutures can be placed with excellent visualization. We recommend intraoperative flow measurements using a transit time flowprobe. Residual blood in the left pleural space may be evacuated using a tracheal suction tube brought through the parasternal assistance port. After confirmation of hemostasis, the robotic system is undocked but all ports are left in place, to be removed under direct videoscopic vision. A chest tube is inserted through the camera port with the left lung inflated so as to avoid injuries to the graft during tube insertion.

Postoperative considerations

There are currently no temporary pacing wires which can be placed endoscopically; other methods of temporary pacing (e.g., endovenous, transthoracic, pacing Swan Ganz) are

**Figure 3.11** Completed anastomosis; note last few bites using the first needle that had previously been “parked.”
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used if necessary. Special attention (neurovascular checks) should be paid to peripheral pulses following cannulation in arrested heart TECAB. Owing to single-lung ventilation during the case, respiratory compromise can occur, and the postoperative chest X-ray may show a degree of atelectasis. The camera port site is usually the most painful area until the chest tube is removed. No sternal precautions are required. MIDCAB and thoracoscopic MIDCAB patients can be extubated in the operating room (OR). We recommend initiation of dual antiplatelet therapy (DAPT: aspirin and clopidogrel) after six hours (or once chest tube drainage is minimal).

**Hybrid coronary revascularization**

**Introduction and definition**

Hybrid coronary revascularization combines surgical and catheter-based therapies for the treatment of coronary artery disease (CAD). Usually, a LIMA to the LAD is placed with PCI to the non-LAD targets.

**Rationale and background**

The hybrid approach is an effort to bring “the best of both worlds” of cardiac surgery and interventional cardiology together for the treatment of multivessel CAD.

Angelini and colleagues reported the first series of six patients, treated with a MIDCAB LIMA to LAD and percutaneous transluminal coronary angioplasty (PTCA) or PTCA and stent in 1996. A decade later, a multicenter trial showed the basic feasibility of combining robotic TECAB and PCI. Twenty-seven patients requiring double vessel revascularization were treated with TECAB LIMA-LAD, and PCI to non-LAD targets. Three-month follow-up angiography showed an excellent LIMA-LAD patency of 96.3% but lower than expected PCI patency of 66.7%. One patient suffered perioperative myocardial infarction (MI). The early reintervention rate, primarily due to stent failures, was 29.3%.

**Current state of hybrid revascularization**

Experience with this technique remains limited. No prospective randomized trials on hybrid revascularization have been published and only three series with large numbers of patients have been reported.

Available data show a low mortality (0–2%) and low morbidity overall (average of ~4.7% in hospital morbidity across all studies), with shorter hospital and intensive care unit (ICU) stays than would be expected with conventional CABG. Immediate LIMA to LAD patency rates range from 92% to 100%. With respect to restenosis rates, the data are mixed. Earlier series, which made use of bare metal stents or angioplasty without stenting, revealed higher 6-month stent restenosis rates, so that in the entire experience thus far, these rates range from 2.3% to 23%, with an average of 11% across all of the literature. When only drug-eluting stents were used in procedures combining MIDCAB and PCI, 97% 1-year patency rates were reported.
In the largest reported series of 226 patients with five-year follow-up, 1.3% hospital mortality, average hospital stay of 6 days and 92.9% 5-year survival rate were found. Five-year freedom from MACCE was 75.2% and reintervention rates were 2.7% with respect to bypass grafts and 14.2% with respect to PCI targets.29

Technical and timing considerations

The timing of the surgical procedure in relation to the PCI has been a subject of some discussion. All hybrid procedures are staged; only the duration between procedures and the order in which they are performed is varied. “Two-staged” hybrid procedures are those in which PCI and CABG are performed in separate operative locations, separated by hours, days, or weeks. “One-stop” procedures are performed in one setting, separated by minutes in a hybrid operating room.27 In a two-stage hybrid procedure, either the surgical or percutaneous intervention can be performed first. In a simultaneous procedure, the surgical intervention is usually performed first.

Percutaneous intervention prior to surgical intervention

Most patients who are treated with a “PCI first” approach undergo acute percutaneous intervention of the culprit lesion for acute coronary syndrome and the LIMA to LAD graft is placed later. Disadvantages of this approach include: the need for antiplatelet agents following PCI necessitates performing the surgical revascularization on DAPT with a slightly increased risk of bleeding1; PCI is performed in a setting in which no protection is afforded by a LIMA to LAD graft; and unless a third procedure (completion angiogram) is performed after the surgical procedure, no imaging of the LIMA-LAD graft is afforded at time of PCI.

Potential advantages to this approach include the decreased risk of ischemia if LAD occlusion is used in a beating-heart surgical approach (due to collateral circulation from the revascularized non-LAD targets). Additionally, there is the opportunity for aggressive multivessel PCI since if a complication occurs or PCI is not successful, surgical revascularization can be performed later.

Surgical intervention prior to percutaneous intervention

Performing PCI after LIMA-LAD grafting allows one to avoid possible DAPT related bleeding complications during the surgical procedure; DAPT can be started after surgery and continued long-term. Additionally, the percutaneous interventions are performed under the protection of a revascularized LAD and affords the opportunity for angiographic evaluation of the LIMA-LAD anastomosis.1

The optimal duration of time between the two interventions is unclear. Patients should at least be able to tolerate lying flat on the angiography table (this may take several days due to postoperative respiratory compromise). It also seems reasonable to delay PCI until the inflammatory milieu following surgery resolves, by perhaps 3–5 days. Additionally, patients may wish for 7–10 days of mental/physical recovery
following surgery. Ideally, PCI is completed at the index hospitalization so that the patient is not discharged without being fully revascularized.  

**Simultaneous procedures**

Two-staged procedures involve more resources (two teams, logistical challenges, costs associated with two separate procedures and possible hospitalization between the procedures) and many patients prefer the simplicity of one inclusive procedure. In centers with hybrid operating rooms, a “one-stop” procedure is possible.

Attractive features about this approach include: monitoring throughout the procedure under general anesthesia so that any complications can be resolved in one setting; a completion angiogram can be done to evaluate the LIMA-LAD graft; and the patient experiences the emotional/psychological benefit of a complete “fix” in one setting. Drawbacks include the need for specialized facilities, increased procedural times, and cost. At this point, the data regarding the effect of DAPT on bleeding in patients undergoing hybrid procedure are mixed (with some reporting increased bleeding and others reporting no such increase; and the effects of protamine reversal on stent patency are unknown).

Srivastava et al. investigated the timing of PCI related to TECAB in hybrid procedure. Most patients (73%) in their study underwent TECAB before PCI and they concluded that the timing of interventions should be individually tailored to the patient’s needs.

**Conclusion**

Improvements in technology and imaging have made a variety of minimally invasive approaches to coronary revascularization available. Despite market forces and financial considerations, it should be emphasized that the procedure is tailored to the individual patient. This is an exciting phase of reinvention for the “Heart Team” concept and it remains to be seen which of these procedures gains momentum in the community at large.

**References**


Chapter 4

Aortic valve repair

Munir Boodhwani and Gebrine El Khoury

Introduction

Aortic valve replacement remains the gold standard treatment for severe aortic valve disease. However, valve repair is emerging as a feasible and attractive alternative to valve replacement in selected patients. Valve repair can reduce or eliminate the risks of prosthesis-related complications including thromboembolism, endocarditis, anticoagulant related hemorrhage, and reoperation due to structural valve deterioration among others. Analogous to the mitral valve, a reconstructive approach to the aortic valve requires a thorough and detailed understanding of the valve anatomy, valve function, assessment and classification of pathologic lesions, and treatment of all affected components of the valve. In this chapter, we review the key features of aortic valve and root anatomy, an approach to valve assessment and lesion classification, and a demonstration of commonly used reparative techniques for aortic valve repair. Furthermore, we review the outcomes of aortic valve repair in unselected cohorts as well as distinct subsets of patients undergoing aortic valve preservation and repair.

Aortic valve anatomy and function

The anatomy of the aortic valve and root is familiar to cardiac surgeons. However, there are some features outlined next that are particularly relevant to aortic valve preserving and repair surgery. Like the mitral valve, aortic valve function involves an important interaction between the valve annulus and leaflets. Importantly, however, the annulus of the aortic valve is not a single structure but rather consists of three different components namely, the sinotubular junction, the ventriculo-aortic junction, and the anatomic crown-shaped annulus which serves as the insertion point of the aortic valve cusps (Figure 4.1). These components work together to facilitate normal valve function and together are termed the “functional aortic annulus.” The atrioventricular (AV) leaflets insert into the aortic annulus proximally at the aorto-ventricular junction (AVJ) and distally at the sinotubular junction (STJ). In a normal AV, the cusps coapt at the center of the AV orifice with a coaptation height that is approximately at the mid-level between the AVJ and the STJ. The height of the sinuses of Valsalva (from the AVJ to the STJ) corresponds to the external diameter of the STJ, which can be useful to size prostheses for aortic root replacement and to assess cusp geometry after AV repair.
As a functional entity, the AV consists of the functional aortic annulus (FAA) and the valve cusps. The integrity of these two functional components (i.e., the cusps and FAA) is the basis for good valvular function, and alteration in one of these components is frequently associated with alteration in the other. Thus, a fundamental principle in AV repair is that lesions of the cusps and the FAA should both be addressed at the time of valve repair.

The anatomy of the subvalvular region of the aortic valve and its surrounding structures also has important implications for aortic valve repair (Figure 4.1). An important observation is that external dissection of the aortic root from its surrounding structures

---

**Figure 4.1** Anatomy of the aortic valve and the functional aortic annulus (FAA). Anatomy of the subvalvular region of the aortic valve. The dotted line marks the limits of external dissection of the aortic root and the proximal suture line for a valve-sparing root replacement procedure using the reimplantation technique.

STJ, sinotubular junction; VAJ, ventriculo-aortic junction.

is limited by the membranous septum (at the junction of the non-coronary and right coronary cusps) and by ventricular muscle (at the junction of the left and right coronary cusps) whereas at all other points, external dissection down to the level of the anatomic valve annulus is possible and necessary when valve-sparing root replacement is performed using the reimplantation technique. Thus, the proximal suture line for the aortic valve reimplantation procedure follows these external limitations in a curvilinear fashion.

**Classification of aortic insufficiency**

Until recently, a major limitation to the more generalized application of aortic valve repair techniques was the absence of a common framework for valve assessment to help guide the approach to valve repair. Important lessons in this regard may be learned from the development of mitral valve repair. The Carpentier classification of mitral valve insufficiency was responsible, in large part, for the development and generalized dissemination of repair techniques for the mitral valve because it provided a common language for cardiologists, anesthesiologists, and surgeons to communicate about disease mechanisms and pathology. Key characteristics of that classification system were that it encompassed the entire spectrum of disease; it clarified and provided insight into the mechanism of insufficiency; it could be consistently applied using different assessment modalities (i.e., echocardiography

**Figure 4.2** Repair-oriented classification of aortic insufficiency.

NCC, non-compaction cardiomyopathy; LCC, left coronary cusp; RCC, right coronary cusp.

### Classification of Aortic Insufficiency

<table>
<thead>
<tr>
<th>AI class</th>
<th>Type I</th>
<th>Type II</th>
<th>Type III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal cusp motion with FAA dilatation or cusp perforation</td>
<td>cusp prolapse</td>
<td>cusp restriction</td>
</tr>
<tr>
<td></td>
<td>Type Ia</td>
<td>Type Ib</td>
<td>Type Ic</td>
</tr>
</tbody>
</table>

#### Mechanism

- **Type Ia**: Normal cusp motion with FAA dilatation or cusp perforation
- **Type Ib**: FAA dilatation
- **Type Ic**: Cusp perforation
- **Type Id**: Normal cusp motion with FAA dilatation or cusp perforation

#### Repair Techniques

- **Primary**
  - STJ remodeling
  - Ascending aortic graft
  - Aortic Valve sparing: Reimplantation or Remodeling with SCA
  - Aortic Valve sparing: Reimplantation or Remodeling with SCA
  - Patch repair
  - Autologous or bovine pericardium
  - Prolapse repair
  - Plication
  - Triangular resection
  - Free margin resuspension
  - Leaflet repair
  - Shaving decalcification patch

- **Secondary**
  - SCA
  - STJ annuloplasty
  - SCA
  - SCA
  - SCA

---

**Figure 4.3** Classification of aortic insufficiency.

AI, aortic insufficiency; FAA, functional aortic annulus; SCA, sudden cardiac arrest; STJ, sinotubular junction.

Over the past decade, we have developed a similar classification of aortic valve insufficiency with the aforementioned characteristics in mind. This classification centers around the idea that the aortic valve, much like the mitral valve consists of two major components, namely the aortic annulus and the valve leaflets. Contrary to the mitral valve, however, the annulus of the aortic valve is not a single anatomic structure. The functional aortic annulus, rather, consists of two separate components, namely the ventriculo-aortic junction and the sinotubular junction. As in Carpentier’s classification of mitral valve disease, regurgitation associated with normal leaflet motion is designated as type I. This is largely due to lesions of the FAA with type Ia aortic insufficiency (AI) due to sinotubular junction enlargement and dilatation of the ascending aorta, type Ib due to dilatation of the sinuses of Valsalva and the sinotubular junction, type Ic due to dilatation of the ventriculo-aortic junction, and lastly type Id due to cusp perforation without a primary FAA lesion. Type II AI is due to leaflet prolapse secondary to excessive cusp tissue or due to commissural disruption. Type III AI is due to leaflet restriction, which may be found in bicuspid, degenerative, or rheumatic valvular disease due to calcification, thickening, and fibrosis of the aortic valve leaflets.

Patients can present with either single or multiple lesions contributing to their aortic insufficiency. For example, patients with isolated type Ib AI (due to dilatation of the sinuses of Valsalva) are expected to have a central regurgitant jet. Thus, the presence of a sinus of Valsalva aneurysm with an eccentric AI jet suggests concomitant leaflet prolapse (type II) or restriction (type III). Further assessment of leaflet anatomy can help to better delineate the different mechanisms contributing to AI. Once the mechanism of AI is well understood, the classification system can help to guide the surgeon in the choice of surgical techniques for correction of the pathology.

**Surgical techniques**

**Exposure and assessment**

Aortic valve repair procedures are generally performed through a median sternotomy. Arterial cannulation is performed distal to any diseased aortic segments, typically in the distal ascending aorta or aortic arch. Alternatively, axillary artery cannulation may be performed in the setting of aortic arch pathology. A single, two-venous cannula is inserted through the right atrial appendage. Following cardioplegic arrest, a transverse aortotomy is performed ~1 cm above the sinotubular junction starting above the non-coronary sinus and the posterior 2–3 cm of aortic wall is left intact. The distal aorta is retracted cephalad. Full thickness 4-0 polypropylene traction sutures are placed at the three commissures and retracted using clamps but not tied in order to permit a dynamic assessment of valve anatomy. Axial traction is applied (perpendicular to the level of the annular plane) on the commissural traction sutures. This maneuver demonstrates physiological aortic valve closure position and the area and height of coaptation.
is observed. Leaflets are inspected to assess mobility, restriction, calcification, and prolapse. A prolapsing cusp will exhibit a transverse fibrous band at this time, also visible on echocardiography\(^7\) (Figure 4.4).

**Interventions on the aortic root and annulus**

Type 1 lesions are most frequently due to dilatation of the various components of the FAA and may occur in isolation or in association with cusp disease. A type 1a lesion occurs due to a supracoronary ascending aortic aneurysm with concomitant dilatation of the STJ. This is corrected by replacing the ascending aorta and remodeling the STJ using a Dacron tube graft. When significant associated AI is present, subcommissural annuloplasty is also performed. Aneurysms of the aortic root (type 1b) are frequently associated with dilatation of the STJ and the AVJ. These are treated using valve-sparing root replacement, preferentially using the reimplantation technique\(^8\) because it provides better stabilization.

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**Figure 4.4** A transverse fibrous band is typically visible on echocardiography (a, b) and surgical inspection (c, d) in the setting cusp prolapse in trileaflet aortic valves and may help in the detection and localization of cusp prolapse.

Adapted from Boodhwani et al. (2011) Assessment and repair of aortic valve cusp prolapse: Implications for valve-sparing procedures, the Journal of Thoracic and Cardiovascular Surgery 4(9):917–25 with permission from Elsevier.
of the ventriculo-aortic junction (VAJ). Aortic root remodeling may also be used to treat aneurysms of the aortic root and is particularly useful when only one or two sinuses are involved.

**Subcommissural annuloplasty**

Subcommissural annuloplasty is typically performed at mid-commissural height, except at the non-coronary/right coronary commissure where it should be performed higher in order to avoid the membranous septum and conduction tissue (Figure 4.5). Care should also be taken in this area when tying the suture in order to avoid a tear in the septum. At the other two commissures, the subcommissural annuloplasty may be performed at a lower level if greater increase in the coaptation surface is desired. A subcommissural annuloplasty reduces the width of the interleaflet triangle, improves cusp coaptation, and may help to stabilize the ventriculo-aortic junction. In the setting of a bicuspid aortic valve, however, subcommissural is not always sufficient for the prevention of future VAJ dilatation. Alternative approaches to annuloplasty of the aortic valve, without root replacement, are currently under development.

**Valve-sparing root replacement—reimplantation technique**

A valve-sparing root replacement using the reimplantation technique provides the most stable form of functional aortic annuloplasty. In addition to patients with aortic root aneurysms, this technique can also facilitate aortic valve repair in patients with moderate root dilatation in the setting of bicuspid aortic valves. The important steps of this procedure are described next.
Aortic root preparation
The key principle is to externally dissect the aortic root as low as possible, given the natural anatomic limitations (i.e., where the root inserts into ventricular muscle). The root dissection is started along the non-coronary (NC) sinus and continued toward the left coronary (LC)/NC commissure. In this area, the subannular region of the AV is fibrous and dissection can therefore be carried to below the level of insertion of the leaflets. Moving toward the right coronary (RC)/NC commissure as well as along the right sinus and the RC/LC commissure, the dissection is limited by non-fibrous portions of the annulus (Figure 4.6). The sinuses of Valsalva are then resected, leaving approximately 5 mm of aortic wall attached and the coronary buttons are harvested.

Prosthesis sizing
The three commissural traction sutures are pulled perpendicular to the annular plane with a slight inward motion to ensure good leaflet coaptation. When the leaflets are coapting adequately, a Hagar dilator is used to size the circle that includes the three commissures and a graft 4 mm larger is chosen, as this graft will sit outside the commissural posts. An alternative approach to prosthesis sizing takes advantage of the principle that in a normally
functioning aortic valve, the height of the commissure (measured from the base of the interleaflet triangle to the top of the commissure) is equal to the external diameter of the sinotubular junction\(^ {13}\) (Figure 4.7). Although various components of the aortic root and the FAA may dilate in the setting of root aneurysms, the height of the commissure remains relatively constant. The height of the commissure is most easily measured at the non-coronary/ left-coronary commissure by first drawing a connecting line between the nadirs of the two adjacent cusps (base of interleaflet triangle) and measuring the distance between this line and the top of the commissure. This height corresponds to the diameter of the graft chosen.

**Proximal suture line**

2-0 Tycron sutures with pledgets are passed from inside to outside the aorta with the pledgets on the inside, starting from the NC/LC commissure and moving clockwise.
Along the fibrous portion of the aortic annulus, these sutures are inserted along the horizontal plane formed by the base of the interleaflet triangles. Importantly, however, along the non-fibrous portions of the annulus where the external dissection of the aortic root is limited by muscle, these sutures are inserted along the lowest portion of the freely dissected aortic root making the proximal suture line slightly higher at the RC/NC and RC/LC commissures compared to the LC/NC commissure (Figure 4.8).

Prosthesis preparation and fixation

A Dacron prosthesis with or without built-in neo-aortic sinuses may be used. To prevent AI, the three commissures must be attached to the prosthesis along the same plane, the new sinotubular junction. Due to external limitations of root dissection, the graft has to be tailored. First, the distance from the base of the interleaflet triangle to top of the commissure is measured at the LC/NC commissure and marked on the graft. Then, at the RC/NC and RC/LC commissures, the distance from the proximal suture to the top of the commissure is measured and used to determine the amount of graft material that needs to be trimmed (Figure 4.9). Thus, the height of the trimmed portion is the difference between height of the unrestricted LC/NC commissure and the distance from the proximal suture line to the top of the respective commissure. The exact shape of the trimmed portion is less important as the prosthesis will accommodate to the external limitations of the aortic root. The pledgeted sutures are then passed through the base of the prosthesis, respecting the spaces between sutures and importantly, the curvilinear contour of the suture line. The commissural traction sutures are pulled up together while tying down the prosthesis to ensure appropriate seating around the aortic annulus.
Valve reimplantation

The commissures are reimplanted first using 4-0 polypropylene sutures while pulling up on the prosthesis and the native commissure and then tied into place. Radial traction is then applied on two adjacent commissural sutures and this clearly delineates the “line of implantation.” This running suture line is performed in small regular steps passing the suture from outside the prosthesis to inside and through the aortic wall, staying close to the annulus, and then back out of the prosthesis.

Leaflet assessment and repair

After valve reimplantation, it is critical to re-examine the leaflets for any unmasked prolapse, symmetry, and the height and depth of coaptation. Prolapse can be repaired using a variety of techniques described next. Cardioplegia is administered through the distal end of the graft with partial clamping to distend the new aortic root, assess root pressure, and signs of left ventricular (LV) dilatation. A limited echocardiographic view may be obtained at this time. The cardioplegia solution is then slowly aspirated out of the prosthesis without distorting the leaflets. This gives another visual assessment of AV in
its physiologic closed state as well as the area and height of coaptation. Coronary ostia are then reimplanted on the graft and the distal anastomosis is performed at the level of normal aorta.

**Cusp repair techniques**

**Cusp prolapse correction**

Cusp prolapse is associated with excess length of the free margin, which can be corrected using either central free margin plication or free margin resuspension. When a single cusp is prolapsing, the two non-prolapsing cusps serve as the reference and are used to estimate the required reduction in the free margin length. When two cusps are prolapsing, the third non-prolapsing cusp is used as a reference to indicate the desired height of coaptation. In the rare instance that all the cusps are prolapsing, the goal is to achieve a cusp coaptation height at the mid-level of the sinuses of Valsalva.

**Free margin plication**

The technique for central free margin plication has been previously described\(^1\) (Figure 4.10). A 7-0 polypropylene suture is passed through the center of the two non-prolapsing reference cusps and gentle axial traction is applied. The prolapsing cusp is

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*Figure 4.10* (a to e) Free margin plication technique for the correction of cusp prolapse. Adapted from Boodhwani M and El Khoury G (2009) Aortic Valve Repair, Operative Techniques in Thoracic and Cardiovascular Surgery 14(4):266–280 with permission from Elsevier
gently pulled parallel to the reference cusp and a 6-0 polypropylene suture is passed through the prolapsing cusp, from the aortic to ventricular side, at the point at which it meets the center of the reference cusp. Next, the direction of traction on the prolapsing cusp is reversed and the same suture is passed from the ventricular to the aortic side of the cusp where it meets the middle of the reference cusp. The length of cusp-free margin between the two ends of this 6-0 suture represents the quantity of excess-free margin which is then plicated by tying this suture with the excess tissue on the aortic side.

The plication is extended by about 5–10 mm onto the body of the aortic cusp by adding interrupted or running locked 6-0 polypropylene sutures. If there is significant excessive tissue, it can be shaved off using a scalpel or scissors keeping sufficient tissue to bring the edges together.

**Free margin resuspension**

Excess length of the cusp free margin may also be corrected using resuspension with polytetrafluoroethylene (PTFE) suture\(^{15,16}\) (Figure 4.11). A 7-0 polypropylene suture is first passed through the center (nodule of Arantis) of the two non-prolapsing cusps, which serves as a reference. A 7-0 PTFE suture is passed twice at the top of the commissure. Next, one arm of the suture is passed over and over the length of the free margin in a running fashion. The suture is locked at the other commissure. A second 7-0 PTFE is then passed in the same fashion along the cusp free margin. The length of the free margin is reduced by applying gentle traction on each branch of the PTFE sutures and applying opposite resistance with forceps at the middle of the free margin. This maneuver is used to plicate and shorten the free margin until it reaches the same length as the adjacent reference cusp-free margin. The same maneuver is applied for the second half of the free margin. This two-step technique for free margin resuspension allows symmetric and homogenous shortening. When the appropriate amount of free margin shortening is achieved, the two suture ends at each commissure are tied.

This technique may be used in isolation or in combination with other cusp repair techniques and is particularly useful in the setting of a fragile free margin with multiple fenestrations or to homogenize the free margin when a pericardial patch is used for cusp augmentation.

**Approach and techniques for bicuspid aortic valves**

Bicuspid aortic valve disease affects not only the valve cusps, but also the FAA. Bicuspid AV may be divided into two general types\(^{17,18}\) (Figure 4.12). Type 0 bicuspid AV do not contain a median raphé, have two symmetric aortic sinuses, two commissures, and a symmetric base of leaflet implantation of the two cusps. This configuration is present in a minority of cases. The mechanism of AI in this setting is usually cusp prolapse of one or both cusps due to the presence of excess cusp tissue.

Type 1 bicuspid AVs, which are significantly more prevalent, have a median raphé on the conjoint cusp and an asymmetric distribution of the aortic sinuses with a large aortic sinus accompanying a large non-conjoint cusp and two smaller cusps fused together.
7-0 PTFE sutured over & over the free margin of the prolapsing cusp

Following resuspension of free margin sutures are exteriorized on the aorta & tied

Tension applied to suture ends shortens free margin of prolapsing cusp

Figure 4.11 Free margin resuspension technique using polytetrafluoroethylene (Gore-Tex) suture for cusp prolapse correction.

with a median raphé. The raphé often attaches to the cusp base in the form of a “pseudo-
commissure,” which has a height lower than that of the true commissures. The raphé
may be restrictive, fibrotic, calcified, or prolapsing. Furthermore, the base of leaflet im-
plantation is typically larger (i.e., occupying a greater proportion of valve circumference)
and higher on the conjoint cusp compared to the non-conjoint cusp. The mechanisms
of AI in type 1 valves can be due to a rigid and restrictive raphé associated with small
fused cusps resulting in a triangular coaptation defect. Alternatively, the raphé may be
short and non-restrictive with well-developed cusps and associated prolapse of the con-
joint cusp. Bicuspid valve anatomy can be anywhere along a spectrum between type 0
and type 1. The general algorithm for the repair of bicuspid aortic valves is presented in
Figure 4.13.

In type 0 valves, the degree of prolapse is assessed by comparing the prolapsing cusp
to the non-prolapsing cusp, similar to trileaflet valves. In the case where both cusps are
prolapsing, the goal is to restore the height of coaptation to the mid-point of the sinuses of
Valsalva. This may be performed using either free margin plication, free margin resuspen-
sion with 7–0 PTFE suture, or both as previously described for trileaflet valves. Thickened,
fibrotic areas of the leaflet (typically central aspect of the free margin) are shaved and lo-
calized decalcification is performed if calcium is present.

In type 1 valves, the median raphé is addressed first. If the raphé is relatively mobile and
only mildly thickened and fibrosed, it is preserved and shaved using a combination of a
scalpel and scissors (Figure 4.14). When a severely restrictive or calcified raphé is present,
a parsimonious triangular resection of this tissue is performed (Figure 4.15). Next, the
Figure 4.13 Algorithm for annulus and cusp management in bicuspid aortic valve repair.
Figure 4.14 Shaving of a non-calcified, fibrous raphé.
Figure 4.15 Resection of a restrictive or calcified raphé (left) and assessment of the quantity of available tissue (right).
quantity of remaining cusp tissue is assessed by putting the two arms of a 6-0 polypropylene suture on the free margin of the conjoint cusp, on either side of the resected raphé. At this point, lack of cusp restriction and good valve opening are signs of the presence of adequate cusp tissue. The leaflet edges are reapprroximated primarily when adequate cusp tissue is present using running locked or interrupted 6-0 polypropylene sutures. In the absence of adequate tissue, a triangular autologous treated or bovine pericardial patch is used for cusp restoration (Figure 4.16).

Next, the free margins of both cusps are compared for the presence of any prolapse, which is corrected using free margin plication or resuspension with PTFE.

**Intraoperative echocardiography**

In addition to providing important information regarding valve anatomy and mechanism of valve dysfunction, post-repair transesophageal echocardiography is mandatory in patients undergoing aortic valve repair. More than trivial to mild residual aortic insufficiency (particularly eccentric jets), coaptation height below the aortic annulus, and coaptation length <5 mm have been shown to be important predictors of late repair failure and warrant aortic valve re-exploration.

**Outcomes**

There are no randomized controlled trials comparing the outcomes of aortic valve repair versus replacement. Data on the durability of AV repair techniques are currently limited to single-center series that are small to moderate in size, with a mean follow-up time of 5–10 years.

Overall, there are few studies reporting the outcome of unselected patients referred for aortic valve repair surgery. The success rate of valve preservation and repair in this context is rarely reported. The patients presenting for aortic valve repair are typically a heterogenous group and span the spectrum from young patients with congenital valve disease to elderly patients with degenerative aortic aneurysms and concomitant AI. As such, outcomes are frequently reported for specific subsets of patients undergoing aortic valve repair.

In a study examining the role of AI classification on surgical techniques and outcome, we evaluated 264 unselected patients undergoing AV repair (mean age 54 ± 16 years, 80% male). Approximately two-thirds of patients were identified as having a single lesion causing AI. Two lesions were identified in 30% and three in 6% of patients. Fifty percent of lesions were type I, 35% were type II, and 15% were type III. The most common set of multiple lesions were prolapse of AV leaflet in combination with type Ia (STJ dilatation, n = 14) or type Ib (aortic root aneurysm, n = 38) disease. The classification of AI correctly predicted the surgical technique utilized in the vast majority of patients (82–100%). Overall survival in this cohort was 95 ± 3% at 5 years and 87 ± 8% at 8 years. Freedom from cardiac death was 95 ± 5% at 8 years. Freedom from aortic valve reoperation and replacement at 8 years was 91 ± 5% and 93 ± 4%, respectively. Importantly, classification of
Figure 4.16 Primary re-approximation (left) or use of pericardial patch for cusp restoration (right).

AI was also predictive of late outcome with patients with type III demonstrating increased late AV reoperation and recurrent AI.

**Valve-sparing aortic replacement**

Results from large cohorts of patients performed in centers with experience with this technique generally show similar outcomes. David et al., pioneers of the reimplantation technique, reported their experience in 289 patients, 228 of which underwent the reimplantation technique and 61 underwent the remodeling technique. Early mortality was 1.7% and 12-year survival was 83%. Late freedom from reoperation at 12 years was 90% with the remodeling technique and 97% with the reimplantation technique ($P = 0.09$). Freedom from recurrent AI at 12 years was 83% after remodeling and 91% after reimplantation ($P = 0.035$). The authors concluded that the reimplantation technique provides more durable outcome.

Schafers et al. reported the outcome of the remodeling approach in 274 patients and found that early mortality was 3.6%, freedom from reoperation was 96% at 10 years, and freedom from recurrent AI was 87% at 10 years.

Our group has reported outcome in 164 consecutive patients who underwent valve-sparing aortic root replacement (74% reimplantation, 26% remodeling) looking specifically at the presence of preoperative aortic insufficiency on late outcome. Severe preoperative AI was present in 57% of patients. In this cohort, early mortality was 0.6% and late survival was 88% at 8 years. Freedom from reoperation was 90% at 8 years and freedom from recurrent AI was 90% at 5 years, and both were independent of preoperative AI severity.

**Bicuspid AV repair**

Unlike the results of valve-sparing aortic root replacement, results of bicuspid aortic valve repair reported in the literature have been quite variable between groups. These differences are largely due to the heterogeneity in the surgical techniques employed, particularly the degree of annular stabilization. Schafers et al. reported freedom from reoperation of 97% at 5 years in those undergoing the remodeling approach, but was only 53% in those not undergoing root replacement for bicuspid valve repair. A more recent update of their experience in 316 patients showed a 10-year survival of 92% and a 10-year freedom from reoperation of 81%. Absence of root replacement was predictive of repair failure. David et al. reported outcome following bicuspid aortic valve repair in 71 patients. Despite low early and late mortality, freedom from reoperation and recurrent AI at 8 years were 82% and 44%, respectively.

In our cohort of 122 patients undergoing bicuspid aortic valve repair, there was no early mortality and late survival was 97% at 8 years. Freedom from late AV reoperation was 98% and 87% at 5 and 8 years, respectively, and freedom from recurrent AI was 94% at 5 years. In our experience, root replacement led to a more durable outcome compared with subcommissural annuloplasty alone. A follow-up study was
performed comparing patients undergoing valve-sparing root replacement using the reimplantation technique to all other forms of annular stabilization in a matched cohort of patients. Patients undergoing the reimplantation technique had significantly lower rates of reoperation and recurrent AI. This confirms the notion that the VAJ in patients with bicuspid AV disease may continue to dilate over time and may cause repair failure.

**Trileaflet AV repair**

Different techniques may be used to correct cusp prolapse in trileaflet aortic valves. Free margin plication and free margin resuspension are the most commonly used techniques. Studies comparing the two techniques demonstrate equivalent durability in terms of freedom from reoperation or recurrent AI.\(^\text{16,28}\) Another important question in the repair of trileaflet aortic valves is the appropriate detection and localization of cusp prolapse. We examined echocardiographic and intraoperative features that could predict the need for cusp prolapse repair in trileaflet aortic valves with or without aortic root pathology. We found that the presence of a preoperative eccentric AI jet, regardless of severity, and the presence of a transverse fibrous band (Figure 4.4) were most useful in the detection and correct localization of cusp prolapse.\(^\text{7}\)

**Valve-related complications**

A consistent finding across all longitudinal studies of aortic valve repair outcome is the low incidence of valve-related events. For prosthetic aortic valve replacements, the rate of thromboembolic events is typically between 1% and 2% per year.\(^\text{29,30}\) For patients with mechanical aortic valves, the rate of anticoagulant-related hemorrhage is also 1–2% per year. Furthermore, valve thrombosis and prosthetic valve endocarditis are infrequent but devastating complications. In contrast, the combined rate of thromboembolism, bleeding events, and endocarditis following aortic valve repair has been reported in several studies to be less than 0.5% per year.\(^\text{6,17,31}\) This is particularly attractive for young patients who continue to accrue the risk of valve-related events over time.

**Conclusions**

Over the past two decades, important advances have been made in the field of aortic valve repair. These include a better understanding of the functional anatomy of the aortic valve, the development of a repair-oriented classification system for aortic insufficiency, the application of valve-sparing techniques to the preservation and repair of regurgitant aortic valves, and the development of cusp repair techniques. Increasing data is now available indicating the durability of aortic valve repair up to 10 years. Further long-term studies and those comparing aortic valve repair to replacement are needed to define the role of aortic valve repair in patients with aortic insufficiency.
References


Introduction

The natural history of untreated severe aortic valve stenosis (AS), with an average survival of 3 years after the onset of angina or syncope and only 1½ years after onset of heart failure, strongly suggests early surgical therapy which represents the only curative option. Since the first pioneering work in the early 1960s, conventional aortic valve replacement (AVR) has become a routine procedure performed more than 200,000 times annually worldwide.

General considerations and literature: Current issues in conventional aortic valve replacement (AVR)

Current outcome in “low-risk” patients

Over the past decades the surgical technique of AVR has evolved to a highly standardized procedure resulting in excellent outcome and patient safety. According to the Society of Thoracic Surgeons (STS) National Database, 30-day mortality decreased over the last decade by 24% despite increased patient age and risk profile. Today, most centers report a 30-day mortality rate of 2–3% in elective “low-risk” patients.

Tissue vs. mechanical valves

According to the STS National Database, a dramatic shift toward the use of bioprosthetic valves occurred over the last decade. Generally, the selection of a tissue valve is supported by the recently updated American Heart Association (AHA) guidelines in patients over 65 years of age. However, the avoidance of a second operation due to potential tissue valve degeneration should be balanced against the cumulative risk for bleeding or thromboembolism of mechanical valves in each individual patient. For quality of life and lifestyle reasons, even younger patients might opt for a tissue valve. Given the lack of evidence proving the superiority of mechanical over tissue valves in younger patients regarding long-term mortality, this recent trend seems to be justified. According to a recent
analysis the merits and drawbacks of tissue and mechanical valves outbalance at an age crossing point of 60 years. In addition, the operative risk for a second surgical AVR has been demonstrated to be not significantly increased in younger patients compared to the primary procedure. Although still evolving, the transcatheter “valve-in-a-valve” option might have further impact on the decision to choose bioprosthetic valves in younger patients in the near future.

**Patient-prosthesis mismatch**

Since the introduction of the theoretical concept of patient–prosthesis mismatch (PPM) following AVR this phenomenon has been of much debate in the literature over the last decade. PPM is generally accepted to be severe if the indexed effective orifice area (IEOA) is less than 0.65 cm²/m² and moderate in patients with an IEOA less than 0.85 cm²/m². The published data on the topic of PPM is very conflicting. According to a recent analysis, severe PPM seems to be associated with impaired short-, mid-, and long-term outcome, and should be always avoided. The potential impact of moderate PPM is more complex. It seems to be well tolerated in elderly patients with preserved left ventricular function, who represent most patients undergoing AVR for AS. On the other hand, moderate PPM should be avoided in patients with impaired left ventricular function or marked hypertrophy and in young and/or physically active patients. To avoid severe PPM in the small aortic annulus both, annular enlargement techniques or full root replacement using a stentless valve results in good hemodynamical outcome without a significant increase in the operative risk.

**Stentless valves**

At time of introduction into clinical practice, the concept of stentless valves was seen as revolutionary. The hope was that these new valves would show hemodynamic performance similar to a native aortic valve and that this benefit regarding low gradients and large effective orifice area would transduce into improved patient outcome and quality of life. In addition, better flow kinetics would result in less stress on the artificial valve leaflets. Thus, improved long-term durability was anticipated.

Now, almost 15 years later some long-term data regarding the durability of the valves became available and are somehow conflicting. Whereas the Medtronic Freestyle valve demonstrated extremely low rates of valvular degeneration at 10-year follow-up, data for the St. Jude Toronto valve were disappointing at 12-year follow-up, despite good 8-year results.

The drawback of all stentless valves is that the implantation itself is technically more demanding. In case of subcoronary implantation, the coronary ostia do not have to be reimplanted, but this technique is prone to increased transvalvular gradients especially in small aortic roots. The other option, a full root replacement seems to be the treatment of choice in case of a small aortic annulus to avoid PPM but the necessity to reimplant the coronary arteries adds complexity. Nevertheless, several randomized trials have proven that stentless valve implantation does not increase the operative mortality in specialized centers but results in beneficial hemodynamic performance associated with accelerated regression of ventricular hypertrophy.
Regarding survival, several studies claimed a benefit due to the implantation of stentless valves. Unfortunately, the evidence is not very valid as most studies were non-randomized and there was a clear bias present toward using stentless valves in younger patients, which certainly affected the reported long-term data. On the other hand, the literature data strongly suggest a significant benefit for stentless valves in case of a small aortic root or impaired left ventricular function.\(^\text{18}\)

For most patients presenting for AVR due to degenerative AS in their late seventies, the easiness and safety of a quick procedure using a stented valve probably outbalance the potential benefits of a more complex stentless valve. In younger patients, where hemodynamic performance, especially during exercise, is a more relevant issue, the potential risks of a reoperation associated with stentless valves\(^\text{19}\) should be taken into consideration. In summary, stentless valves are an excellent option in carefully selected patients but more data regarding the long-term durability and valve designs allowing for an easier implantation technique are required to further increase the acceptance of the “stentless” concept.

**Minimally invasive access aortic valve replacement**

Minimally invasive access aortic valve replacement (MA-AVR) was introduced more than 10 years ago.\(^\text{20}\) It facilitates standard AVR using either an upper partial sternotomy or a right lateral mini-thoracotomy. Both approaches have been proven to be safe and feasible, are less invasive regarding cosmetics and surgical trauma and spare sternal stability compared to full-sternotomy AVR. The upper sternotomy access is probably more “straightforward” and does not require any special instruments.\(^\text{21}\) On the other hand, the lateral approach provides the benefit of not dividing the sternum at all, but usually requires a set of special minimally invasive instruments and is associated with prolonged cross-clamp times reflecting the technical challenges.\(^\text{22}\)

Several studies have shown that MA-AVR can be performed as safely as with a full sternotomy without affecting the quality of the valve procedure itself. Furthermore, a recent meta-analysis\(^\text{23}\) demonstrated a significant benefit for the MA-AVR technique regarding length of hospital stay, length of intensive care stay, and length of ventilation. Tabata et al.\(^\text{21}\) reported remarkably good results in elderly patients (>80 years, \(n = 179\)) with the MA-AVR technique resulting in a 30-day mortality rate of 1.7% only despite the age of this particular patient group. In another recent study, MA-AVR was even identified as an independent factor for decreased 30-day mortality in a subgroup of high-risk elderly patients.\(^\text{24}\)

Although safety of the minimally invasive approach is clearly proven and significant benefit regarding outcome is most likely, MA-AVR is still not standard of care more than 10 years after its introduction. For example, in 2008 only 8.3% of all isolated AVR procedures were performed using a minimally invasive access in Germany.\(^\text{25}\)

MA-AVR is well suited for younger patients as it facilitates the use of “classic” valve prosthesis with known long-term durability while at the same time offering a less invasive option is certainly appreciated by the patients. Regarding elderly high-risk patients, MA-AVR in combination with a new sutureless valve prosthesis\(^\text{26}\) may become an intermediate step between conventional AVR and transcatheter techniques.
Older patients

The prevalence of AS increases with age, it reaches 8.1% at 85 years. Combined with the phenomenon of the aging population, AS is expected to become a major factor in cardiovascular practice in the near future. After the onset of symptoms, the prognosis of AS is grave and it is even worse in presence of advanced age. Given the poor natural history of AS in older people, surgical valve replacement seems to be justified even in octogenarians to improve survival.

Over the past few years several groups have demonstrated that today, conventional surgical aortic valve replacement is feasible in octogenarians with an acceptable outcome. Consistent with the good outcomes observed in older people, age alone has been shown not to be an independent risk factor for conventional AVR. In addition to the known improvement of short-term outcome by surgical intervention, it has been demonstrated recently that surgical AVR in elderly patients is also associated with an excellent long-term outcome.

Today, conventional AVR clearly leads to a significant survival benefit even in octogenerians. On the other hand, survival alone should probably not be the preliminary endpoint in these patients. Therefore, several groups have investigated quality of life (QoL) after conventional AVR over the past years reporting significant benefit. However, some studies have demonstrated that QoL may not to be significantly different after AVR compared to an age-matched “healthy” population.

Current issues in transcatheter aortic valve implantation (TAVI)

The concept of transcatheter valves

Given the good outcome of conventional AVR, the question is: Do we really need anything new? According to the data of the European Heart Survey one-third of all elderly patients suffering from severe symptomatic AS were never referred to a cardiac surgeon because the referring cardiologists believed the surgical risk to be unacceptably high. A similar “non-referral” pattern has been demonstrated in a study from California where even 61% of patients with severe AS never underwent aortic valve replacement. Although the observed “non-referral” pattern can be partially explained by the fact that the referring physicians are often not aware of the true outcome of conventional AVR in elderly patients at present, it still clearly demonstrates the need for a less invasive option in carefully selected elderly high-risk patients.

The idea itself is not new and aortic valve balloon valvuloplasty was advocated in the 1980s for selected patients, but it became quickly evident that this technique is associated with modest and short-lived clinical improvement only. After the development of a valve stent the concept regained interest and finally resulted in its first human implantation in 2002 using an antegrade transfemoral transseptal approach. After initial pioneering, TAVI has evolved to an almost routine procedure in specialized centers. Valve delivery is either performed using a retrograde transvascular approach.
(transfemoral, transsubclavian, transaortal) or the surgical antegrade transapical access. Theoretically, the transcatheter concept offers several advantages:

1. The technique facilitates valve implantation with minimal surgical trauma only (transapical) or even with a purely percutaneous approach (transfemoral) and avoids sternotomy.

2. General anesthesia is not required for the transfemoral approach and even when using the apical technique, it can be avoided in selected patients.\textsuperscript{41}

3. The technique allows for valve implantation off-pump, thus avoiding the potentially harmful effects of cardiopulmonary bypass. However, potential drawbacks such as procedure-related complications (vascular injury, ventricular tear, paravalvular leak, valve dislocation, and so on) must be kept in mind.

**Which patients should undergo TAVI instead of conventional AVR?**

Although the concept itself offers some obvious advantages, the benefit of TAVI compared to conventional AVR is unproven yet. Given the excellent results of conventional AVR and the unknown long-term durability of the TAVI valves, the technique should stay restricted to “true” elderly high-risk patients until convincing scientific data is available justifying a broadening of the indication. Otherwise, a development similar to the inglorious story of coronary artery bypass graft (CABG) versus PCI might repeat itself. Clinical practice must stay supported by best scientific evidence available. At present most groups accept the recommendations recently published by the European Association for Cardio-Thoracic Surgery (EACTS) and ESC.\textsuperscript{42} Accordingly, patients are eligible for TAVI if they present with advanced age (>75) AND additional risk factors (STS-score >10%, logistic EuroSCORE (ES) >20%) such as severe respiratory dysfunction, chest radiation, mediastinitis, previous CABG with patent left internal mammary artery (LIMA), and other risk factors not represented by the STS or EuroSCORE (i.e., porcelain aorta, liver failure, immobility, or severe hematological disorders).

The true risk of this special subgroup of patients is hard to estimate. In addition to scoring systems issues as biological age and frailty are not routinely measurable. On the other hand, scoring systems are needed to compare the outcome of different techniques. It is well accepted that the logistic EuroSCORE generally overestimates the true risk\textsuperscript{43} and the STS-score should be probably favored as it is more accurate in these patients.\textsuperscript{44}

**Transfemoral versus transapical access**

TAVI is feasible using either the retrograde transfemoral, or the antegrade transapical approach with good outcomes.\textsuperscript{45,46} There is currently no scientific evidence proving the superiority of the one or the other approach. The strengths of the transfemoral access are certainly that it can be performed under local anesthesia. On the other hand, the transapical approach is clinically advantageous due to the direct and antegrade access to the aortic valve, hence very precise device manipulation and positioning is feasible. In addition, sheath size
and quality of the femoral vessels are not an issue with the apical access. Another advantage of the antegrade transapical approach might be the fact that this technique is associated with limited manipulations around the aortic arch only. This might result in a lower stroke rate compared to the transfemoral approach especially in “high-risk” patients with a calcified aortic arch. In patients with severe lung dysfunction, the awake transfemoral approach might be advantageous whereas the apical approach should be favored in case of stenotic or calcified femoral vessels. In addition, there are other approaches that include transaortic and trans-subclavian routes which are appropriate in selected patients.

In conclusion, for most patients both options will lead to good results. A “transfemoral first strategy” is not supported by any scientific evidence although advocated by some groups. When comparing the results in regard to the access site, the overall risk profile (logistic EuroSCORE and most importantly STS-score) must be taken into account for a “fair” comparison.

Current outcome of TAVI

After an initial pioneering phase, the results have now stabilized. Unfortunately, most groups seem to favor a “transfemoral first strategy” which results in two groups of patients hardly comparable. In the transfemoral group a 30 d-mortality rate of 7% with a logistic EuroSCORE less than 25% has to be expected. In the transapical group, patients usually have a higher risk profile (logEuroSCORE >30%) that translates to a higher 30 d-mortality rate of approximately 10%.

Over recent years, TAVI emerged to become the treatment of choice for inoperable patients and the preferred alternative for high-risk patients with severe, symptomatic aortic stenosis. The randomized PARTNER trial reported the benefit of TAVI in patients with inoperable aortic stenosis. Evidence continues to emerge rapidly as ongoing trials are conducted. The PARTNER trial reported no structural valve deterioration requiring surgical aortic valve replacement (SAVR) was detected after 5 years and the valve area as well as the mean transvalvular gradient remained stable. The reported durability of TAVI devices appears sufficient for high high-risk patients, but long-term studies are necessary to prove comparable durability to SAVR valves. As regards Vascular complication rates, this has significantly declined as the size of TF-TAVI delivery sheaths has decreased significantly compared with the first-generation systems.

The results of randomized trials of TAVI in intermediate-risk patients are eagerly awaited.

Technical key steps

Conventional AVR

The technique of conventional full-sternotomy AVR today is a highly standardized procedure. Therefore, we would just like to share our approach for the small aortic root. In case of younger patients, we believe that the full root replacement is the best solution to avoid any PPM. A mechanical conduit is a good choice to avoid a potential risky redo
root replacement in the future in younger patients. If the patient decides to have a tissue valve, the long-term durability of the Freestyle valve seems to be excellent and comparable to a homograft. In case of elderly “active” patients we would favor a posterior root enlargement in combination with a modern supraannular stented tissue valve to keep the procedure relatively straightforward. In case of elderly rather “inactive” patients we believe that with the use of a modern supraannular biological stented valve, acceptable hemodynamic performance can be anticipated in most patients and a moderate PPM is acceptable obviating the need for more complex procedures in this patient group.

**Minimally invasive access AVR**

We believe that minimally invasive access AVR should be increasingly used in isolated aortic valve procedures. The lateral parasternal access offers the advantage of completely sparing the sternum and several groups have reported excellent outcome with this approach. However, reported cross-clamp duration is rather long with this technique. In comparison we favor the upper partial mini-sternotomy, as this technique is technically straightforward translating into shorter procedure and cross-clamp times and does not require special instruments.

In most cases, we use a 6–8 cm long skin incision and a J-shaped mini-sternotomy into the fourth or fifth right intercostal space. Usually a conventional chest X-ray is sufficient to plan the procedure avoiding the radiation and the contrast load of a CT-scan. The access allows for standard cannulation of the ascending aorta and the right atrial appendage in most patients (Figure 5.1). Alternatively, the venous cannula can be placed through an

![Figure 5.1](image-url) Minimally invasive access aortic valve replacement (AVR).
additional epigastric incision or a percutaneous venous cannula can be used with vacuum assisted drainage. Placement of the vent into the upper right pulmonary vein is almost always possible; in rare cases, venting of the pulmonary artery is an option. Once access is established, the procedure can be performed similar to a full sternotomy procedure using antegrade cardioplegia.

A few pitfalls were identified over time:
1. A typical site of bleeding is the right internal thoracic artery (RITA) due to the J-shaped sternotomy.
2. Placement of the epicardial pacing lead and the chest drain is a lot easier and safer to achieve once the heart is still unloaded on-pump.
3. The limited access does not allow for full visualization of the right and left ventricle—transesophageal echo (TEE) is mandatory to identify potential ventricular distension. Deairing is relatively difficult—therefore CO$_2$ field flush should be routinely used.

**TAVI (focusing on the surgical transapical approach):**

Specific issues observed during the learning-curve, in addition to useful tips and tricks with the transapical technique using the Edwards SAPIEN prosthesis are highlighted here.

**The setup**

The optimal environment for TAVI procedures is a fully equipped hybrid operative room (OR). If such a room is not available, an “upgraded” cath-lab should be favored over a regular OR with a mobile C-arm as imaging quality is key. In addition, a TEE and a regular cardiopulmonary bypass system (CPB) should be available. The procedures should be performed by a specialized team—made up of surgeons, cardiologists, and anesthetists—to ensure optimal patient safety. The setup should be designed with potential “bail-out” scenarios in mind, ranging from simple procedures like surgical femoral cut-down to complex worst-case settings like redo aortic arch replacement in type A dissection.

In order to provide immediate CPB support if necessary, a femoral “safety-net” (percutaneous venous wire in addition to the arterial sheath) should be placed prior to skin incision.

**Apical access**

Although transapical valve implantation has been proven feasible in awake patients, general anesthesia is used in most cases. When trying to identify the optimal access site, echocardiography might be helpful to locate the aple. Alternatively, the sixth intercostal space with an incision of 5–6 cm beginning at the mid-clavicular line to the lateral aspect usually provides good exposure (Figure 5.2). In patients with enlarged ventricles, a more lateral approach is chosen. Once an intercostal space is slightly opened the apex can be easily palpated and, accordingly, an intercostal space higher or lower can be selected prior to insertion of the rib spreader without significantly increasing the overall trauma. With
the help of four to six pericardial stay-sutures, the exposure of the apex is then optimized. The stay-sutures allow for regular bilateral lung ventilation.

Although different techniques have been suggested with good results, we always use two separate 2-0 Prolene purse strings (large medium half (MH) needle) with five small Teflon pledget-supported interruptions to secure the apex. Sufficiently deep bites should be taken to avoid tearing of the epicardium. The optimal target site is the muscular spot cranial to the anatomical left ventricular apex lateral of the left anterior descending artery (LAD) to avoid the fatty tissue at the true apex.

After the valve is implanted both purse strings are tied. In case of high systolic blood pressure, a brief episode of rapid ventricular pacing might be used. If residual bleeding is present, deep felt strip supported 2-0 Prolene U-stiches provide adequate haemostasis. “Uncontrollable” apical bleeding or tearing requires temporary CPB support to unload the ventricle. In case of persistent arterial bleeding without a clear source at the apex the rare event of annular rupture is suspected and ruled out by repeat root angiography.

**Imaging: Optimal angulation of the C-arm**

As already mentioned, we believe that good imaging quality is one of the key steps for a successful TAVI program. A new imaging modality (DynaCT) was developed and might
be of utmost help to achieve a perfectly perpendicular angulation of the C-arm. If not available, however, the optimal angulation (hint: start at LAO/cranial 10°/10°) must be identified by repeat root angiography. The importance of a truly perpendicular angulation of the C-arm cannot be emphasized enough and is often underestimated at the beginning of each team’s learning-curve. Figure 5.3 demonstrates a non-perpendicular (A) versus an optimal angulation (B). This ensures precise and controlled positioning of the prosthesis.

**Valve positioning and implantation**

Ideally, the valve should be positioned one-third to one-half above the aortic annulus but strictly subcoronary. In our experience, too low a position is associated with a higher rate of paravalvular leak. On the other hand, a high position might result in coronary obstruction—a rare but devastating complication. The distance between the aortic annulus

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**Figure 5.3** Optimal C-arm angulation: (a) non-perpendicular, (b) perpendicular.
and the coronary ostia can be usually assessed on the preoperative coronary angiogram. If in doubt, an additional CT-scan is indicated. A rather wide aortic root configuration (pronounced aortic sinus) allows for a more “aggressive” positioning close to the ostia, whereas in a small more tubular shaped root, a position on the “lower side” is more advisable.

In contrast to the femoral access, the transapical approach allows adjusting the tilting of the valve within the aortic annulus by either tightening the guidewire or giving some extra slack (Figure 5.4). Furthermore, some minor positional adjustments are feasible even during valve implantation by stepwise balloon inflation. The implantation sequence is as follows:

1. The valve is positioned including adjustment of the wire tension and all team members agree after the final angiographic control.
2. Ventilation is stopped to minimize side motion.
3. Rapid pacing is initiated (180–220 bpm, in case of “non-capture” try a slower rate to avoid 2:1 conduction).
4. The anesthetist confirms: “No output.”
5. A final contrast injection into the root is given during the rapid pacing. This allows for implantation into the contrasted aortic root and thus for optimal visualization of all key target structures, including the aortic annulus and the coronary ostia.
6. The balloon is gradually inflated to 50%.
7. If required final adjustments are made (to avoid uncontrolled jumping due to initial friction between the sheath and the catheter it is best to manipulate the whole system only).
8. Once the team is satisfied, full inflation is performed.

Potential complications and “bail-out” suggestions

Given the high-risk nature of the patients treated with the TAVI technique, a variety of complications might occur. We would like to share the more frequent complications and how we would react according to the specific situation:

- **Valve deployed too low:** The delivery system should be retrieved immediately to be prepared for a second valve-in-a-valve implantation with a slightly higher position.

![Figure 5.4](image.png) Adjustment of the valve tilting by wire manipulation.
Valve deployed too high, leading to coronary occlusion or impingement: If a guidewire can be placed, consider stent-implantation. If not, sternotomy and surgical bypass grafts beating-heart on-pump should be performed. To decrease the time until myocardial reperfusion retrograde continuous coronary sinus perfusion can be established immediately after start of CPB especially in case of left main occlusion.

Paravalvular leak (>grade 1+): Reballooning adding 1 mL of extra volume should be attempted.

Central leak (>grade 1+): If one leaflet is not moving mobilization by pigtail manipulation might be feasible. Valve function often dramatically improves once the arterial pressure has fully recovered. In case the maneuver is not successful consider second valve-in-valve implantation eventually slightly higher to avoid interference of the native aortic valve cusps.

Hemodynamical instability: Low-dose epinephrine (2–10 mL of 1 mg diluted to 100 mL saline) into the aortic root over the pigtail is often helpful. In case of persistent low-output convert to CPB using the “Safety-Net” for reperfusion. Bridge with chest compressions until full CPB flow is established. To prevent left ventricular distension (especially in case of higher degree of aortic regurgitation) consider apical venting.

References
REFERENCES


Chapter 6

Open and endovascular treatment options in thoracic aortic surgery

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Introduction

The thoracic aorta is divided into the proximal aorta, the transverse arch, and the descending and thoracoabdominal aorta. Each segment is addressed differently with regard to pathology. Open endovascular and hybrid repairs have emerged for treating these different segments. A full median sternotomy is the standard approach for proximal aortic disease and proximal and transverse arch repairs. Other minimally invasive approaches such as upper mini-sternotomy and right mini-thoracotomy have emerged for treating proximal aortic and arch disease. Until recently, a left thoracotomy and thoracoabdominal approach has been the sole approach for treating lesions of the descending and thoracoabdominal thoracic aorta. In the mid-1980s, Volodos and associates reported the first aortic repair with a self-fixing endoprosthesis. In 1991, Parodi and colleagues popularized the technique by using a stent graft to treat an abdominal aortic aneurysm, and 3 years later, Dake and colleagues described the use of a homemade stent graft to treat thoracic aortic aneurysms. These initial attempts to treat aortic aneurysms with a minimally invasive procedure led to robust research and development of this technology. As a result, the United States Food and Drug Administration (FDA) approved two devices for treating abdominal aortic aneurysms in 1999 and the first device for the endovascular treatment of thoracic aortic aneurysms in 2005.

Diagnostic modalities in thoracic aortic surgery

Different imaging modalities can provide critical information to guide treatment options in the thoracic aorta. The availability of imaging equipment and experienced operators varies among institutions, and this variability results in differences in current thoracic aortic practices among different centers. Nevertheless, recent guidelines attempt to standardize image acquisition and reporting with regard to basic key points: location of aortic pathology (including calcification and extension of abnormalities into branch vessels); maximum external aortic diameters; evidence of rupture or internal filling defects; and comparison with previous imaging studies.

Although plain radiography of the chest and abdomen can aid the initial suspicion or even diagnosis of a thoracic aortic aneurysm (characterized by a convex shadow to the right of the cardiac silhouette, widening of the descending thoracic aortic shadow with a
rim of calcification, and a convexity in the right superior mediastinum), the results may also appear completely normal. Aneurysms of the mid and lower descending thoracic aorta can reside undetected within the cardiac silhouette. Computed tomography (CT)—with or without intravenous contrast agents—of the chest, abdomen, and pelvis can image the entire thoracic and abdominal aorta with multiplanar and three-dimensional aortic reconstructions. Measurements should be taken in standard anatomic locations and should be obtained perpendicular to the direction of blood flow. By detecting aortic dissections (acute and chronic), aneurysms, mural thrombi, inflammatory reactions around saccular aneurysms, contained aortic ruptures, and mediastinal and retroperitoneal hematomas, CT scanning permits accurate diagnosis of thoracic aortic pathology. In patients with previous thoracic aortic surgery, a CT scan can provide valuable information with regard to the results of that surgery (i.e., the integrity of previously placed Dacron grafts or the position of previously placed endovascular stent grafts), as well as the fate of the remaining native aorta. This modality is also a useful tool for follow-up evaluation and comparison. Moreover, in patients with proximal and arch aneurysms and previous sternotomies for whom a debranching hybrid or a traditional open procedure is being considered, CT scanning provides valuable information regarding the proximity of the sternum to the thoracic aorta or the relationship of a previous left internal thoracic mammary artery bypass to the back of the sternum. The frequent use of CT scanning for a multitude of indications has led the discovery of numerous asymptomatic thoracic and abdominal aortic aneurysms that a few decades ago would have gone undetected until rupture or death.

Although radiation exposure is not inconsequential, in these patients the impact on renal function is of more concern. Contrast-induced nephropathy, defined as an increase of 25% or more in the serum creatinine level compared to the baseline level within 1 to 4 days after contrast administration, is responsible for 10% of hospital-acquired cases of renal failure and is the major adverse effect of CT scanning with an intravenous contrast agent. This complication is associated with patient-related risk factors such as congestive heart failure, advanced age, anemia, chronic renal disease, reduced effective circulating volume, and the type and volume of contrast agent. Non-ionic, low-osmolar contrast medium is used in most studies. Preoperative hydration with sodium chloride and sodium bicarbonate has proven quite helpful. Use of oral N-acetylcysteine has no consistent efficacy. For long-term follow-up, since in the asymptomatic patient the primary diagnostic feature is the outer diameter of the aorta, CT scanning without the use of intravenous contrast is adequate for routine surveillance in most cases.

Magnetic resonance angiography (MRA) can be another useful tool for imaging the entire aorta, because this approach requires no exposure to ionizing radiation and offers excellent visualization and detection of branch-vessel stenosis. However, gadolinium, the contrast material used for MRA, has been implicated in nephrogenic systemic fibrosis in patients with advanced renal insufficiency. For patients who require long-term follow-up observation, MRA can be an excellent imaging tool.

Other diagnostic modalities for visualizing the thoracic aorta include two-dimensional (2D) echocardiography (transthoracic and transesophageal), which provides excellent visualization of the aortic root and the ascending aorta. In addition, this approach can assess wall-motion abnormalities, detect and grade aortic
Insufficiency, and identify other valvular abnormalities and intracardiac defects.\textsuperscript{11} Echocardiography is considered the diagnostic imaging procedure of choice in patients with unstable proximal aortic dissection and is cost-effective in following up most aortic diseases.\textsuperscript{13,14} Invasive aortic angiography, once considered the gold standard, has been replaced by CT scanning and MRA except for intraoperative use during in endovascular aortic procedures. A 3D image fusion of a preoperative CT with live fluoroscopy and carbon dioxide digital subtraction angiography (DSA) instead of iodine DSA has been used in patients with renal insufficiency.\textsuperscript{15} Cardiac catheterization still plays an important role in preoperative planning and diagnosis, especially in patients with aortic root pathology, known coronary artery disease, and prior coronary artery bypass.

**Preoperative assessment before thoracic aortic surgery**

Before any elective thoracic aortic procedure, every patient should undergo a detailed evaluation, with an emphasis on the assessment and optimization of pulmonary, cardiac, and renal status. With regard to pulmonary assessment, every patient should undergo arterial blood gas measurement and spirometry. Patients with a forced expiratory volume of more than 1.0 L in 1 second (FEV\textsubscript{1}) and a partial pressure of carbon dioxide (PaCO\textsubscript{2}) of less than 45 mmHg are considered surgical candidates. Poor preoperative pulmonary function does not preclude repair of an aneurysm or dissection, but special consideration must be given to preserving the left recurrent laryngeal nerve, the phrenic nerve, and diaphragmatic function. Smoking cessation, exercise, weight loss, and treatment of bronchitis a few months before the repair procedure can be beneficial in patients with borderline pulmonary function.

Preoperative cardiac evaluation consists of transthoracic echocardiography to evaluate cardiac and valvular function. A dipyridamole-thallium myocardial perfusion scan to identify reversible ischemia in the myocardium can be beneficial, especially in older and less mobile patients with peripheral vascular disease. If any of these tests suggests coronary artery disease, or if the left ventricular ejection fraction is less than 30%, cardiac catheterization and coronary angiography should be performed. Any significant coronary artery or valvular disease can be addressed in the same procedure as the proximal aortic surgery. If the repair involves the distal aorta, coronary revascularization should be performed before the thoracic aortic procedure.

Baseline renal function is extremely important, because in up to 25–30% of patients requiring thoracoabdominal aortic replacement, significant renal artery stenosis may be encountered. Renal artery endarterectomy, stenting, or bypass may be necessary in selected patients. In the event of precipitous decline in renal function, temporary hemodialysis may be necessary after surgery.

**Surgical indications for replacement of the proximal aorta and/or aortic root**

**Ascending aortic dissection and variants**

Acute ascending aortic dissection (Stanford A or DeBakey type I or II), defined as occurring within 2 weeks after the onset of pain, and spontaneous aortic rupture are the
two main emergency indications for intervention and replacement of the ascending aorta. The timing of intervention is critical because of two potential severe cardiac complications related to disruption of normal anatomic relationships: (1) acute aortic regurgitation (AR), manifesting as an insignificant diastolic murmur or even as congestive heart failure and cardiogenic shock; and (2) myocardial infarction due to extension of the dissection into the coronary ostia or compression of the coronary arteries. Because the latter condition is an infrequent complication of acute type I aortic dissection, it is likely to be misdiagnosed as primary myocardial infarction and treated inappropriately. Another complication of proximal aortic dissection is heart failure, which can have an atypical presentation and possibly a delayed diagnosis. Pericardial tamponade, a frequent complication of acute ascending aortic dissection, necessitates immediate repair. Syncope due to cardiac, neurologic, vascular, and volume-related causes is another manifestation of acute type A (or type I) aortic dissection. It requires special attention and prompt intervention because affected patients have a significantly greater risk of death than patients without a history of syncope.

Malperfusion (cerebral, visceral and lower extremity) associated with acute Type I aortic dissection predicts poor outcomes and deserves special consideration. A significant dilemma with regard to the method and timing of intervention exists in the case of patients who present with stroke. According to recent data from the International Registry of Acute Aortic Dissection (IRAD), stroke was the presenting symptom in 6% of patients with acute proximal aortic dissection. These patients tended to be older, to be hypertensive, and to have aortic-arch-vessel involvement. They had less surgical treatment and significantly higher in-hospital mortality and morbidity but not long-term mortality. In these patients, aggressive surgical intervention and its effect on in-hospital morbidity need to be examined and tailored to each patient's circumstances, including age, comorbidities, and potential for meaningful recovery.

Intramural hematoma (IMH) is a variant of aortic dissection and a dynamic process. Ten to twenty percent of patients with a clinical picture of aortic dissection have IMH without an intimal tear on diagnostic imaging. According to some reports, a microscopic tear in the intima, versus hemorrhage of the vasa vasorum within the media, can also result in an intramural hematoma. Intramural hematoma has the same indication for surgical intervention as acute type A (type I) aortic dissection, except in very elderly individuals or patients with multiple comorbidities, in whom medical management with blood pressure control and serial imaging is essential.

Chronic dissection of the ascending aorta, defined as dissection that occurs more than 6 weeks after the onset of initial symptoms, is not an emergency, but the threshold for intervention is low. In these patients, the thoracic aorta tends to dilate, and the dissection should be managed like an enlarging aneurysm.

Penetrating atherosclerotic ulcer (PAU), or ulceration of the internal elastic lamina that allows hematoma formation within the media of the aortic wall, can occur anywhere in the aorta but is most commonly located in the descending thoracic aorta and can result in IMH or aortic dissection. It can be treated more or less aggressively. Its presence in the
ascending aorta is another surgical indication for non-urgent replacement. Patients with connective tissue disorders and acute type A (type I) aortic dissection require replacement not only of the ascending aorta, but also of the aortic root.

**Ascending aortic aneurysm**

The most common indication for ascending aortic replacement is a degenerative aneurysm. All symptomatic patients are referred for urgent or emergent repair. According to the current recommendations, surgical repair is recommended in suitable candidates when the ascending aorta or sinus reaches a diameter of 5.5 cm in asymptomatic patients, or when the growth rate exceeds 0.5 cm per year regardless of the size. In patients with genetic disease, an aortic or sinus diameter of 5 cm is an indication for repair unless the patient has a family history of aortic dissection, which could lower the threshold for repair. For patients who undergo any cardiac operation, the recommended size for ascending aortic replacement is 4.5 cm. In patients with a connective tissue disorder, aortic root repair or replacement is required in addition to ascending aortic replacement.

**Bicuspid aortic valve**

A bicuspid aortic valve is the most common cardiovascular defect, having a prevalence of 1–2% and affecting four times as many males as females. Bicuspid aortic valve (BAV) may be associated with thoracic aortic aneurysm formation, aortic dissection, and coarctation. A normally functioning BAV and an ascending aorta exceeding 5 cm in diameter is an indication for ascending aortic replacement. Because as many as 15% of patients with proximal aortic dissection have BAV, and 12.5% of patients with an ascending aortic diameter of less than 5 cm could have aortic dissection, an abnormally functioning BAV alone may be an indication for ascending aortic repair. Even though current guidelines suggest replacing the ascending aorta during aortic valve replacement in patients with BAV when the diameter of the ascending aorta is greater than 4.5 cm, this recommendation is not supported by all. The mortality rate associated with elective repair with or without ascending aortic replacement should be less than 1%. Bicuspid aortic valve is more likely to cause AR in younger patients and aortic stenosis (AS) in older ones. Aortic regurgitation and a dilated sinotubular junction in patients with BAV indicate the need for root repair or replacement.

**Infection**

Infection of a previously placed Dacron graft is an indication for proximal aortic replacement. Fungal or bacterial endocarditis is another indication for aortic root replacement with additional proximal ascending aortic replacement.

**Porcelain aorta**

A porcelain aorta with an eggshell appearance due to extensive calcification, as seen on a CT scan or a simple chest radiogram, can be found during operations for valvular heart
disease or coronary artery disease. Aortic cross-clamping and direct ascending aortic cannulation for arterial inflow is prohibited in these patients because these maneuvers pose an extreme risk of embolic stroke. Replacing the ascending aorta with a tube graft has been recommended, in addition to other suggested techniques for dealing with the porcelain aorta.32,33

**Special considerations: Pregnancy**

Increases in blood pressure, maternal blood flow, and stroke volume can lead to greater aortic wall tension and shear forces, especially during the third trimester of pregnancy and the peripartum period, resulting in a higher incidence of dissection during that period.27,34 In cases of acute proximal dissection during the first and second trimester of pregnancy, emergent repair is indicated, with additional aggressive fetal monitoring and the involvement of an experienced high risk maternal-fetal team.27 Cardiopulmonary bypass and hypothermia can be detrimental, potentially even resulting in fetal loss. If the proximal aortic dissection occurs during the third semester of pregnancy, a cesarean section followed by aortic repair provides the best chance for survival of both the unborn child and the mother.27

**Surgical indications for repair/replacement of the aortic arch**

Rarely is aortic pathology confined to the aortic arch, sparing the remainder of the aorta. As a result, the indications for surgical intervention in the aortic arch are quite similar to those for treating the ascending or descending aorta. Acute type A (type I) aortic dissection with a tear inside the arch and marked dilation of the arch (to >5 cm) is an indication for aortic arch replacement in addition to ascending aortic replacement.27 Proximal aortic dissection alone, without arch dilatation, is not considered an indication for aortic arch replacement. In an attempt to decrease the rate of late reoperations on the distal aorta, a few surgeons35,36 have advocated extensive total arch replacement at the time of the initial ascending repair. Others have advocated antegrade stent delivery into the descending thoracic aorta to promote distal aortic remodeling and, possibly, to help patients with malperfusion.37,38 In patients with a previous ascending aortic repair and remaining distal dissection, we replace the aortic arch if there is evidence of continuous enlargement (0.5 cm/year) during the follow-up period or if the diameter of the aortic arch is 5.5 cm or greater. In patients with connective tissue disorders and a remaining dissecting aortic arch, we proceed with arch replacement when the aortic diameter is ≥5 cm.

Fusiform or saccular aneurysms are another indication for replacement of the aortic arch. Saccular aneurysms of the aortic arch are rarely encountered and are usually secondary to an infection (mycotic aneurysm), degeneration of a heavily atherosclerotic penetrating ulcer, trauma, previous surgery, or focal dissection.37,39 In all of these circumstances, it is our practice to intervene surgically to replace or exclude the aneurysm.
Surgical indications for repair/replacement of the descending and the thoracoabdominal aorta

Descending thoracic and thoracoabdominal aneurysms

According to Elefteriades, who reported the natural history of 1,600 patients with thoracic aortic aneurysms and dissections, aneurysms greater than 6.0 cm in diameter are associated with a yearly rupture rate of 3.6%, a dissection rate of 3.7%, a death rate of 10.8%, and a rupture, dissection, or death rate of 14.1%. The growth rate of thoracic aortic aneurysms varies; descending and thoracoabdominal aneurysms grow at a rate of 0.19 cm/year. Fast-growing aneurysms are more likely to rupture. No level A or B scientific evidence from prospective, randomized studies is available regarding the timing of operative intervention according to aneurysm size. Practice guidelines recommend that an asymptomatic descending thoracic aneurysm be repaired at an aortic diameter of 5.5 cm. Our practice is to proceed with surgical intervention in patients with a family history of Marfan syndrome and aneurysms 5.0 cm or greater in diameter; patients without a family history of Marfan syndrome and aneurysms of 5.5 cm or larger; and patients with aneurysms that have a documented growth rate of more than 1 cm/year. We also intervene for rapidly expanding aneurysms, those more than twice the diameter of the normal contiguous aorta, and those that produce symptoms.

Type B or DeBakey type III aortic dissection and its variants

In the acute phase of the dissection, the following conditions are considered specific indications for immediate intervention: a contained rupture; a rapidly expanding aortic diameter; increasing periaortic or pleural fluid; uncontrollable pain; persistent hypertension not responding to medical therapy; evidence of malperfusion manifesting as lower-extremity ischemia; and renal or mesenteric ischemia. Acute dissection superimposed on a chronic dissection or an existing aneurysm needs special consideration and is another indication for surgery. In uncomplicated cases of acute type B (type IIIa, type IIIb) aortic dissection, medical therapy alone is satisfactory even though it does not improve long-term survival. Remodeling of the distal aorta and thrombosis of the false lumen induced by the stent graft after endovascular intervention has been reported, but long-term results are not yet available. In chronic distal aortic dissection, late complications occur in 20–50% of patients. Crawford found that in 23% of patients who presented with rupture of a chronically dissected aorta, the descending aorta was between 5 and 6 cm in diameter. We intervene when the diameter of a chronic dissecting aneurysm reaches 5.5 cm in patients with no genetically triggered thoracic aortic disease and 5 cm in patients with genetic thoracic aortic disease.

With IMH of the descending or thoracoabdominal aorta, the indications for intervention are similar to those in acute type B (type IIIa, type IIIb) lesions. Recurrent pain, increasing hematoma size, and aortic leak are indications for urgent repair. With regard to PAU, there is controversy about the indications for intervention. Eighty percent (80%) of these patients may have an associated IMH. Although it is usually our practice
to intervene in patients with PAU who are acceptable surgical candidates, it is unclear whether any surgical intervention affects long-term survival in these patients, who usually have multiple comorbidities.\textsuperscript{42}

**Treatment options for aortic root and ascending aortic pathology**

Surgical treatment of thoracic aortic pathologies involving the proximal aorta is traditionally performed via a median sternotomy with the aid of cardiopulmonary bypass. A variety of different procedures, with or without circulatory arrest, are used, ranging from a straightforward ascending aortic replacement with a Dacron tube graft to replacement of the entire proximal aorta and the hemiarch, with additional aortic root replacement and reimplantation of the coronary arteries. In all cases, intraoperative transesophageal echocardiography is performed, and near-infrared spectroscopy (NIRS) probes are placed over the cranium to monitor cerebral perfusion pressure and regional cerebral oxygen saturation (rSO\textsubscript{2}). For arterial inflow, different cannulation strategies have been implemented: since 2008, innominate artery cannulation has been our preferred strategy for proximal aortic aneurysms and aortic dissections unless the patient’s condition (i.e., in extremis or hemodynamically unstable) indicates using an alternative site.\textsuperscript{47–48} Our previous preferred approach, right axillary artery cannulation, is currently our second choice, followed by femoral and/or direct aortic cannulation if the patient is hemodynamically unstable. An 8-mm graft is sewn to the right axillary or innominate artery as previously described elsewhere.\textsuperscript{47–48} Antegrade and retrograde cardioplegia is administered for myocardial protection throughout the procedure.

Regardless of whether we are treating an ascending aortic aneurysm involving the proximal arch or a proximal dissection, we perform an open distal anastomosis.\textsuperscript{37,47–48} Only in the rare case in which the distal ascending aorta and arch are absolutely normal, not at risk, and without dissection do we use a cross-clamp. In cases of open distal anastomosis, hypothermia to 24°C is targeted. Moderate hypothermia (24–28°C) is our usual practice for elective total arch and hemiarch replacements.\textsuperscript{49} Ice is placed around the patient’s head, and mannitol and hydrocortisone are administered to prevent cerebral edema. Systemic circulatory arrest is initiated once the target temperature is reached. Once the proximal innominate artery is secured, the pump flows are decreased to 10–15 mL/kg/min. This provides unilateral antegrade perfusion via the right common carotid artery. Additional or bilateral perfusion can be achieved by adding a 9F Pruitt\textsuperscript{\textregistered} perfusion catheter (LeMaitre Vascular, Inc.; Burlington, Massachusetts, USA), which is inserted into the left common carotid artery by direct access once the arch is open. After completion of the distal anastomosis, pump flow is re-established via the innominate artery to its full level, and the period of circulatory arrest is ended. The newly placed Dacron graft is clamped, and the proximal aortic pathology (involving the aortic valve [AV]) is addressed.
The following options cover the entire spectrum of treatment for AV pathology. The repair can be as simple as (1) AV commissural plication for patients with mild-to-moderate regurgitation and a normal sinus of Valsalva segment, or (2) AV resuspension with or without commissural plication in patients with proximal dissection with or without regurgitation in whom the false and true lumens extend through the aortic annulus. The following conditions are indications for aortic root replacement: aortic root aneurysm (annuloaortic ectasia); Marfan syndrome or other connective tissue disorder; endocarditis of the AV with extensive involvement of the root; endocarditis of a prosthetic AV; recurrent perivalvular leak; and a small aortic root requiring a new AV prosthesis. In cases of complex proximal dissection with or without a dilated sinus of Valsalva, aortic root replacement can be considered. The coronary artery reattachments are performed by using either free buttons or an inclusion technique. Patients with type A (DeBakey Type I) aortic dissection undergo aortic root replacement with a composite Valsalva valved graft (Terumo, VASCUTEK, Inchinnan, Scotland) or, less commonly, a valve-sparing procedure if the aortic valve leaflets are normal. In our practice, in cases of acute proximal dissection in which the aortic root is involved and requires replacement, we either place a composite Valsalva valved graft with an attachment of free coronary buttons or place a bioroot (Medtronic Freestyle Bioroot). We very rarely perform AV-sparing procedures in patients with aortic dissection.

We consider AV repair with AV-sparing techniques in cases of non-dissection in young patients with BAV, mild-to-moderate dilation of the sinus of Valsalva, and mild-to-moderate AR; in all young individuals with AR and dilated sinuses of Valsalva; and in patients with connective tissue disorders in whom the AV leaflets are of suitable quality for repair. We prefer the David I reimplantation technique of valve-sparing aortic root replacement over the remodeling procedure (Yacoub or David II technique). In the remodeling procedure, the sinuses and the ascending aorta are replaced with three “tongues” to simulate the normal sinuses. These tongues are sewn to the scalloped contour of the aortic annulus. In the reimplantation procedure (David I), the Dacron graft (we use a Valsalva non-valved graft) is placed around the skeletonized AV and is secured below the annulus. The remnant of sinus tissue and the annulus are sewn to the inside of the graft. This technique stabilizes the annulus and prevents future dilation, especially in patients with connective tissue disorders. The remodeling technique can lead to aortic annular dilation. The surgeon’s experience and degree of confidence play a critical role in successful and durable valve-sparing procedures.

Treatment options for aortic arch pathology

The treatment armamentarium for repair/replacement of the aortic arch includes open surgical repair, hybrid repair, and endovascular replacement of the aortic arch. The choice of repair technique for the various thoracic arch lesions is influenced by the patient’s comorbidities and age.
Open aortic arch repair

The first open aortic arch repair was reported by Cooley and DeBakey in 1955.\textsuperscript{53} This was for its time an extremely challenging operation that involved a considerable risk of stroke and death. Because of advances in cardiopulmonary bypass techniques, simplification of surgical technique, and the development of protective adjuncts—such as selective antegrade cerebral protection and moderate hypothermia—for better brain protection, recent outcomes are a substantial improvement over those obtained in the past.\textsuperscript{54–56} As previously mentioned, our preferred route for arterial inflow in treating ascending aortic lesions and performing arch reconstruction is via an 8-mm Dacron graft anastomosed end-to-side to the innominate artery.\textsuperscript{47–48} Although the first arch reconstructions were enabled by deep hypothermic circulatory arrest (DHCA), this technique has adverse effects on the coagulation system and is limited to 30 minutes at 18°C.\textsuperscript{57} Retrograde cerebral perfusion, introduced by Ueda\textsuperscript{57} in 1990 as an adjunct to DHCA, yields better results by routing oxygenated blood through the superior vena cava and flushing air and debris out of the cerebral circulation. Despite initial adoption by our surgical group,\textsuperscript{58} retrograde cerebral perfusion failed to improve neurologic and metabolic outcomes,\textsuperscript{59} and antegrade cerebral perfusion has become the preferred means of brain protection for our group, as well as for others.\textsuperscript{60} In addition, moderate or even mild hypothermia (26–30°C) may be safe and effective for brain protection, although the upper safe temperature limit has not yet been determined.\textsuperscript{49,61,62} The open arch repair technique varies from the traditional “island-and-en bloc” supra-aortic-arch-vessel anastomosis to the four-branched arch graft and the Y-graft technique.\textsuperscript{63,64} In cases of extensive aneurysmal disease also involving the descending thoracic or thoracoabdominal aorta, the elephant trunk procedure as described by Hans Borst is used.\textsuperscript{65}

Here is how we conduct the operation: After cardiopulmonary bypass has been established, cooling of the patient is initiated. For open arch reconstruction, we prefer the Y-graft technique,\textsuperscript{55,71} although we use the island technique as needed, depending on the patient’s anatomy. During cooling, the arch vessels are dissected, and the left subclavian and left common carotid arteries are bypassed with an off-the-shelf trifurcated graft (Terumo, Vascutek). Once the targeted temperature has been achieved (24°C), the innominate artery is snared or clamped, and blood flows are decreased to 10–15 mL/kg/min. Antegrade cerebral perfusion is initially established unilaterally via the innominate artery, and then bilaterally by adding a balloon-tipped catheter at the proximal end of the Y-graft. In the event of a significant decline in the left-sided NIRS, or a known large dominate left vertebral artery, an additional perfusion cannula can be added to the origin of the left subclavian artery. The arch is opened, and the main body of the Y-graft is anastomosed to the innominate artery. After de-airing has been performed, the Y-graft is clamped, and the distal anastomosis is performed, usually between the left subclavian and left common carotid artery. For the elephant trunk, we use Terumo’s (Terumo, VASCUTEK, Inchinnan, Scotland) skirted elephant-trunk graft. If a dissecting arch has extensive aneurysmal disease in the descending aorta, the elephant trunk technique is required. The graft is placed inside the true lumen of the dissecting descending thoracic aorta, or a fenestration is created and the graft is placed inside a common lumen.
For patients in whom the descending thoracic aorta is amenable to future endovascular therapy, we perform the frozen elephant trunk procedure with our custom-made frozen elephant trunk graft. After the distal anastomosis has been completed, the graft is clamped, and the proximal part of the operation takes place. At that point, pump flows are restored to normal, and systemic perfusion is re-established. After completion of the proximal reconstruction, the main body of the Y-graft is anastomosed to the main aortic graft at an angle that will minimize kinking of the Y-graft. We rewarm patients to a nasopharyngeal temperature of 36.5°C. Throughout the procedure, we monitor the NIRS and use retrograde and antegrade cardioplegia for myocardial protection.

**Hybrid arch repair**

“Hybrid” arch repair is a combination of open supra-aortic vessel debranching and the endovascular exclusion of pathologic conditions that affect the aortic arch. The first hybrid arch repair was described by Volodos and colleagues in 1991. It has been advocated as an effective alternative that produces acceptable mortality and morbidity rates in patients at high risk from traditional open procedures. Our technique for aortic arch debranching has previously been reported. Via a median sternotomy, we reroute the supra-aortic arch vessels by using commercially available branched grafts (Terumo, Vascutek). First, we create the proximal anastomosis between the main trunk of the bifurcated or trifurcated Y-graft and the ascending aorta by applying a partial occluding clamp to the ascending aorta. We then create the individual distal anastomoses: first to the left subclavian artery, then to the left common carotid artery, and last to the innominate artery. The endovascular portion of the procedure is then carried out by performing antegrade or retrograde stent graft delivery to exclude the aortic arch pathology. The complexity of the hybrid procedure depends on the extent of the aortic disease. In an attempt to avoid a median sternotomy, extra-anatomic bypass for full rerouting of the arch vessels has been also reported. Cardiopulmonary bypass is not required unless the ascending aorta is aneurysmal and needs to be replaced. Off-pump coronary artery bypass can be added as necessary.

Direct comparison of the hybrid procedure and open arch surgery may be unfair because of a lack of homogeneity in the patient populations. Newer endovascular stent grafts are currently on trial for hybrid procedures of the aortic arch.

**Endovascular repair of the aortic arch**

Custom-made branched grafts have been used for patients’ specific anatomy and pathology. Various endovascular techniques have been described in an attempt to overcome the lack of available technology. Because reports are limited, it is difficult to compare this approach to hybrid or open arch repair.

**Treatment options for descending and thoracoabdominal aortic pathologies**

Open and endovascular treatment options are available for various aortic pathologies involving the descending and thoracoabdominal aorta (Figure 6.1).
Descending thoracic aorta

Descending thoracic aneurysms: Open surgical repair

No level A or B scientific evidence from prospective, randomized studies exists regarding the timing of operative intervention according to aneurysm size. The following conditions justify operative intervention: aneurysms with a diameter of 5.0 or larger in patients with a family history of Marfan syndrome; aneurysms with a diameter of 5.5 cm in patients without a family history of Marfan syndrome; aneurysms with a documented growth rate of more than 1 cm/year; and aneurysms that are rapidly expanding, are more than twice the diameter of the normal contiguous aorta, or are producing symptoms.

Open surgical repair is performed via a left posterolateral thoracotomy. The following techniques are appropriate for the open surgical treatment of descending thoracic aneurysms.

**Clamp-and-sew technique**—Before cross-clamp application, heparin is given (1.5 U/kg). The cross-clamp is applied whenever possible distal to the left subclavian artery. In patients with aortic dissection, the clamp is most commonly applied just distal to the left common
carotid artery. In cases involving an enlarging thoracic aneurysm secondary to chronic dissection, the thrombus is removed from the false lumen; then the septum is divided, and the true lumen is opened. Small proximal intercostal vessels that give rise to active back-bleeding are oversewn. Large distal intercostal vessels with slow back-bleeding are usually considered for reattachment. After completing the proximal anastomosis and applying the intercostal patch, we perform an open distal anastomosis. In chronic dissection, the septum is fenestrated during reconstruction of the distal anastomosis to allow inflow into both the true and false lumens distally.

**Clamp-and-sew technique with left-sided heart bypass**—Partial left-sided heart bypass (LHB) is used as an adjunct to provide distal aortic perfusion and maintain blood flow to visceral vessels and the spinal cord during the repair. This technique is used most for extent I and II TAAA repairs (Figures 6.2 and 6.3). The LHB circuit is established through an outflow cannula inserted into the left atrium via the left inferior pulmonary vein, and through an inflow cannula in the lower descending thoracic aorta or, less frequently, in a femoral artery. Left-sided heart bypass is preferred if the repair is prolonged and complicated, because LHB lowers the risk of paraplegia and paraparesis after thoracoabdominal aortic aneurysm repair, especially extent II repair.73

*Figure 6.2* Right lateral decubitus position for a left posterolateral thoracotomy, which extends from the left scapula to the left, toward the umbilicus. Printed with permission from Baylor College of Medicine
Deep hypothermic circulatory arrest (DHCA)—If the aneurysm extends proximally into the distal arch and cross-clamping is not possible, DHCA may be necessary to construct an open proximal anastomosis. Cardiopulmonary bypass is usually initiated via the femoral artery and vein, or via the junction of the inferior vena cava with the right atrium. The patient is cooled to a target temperature of 18°C. When the targeted temperature is achieved, the proximal aorta is opened with a distal clamp in the mid-descending aorta or lower to allow flow of 2–3 L/min. Once the proximal anastomosis is completed, the pump is restarted, usually via a pre-attached 8-mm side graft just below the distal arch anastomosis. The graft is cross-clamped, and the open distal anastomosis is performed during rewarming with the patient on cardiopulmonary bypass.

Descending thoracic aneurysms: Endovascular repair (TEVAR)

In March 2005, the FDA approved for commercial use the Gore TAG thoracic endograft (W.L. Gore and Associates, Flagstaff, AZ, USA) for treatment of descending thoracic aneurysms. Since then, more devices have gained approval. Despite the sole indication approved by the FDA in 2005, thoracic aortic endografting is rapidly emerging as the treatment of choice for a variety of thoracic pathologies. Recently, the FDA has approved endovascular therapy for both traumatic injury and aortic dissection of the descending thoracic aorta. During the evaluation for endografting in the descending thoracic aorta, the following points should be addressed: the proximal landing zone and its relationship...
to the origin of the great vessels (left subclavian and left common carotid artery); the
distal landing zone and its relationship to the celiac axis; the iliofemoral artery’s diameter;
the presence of calcification, thrombus, or dissection; the tortuosity of the thoracic aorta;
and the potential for compromise of critical branch flow. Depending on the size of the ac-
cess vessels, the native iliofemoral vessels or iliac-conduit or aorto-conduit access is used.
Left subclavian artery revascularization with left carotid-to-subclavian artery bypass or
transposition is an absolute indication in patients with a patent left internal mammary
artery and prior coronary artery bypass, a functioning arteriovenous fistula in the left
upper extremity, or a dominant left vertebral artery. Coverage of a long segment of the
descending thoracic aorta is a relative indication for left subclavian revascularization for
spinal cord protection.

The following are the basic procedural steps: the femoral artery is accessed (percutan-
eously or open), and heparin (5,000 U) is administered. Under fluoroscopic guidance, a
soft wire is advanced into the ascending aorta. In cases of acute or chronic aortic dissec-
tion, using intravascular ultrasound (IVUS) to confirm the placement of the guidewire
inside the true lumen of the thoracic aorta is recommended. Occasionally, accessing the
true lumen can be challenging, in which case inserting the soft wire via the right brachial
artery and snaring this wire via the femoral artery can be very helpful. The soft wire is
exchanged for a stiff Lunderquist guidewire, and the sheath, stent endograft, or both are
advanced under fluoroscopy. Before the endograft is placed, preoperative arch and de-
scending thoracic angiography, IVUS, or both are necessary to confirm the origin of the
left subclavian artery, the left common carotid artery, and the celiac axis. During deploy-
ment of the endograft, the systolic pressure is kept below 100 mmHg; immediately after
deployment, we raise the mean pressure to at least 90 mmHg and/or the systolic blood
pressure to 150–170 mmHg for spinal cord protection. The sheath is removed, and the
femoral artery is repaired under direct vision or percutaneously. Protamine is given to re-
verse heparin. Preferably, the patient is extubated in the operating room. A cerebrospinal
fluid drain is used for spinal cord protection during the TEVAR when we cover more than
15 cm of the descending thoracic aorta and when the patient has previously undergone
open or endovascular abdominal aortic aneurysm replacement.

**Descending thoracic aortic dissection: Acute Stanford type B, or DeBakey type IIIA, and/or DeBakey type IIIB aortic dissection**

**Special considerations**

The initial treatment for all patients with suspected or confirmed acute aortic dissec-
tion is aggressive blood pressure control or anti-impulse therapy to stabilize the dissec-
tion and to prevent rupture. Intravenous beta-adrenergic blockers, direct vasodilators,
calcium channel blockers, and angiotensin-converting enzyme inhibitors are used.
Beta antagonists are administered to all patients unless there are strong contraindi-
cations. Medical therapy provides better outcomes in non-complicated acute descending
thoracic dissection than open surgical therapy.77 Serial CT scanning of the chest and
abdomen during the patient’s hospitalization is recommended, and meticulous follow-up after hospital discharge and aggressive blood pressure control are imperative. Surgical intervention is indicated in cases of complicated acute type B, IIIA, or IIIB aortic dissection, which are characterized by contained rupture, malperfusion, continuous pain, uncontrollable hypertension, and periaortic hematoma. Three goals should be achieved during any open or endovascular repair for acute type B aortic dissection: exclude the primary tear, eliminate all aneurysmal disease, and permit perfusion to all distal organs and major aortic branches. Endovascular therapy is becoming the preferred approach for complicated acute descending thoracic aortic dissection. According to the IRAD registry, TEVAR is associated with lower 5-year mortality than medical therapy. For patients with a connective tissue disorder, endografting is not recommended, and endovascular stent grafting, if needed, may be used as a bridge to later definitive repair.

**Chronic Stanford type B (type IIIA and/or type IIIB) aortic dissection**

The presence of symptoms, evidence of an enlarging dissecting thoracic aneurysm, and acute dissection superimposed on a chronic aneurysm with imminent rupture or malperfusion are the indications for surgical intervention in chronic descending thoracic aortic dissection. The same open technique used to treat open thoracoabdominal aortic aneurysms (described next) can be used with these patients. Special attention is given to the septum, which should be divided to identify the true and false lumens and all the important branch vessels.

With regard to endovascular therapy, recent 5-year results of the INSTEAD-XL trial (Investigation of Stent-grafts in Aortic Dissection) revealed that TEVAR improved 5-year aorta-specific survival and delayed disease progression when used in addition to optimal medical treatment. In stable type B dissection with suitable anatomy, the conclusion was that pre-emptive TEVAR should be considered to improve late outcome.

We consider treatment options tailored to each patient’s anatomy, age, and comorbid conditions. The endovascular repair, with regard to technical considerations, can be challenging—even more so than in acute disease. The principles followed during TEVAR in patients with acute descending thoracic dissection are also followed during TEVAR in patients with chronic dissection.

**Thoracoabdominal aorta**

**Thoracoabdominal aortic aneurysms (TAAA): Open repair**

Surgical repair of TAAA is categorized by the extent of aortic replacement according to the Crawford classification. Extent I thoracoabdominal aortic aneurysm repair (TAAA ext I) involves the descending thoracic aorta, beginning near the left subclavian artery, and extends into visceral vessels (celiac, superior mesenteric, and both renal arteries). Extent II repair (TAAA ext II; Figure 6.1) also begins near the left subclavian artery but extends distally into the aortic bifurcation. Extent III repair (TAAA ext III) extends from the lower descending thoracic aorta (below the sixth rib) into the
abdomen. Extent IV repair (TAAA ext IV) begins at the diaphragmatic hiatus at the level of the visceral vessels and often involves the entire abdominal aorta. Exposure is achieved by thoracoabdominal incision. In TAAA ext I and ext II repair, we routinely use LHB, permissive hypothermia, and cold (4°C) crystalloid solution (25 g of mannitol and 125 mg of methylprednisolone in 1 L of Ringer’s lactate solution) for renal perfusion and protection.\textsuperscript{73,81,82} Cerebrospinal fluid drainage, in addition to sequential cross-clamping and selective reimplantation of intercostal or lumbar arteries, is used for spinal cord protection,\textsuperscript{83,84} especially in ext I and II repairs. The steps of the operation have been previously described (Figure 6.2). Left heart bypass is initiated (Figure 6.3), the cross-clamp is placed for performing the proximal anastomosis (Figure 6.4), and large intercostal arteries with slow back-bleeding are reimplanted (Figure 6.5). For extensive aneurysms (“mega aorta”) involving the ascending aorta, transverse arch, and descending thoracic aorta, we proceed with staged operations. When the descending or thoracoabdominal component is symptomatic or is disproportionately large (compared with the ascending aorta), the distal segment is treated during the initial operation, and repair of the ascending aorta and transverse aortic arch is performed as a second procedure. A reversed elephant trunk repair can be performed during the first operation.\textsuperscript{85} Frozen elephant trunk repair can be performed in patients with ascending and arch aneurysms that extend through the upper or the entire descending thoracic aorta.\textsuperscript{86} Although spinal cord ischemia and renal failure warrant special consideration postoperatively, the most common complication after extensive repair is respiratory

\textbf{Figure 6.4} After LHB is established, placement of the cross-clamp and performance of the proximal anastomosis follow.

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failure. In addition, the vagus and left recurrent laryngeal nerves are susceptible to injury. Vocal cord paralysis can be treated by direct cord medialization. In patients with patent left internal thoracic artery grafts from prior coronary artery bypass in whom there is need to clamp proximal to the left subclavian artery, a left common carotid-to-subclavian bypass is performed before TAAA repair.

**Completion elephant trunk repair**

This repair can be performed with endovascular techniques in patients whose aneurysm ends at the diaphragm, whereas open repair is necessary in patients with more extensive pathology. Occasionally, advancing a stent graft in retrograde fashion from the femoral artery into the elephant trunk can be very challenging; advancing a wire antegrade via the right brachial artery may be useful in these cases. For the past few years, in cases in which the completion stage can be performed endovascularly, we have been placing a short (10-cm) stent inside the trunk of the elephant graft to facilitate the second/completion stage.\textsuperscript{86,66}

**Thoracoabdominal aortic aneurysms (TAAA): Hybrid and endovascular repair**

A combination of open surgery to reroute the blood supply of the visceral vessels to avoid visceral ischemia, allowing their aortic origin to be covered by stent graft, is the

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*Figure 6.5* Intercostal patch placement.  
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mainstay of hybrid therapy for TAAA. The endovascular portion of the hybrid therapy procedure can be performed concomitantly with the open portion, or it can be done later as a separate procedure. The results of these procedures vary.\textsuperscript{87,88} We do not favor the hybrid approach for TAAA. Although it requires a less extensive incision than does thoracoabdominal exposure for TAAA, debranching usually requires substantial retroperitoneal or transperitoneal exposure. Total endovascular repair for TAAA with the use of fenestrated and branched endografts has been used extensively with promising results.\textsuperscript{89} However, mortality and spinal cord ischemia risks remain considerable.

**Conclusion**

Innovative and standard open surgical approaches are used to treat the various thoracic aortic pathologies. Having open, endovascular, and hybrid repair options creates an opportunity to maximize the benefit of repair for the individual patient.

**References**


Mitral valve repair: Conventional open techniques

A. Marc Gillinov and Tomislav Mihaljevic

Mitral valve repair: Indications and results

Mitral valve repair vs. mitral valve replacement

Mitral valve repair is the preferred surgical option for nearly all patients with mitral regurgitation (MR). Advantages of mitral valve repair over mitral valve replacement include better preservation of left ventricular function, greater freedoms from endocarditis and anticoagulant-related hemorrhage, and, in some cases, improved survival.\(^1\)\(^-\)\(^4\) Mitral valve repair has particular advantages in younger patients, who require lifelong anticoagulation if they receive mechanical prostheses. Mitral valve repair can be achieved in more than 90% of patients with MR caused by prolapse.\(^1\)\(^-\)\(^5\)

Durability of mitral valve repair

The durability of mitral valve repair is widely recognized to be excellent.\(^1\)\(^-\)\(^7\) However, it is clear that not all mitral valve repairs last a lifetime. In fact, a recent single center series reports an alarmingly high incidence of recurrent MR in patients who had repair for prolapse.\(^8\) Other experienced centers report better durability.\(^1\)\(^-\)\(^7\) Among patients having repair for posterior leaflet prolapse, the most common finding for 10-year freedom from reoperation is 97%, and 10-year freedom from moderately severe or severe MR is 80% to 90%.\(^7\)\(^-\)\(^9\) Durability of repair for anterior leaflet prolapse has been somewhat lower in most series.\(^7\)\(^-\)\(^10\) However, changes in surgical technique have improved results in patients with anterior prolapse. With the elimination of chordal shortening, standardized correction of anterior prolapse with artificial chordae or chordal transfer, and routine use of an annuloplasty, durability of repair of anterior (or bileaflet) prolapse is similar to that for repair of posterior prolapse.\(^7\)

Indications for mitral valve repair (vs. replacement)

There are no specific anatomic contraindications to mitral valve repair in patients with mitral valve prolapse. However, clinical judgment must be applied on a case-by-case basis. If an elderly patient with multiple comorbidities has complex valvar pathology (bileaflet prolapse, annular calcification), bioprosthetic mitral valve replacement should
be considered. Conversely, mitral valve repair is preferred in a younger, healthier patient who has a similarly complex mitral valve.

**Approaches to the mitral valve**

Most mitral valve surgery is performed via median sternotomy. Advantages to median sternotomy include central cannulation, good surgical exposure, excellent access for de-airing the heart, and ability to perform concomitant procedures. Nevertheless, in a patient with isolated mitral valve disease, minimally invasive approaches should be considered. Currently applied less invasive approaches to the mitral valve include partial sternotomy (upper or lower), right mini-thoracotomy, and robotically assisted right chest approaches. In our practice, standard median sternotomy is indicated when concomitant procedures (e.g. coronary artery bypass grafting, aortic valve replacement) are necessary. Most other patients requiring mitral operation, including those with atrial fibrillation (AF), are approached minimally invasively.

**Median sternotomy and mitral valve repair: Technical considerations**

Before incision, the transesophageal echocardiogram is carefully studied. This is necessary to identify the precise mechanism(s) of MR and to formulate the final operative plan. The heart is exposed through a standard median sternotomy. In selected patients, a limited skin incision (10–12 cm) is employed for improved cosmesis. Cannulation is achieved via the ascending aorta, superior vena cava (right angle cannula), and inferior vena cava. Cardiopulmonary bypass is established, and antegrade and retrograde cardioplegia catheters are placed. The aorta is cross-clamped, and the heart arrested with antegrade and retrograde cardioplegia. Thereafter, retrograde cardioplegia is administered every 15 minutes. The operative field is flooded with $\text{CO}_2$ at 6 l/min. If the left atrium is small or the operation is a reoperation, the mitral valve is accessed via a transseptal incision that is carried onto the dome of the left atrium. In most other cases, the mitral valve is approached by a standard incision in the left atrium; this incision is constructed anterior to the right pulmonary veins and is taken beneath the superior and inferior vena cavae to enhance exposure. A self-retaining retractor with three blades is positioned in the left atrium, exposing the mitral valve. Next, systematic valve examination is undertaken, assessing each segment of the anterior and posterior leaflets, and clearly identifying site(s) of prolapse.

**Repair techniques**

Recent increased interest in minimally invasive approaches to mitral valve surgery has been complemented by introduction (or reintroduction) of surgical techniques that simplify mitral valve repair. These mitral valve repair techniques help to reduce operative time and can be applied through both minimally invasive and standard sternotomy approaches (Table 7.1). The specific repair technique applied depends primarily upon the site of prolapse. All leaflet and chordal repair techniques are accompanied by an annuloplasty. In
patients with degenerative disease, durability does not appear to be strongly influenced by type of prosthetic annuloplasty. Therefore, in such patients, we generally favor a posterior flexible band placed from trigone to trigone. It is technically simpler to use a flexible band than it is to employ a rigid ring. The band is sized according to the surface area of the anterior leaflet.

### Posterior prolapse

Approximately 75% of patients with MR caused by degenerative disease have isolated prolapse of the posterior leaflet, most commonly the P2 segment (middle scallop). The classic technique for managing this is quadrangular resection, with or without sliding repair. The sliding repair was developed to reduce the risk of post-repair systolic anterior motion (SAM) in the setting of excessive leaflet tissue and/or a small, hyperdynamic left ventricle. In our clinical practice, we have generally replaced standard quadrangular resection and sliding repair with triangular resection and folding plasty, respectively; these two simplified techniques for correction of posterior leaflet prolapse reduce the number of surgical maneuvers and thereby decrease operative time. When posterior prolapse is extensive or diffuse, we apply artificial chordae without leaflet resection.

### Triangular resection

In the patient with segmental posterior leaflet prolapse, MR is caused by lack of coaptation at the site of chordal rupture or elongation. Therefore, it is logical to target the prolapsing free edge of the leaflet when addressing this problem. A triangular resection entails resection of the portion of the free edge that prolapses, with incisions in the leaflet

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**Table 7.1 Repair techniques: Evolution**

<table>
<thead>
<tr>
<th>Site of prolapse</th>
<th>Classic technique</th>
<th>Simplified technique</th>
<th>Alternate technique(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior-low risk of systolic anterior motion (SAM)</td>
<td>Quadrangular resection</td>
<td>Triangular resection</td>
<td>Edge-to-edge</td>
</tr>
<tr>
<td>Posterior-high risk of SAM</td>
<td>Sliding repair</td>
<td>Folding repair</td>
<td>Edge-to-edge</td>
</tr>
<tr>
<td>Posterior-extensive resection</td>
<td>Sliding repair</td>
<td>Artificial chordae</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>Chordal transfer</td>
<td>Artificial chordae</td>
<td>Edge-to-edge</td>
</tr>
<tr>
<td>Commissure</td>
<td>Leaflet resection or chordal transfer</td>
<td>Commissuroplasty</td>
<td></td>
</tr>
<tr>
<td>Bileaflet-posterior predominant</td>
<td>Sliding repair ± anterior leaflet procedure</td>
<td>Triangular resection, large annuloplasty</td>
<td>Edge-to-edge</td>
</tr>
<tr>
<td>Bileaflet-balanced, no flail</td>
<td>Sliding repair ± anterior leaflet procedure</td>
<td>Large annuloplasty alone</td>
<td>Edge-to-edge</td>
</tr>
</tbody>
</table>
angled toward one another as the incision approaches the annular level (Figure 7.1).\textsuperscript{12,13} No annular plication sutures are necessary; this simplifies the procedure and reduces the risk of circumflex artery distortion or kinking. After triangular resection, care should be exercised not to use too small an annuloplasty, as this may increase the risk of SAM.\textsuperscript{14} We most frequently employ a posterior flexible band of labeled size 34–38 mm.

**Folding plasty**

The folding plasty is used to treat posterior leaflet prolapse when there is a high risk of SAM, replacing the sliding repair in most of these cases.\textsuperscript{15} The prolapsing portion of the posterior leaflet is resected as for a quadrangular resection, leaving tall posterior leaflet remnants on either side (Figure 7.2). A suture is passed through the mid-portion of the cut leaflet edge on each side, and this suture is then passed through the annulus at the mid-portion of the area of resection; this maneuver reduces the posterior leaflet height. If necessary, suture placement is modified to ensure that the leaflet remnants are of similar height. Leaflet tissue is then approximated to the annulus, closing the gap at the annular level, and uniformly reducing the height of the posterior leaflet in this region. The leaflet edges are reapproximated in the middle and an annuloplasty completes the repair.

**Artificial chordae**

There has been considerable recent interest in the application of artificial expanded polytetrafluoroethylene (ePTFE) chordae (Gore-Tex, W.L. Gore and Assoc, Flagstaff, AZ) for correction of posterior leaflet prolapse. We use artificial chordae when there is diffuse posterior leaflet prolapse. If the prolapsing segment is very large, its resection may leave inadequate tissue for restoration of valve competence. In such cases, we create artificial chordae. The needle of an ePTFE suture is passed twice through the tip of a papillary muscle, creating a figure-of-eight stitch. Each of the needles is then passed twice through the free edge of the posterior leaflet, traversing from the ventricular to the atrial aspect each time. In most cases of diffuse prolapse, two sets of chordae are necessary. The ePTFE sutures are left untied, and the annuloplasty is placed. The ventricle is then filled with saline, and the sutures tied at a length that prevents leakage. In general, chordae to the
REPAIR TECHNIQUES

The posterior leaflet are quite short, distracting the tip of the leaflet into the ventricle. The posterior leaflet then provides an excellent surface of coaptation for the more mobile anterior leaflet.

**Anterior prolapse**

Correction of anterior leaflet prolapse is traditionally more challenging than is correction of posterior leaflet prolapse. Classic techniques for management of anterior leaflet prolapse include chordal transfer, which usually requires manipulation of the posterior leaflet; chordal shortening, which is associated with reduced durability; and triangular resection.\(^{16}\) Management of anterior prolapse by creation of artificial chordae or the edge-to-edge repair simplifies the procedure.

**Artificial chordae**

As for posterior prolapse, artificial chordae used to treat anterior prolapse are constructed of ePTFE. The key challenge with application of artificial chordae for anterior prolapse is determination of chordal length, and there are many techniques for estimating chordal length.\(^{17,18}\) We generally create artificial chordae to the anterior leaflet using the same technique.

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**Figure 7.2** Folding plasty. (a) The posterior leaflet is tall. Quadrangular resection of the prolapsing portion is performed. (b) Sutures are passed through the mid-points of the cut leaflet edges and then through the annulus in the region of the defect. (c) Traction on these sutures folds the posterior leaflet toward the annulus, reducing its height. (d) The leaflet edges are sutured to the annulus, each bite reducing the height of the posterior leaflet and the leaflet edges are reaproximated in the middle. (e) Annuloplasty completes the repair.

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described earlier for posterior leaflet prolapse (Figure 7.3). The ePTFE suture is affixed to a papillary muscle as a figure-of-eight stitch. Care is taken not to entrap other, normal chordae in this suture. Each needle is passed twice through the free edge of the prolapsing anterior leaflet. The annuloplasty is placed and then the ventricle insufflated with saline. The chordae are tied at a length that ensures valve competence. Great care must be exercised to ensure that chordae to the anterior leaflet are not too short; this is the most common error.

Alternatively, a caliper may be used for direct measurement and construction of chordal loops, as described by Von Uppell and Mohr. With this technique, the caliper is used to measure the length of a normal chord or, if there is no reference chord, the distance from the papillary muscle head to the annulus. Chordal loops of this length are constructed.

Figure 7.3  Creation of artificial chordae. (a) A figure-of-eight suture is passed through the tip of the papillary muscle. (b) Each needle is passed twice through the free edge of the unsupported leaflet. (c) After placing the annuloplasty and insufflating the ventricle, the ePTFE sutures are adjusted until the valve does not leak. The sutures are then tied at this length on the atrial aspect of the leaflet. (d) Completed chordae; each suture creates two chordae. In most instances, one or two sets of chordae are used to support the anterior leaflet.

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and affixed to a papillary muscle; for repair of anterior prolapse, the length is most commonly 22–24 mm. Finally, the loops are affixed to the free edge of the prolapsing leaflet with a Gore-Tex suture (Figure 7.4). This technique may also be applied for correction of posterior leaflet prolapse, in which case the chordae are generally 12–14 mm in length.  

**Figure 7.4** Creation of pre-measured artificial chordae. (a) A caliper is used to measure a normal chord to the anterior leaflet. The caliper is then locked. (b) A group of chordal loops is fashioned from a single stitch by tying the loops around the caliper, locking each loop to ensure that its length is constant. (c) The set of chordal loops is affixed to a papillary muscle using pledgets, and the loops are attached to the unsupported free edge of the anterior leaflet.

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and affixed to a papillary muscle; for repair of anterior prolapse, the length is most commonly 22–24 mm. Finally, the loops are affixed to the free edge of the prolapsing leaflet with a Gore-Tex suture (Figure 7.4). This technique may also be applied for correction of posterior leaflet prolapse, in which case the chordae are generally 12–14 mm in length.  

**Edge-to-edge repair**

Described by Alfieri and coworkers, the edge-to-edge repair is the simplest maneuver for correction of prolapse. With this technique, the prolapsing segment of the anterior leaflet is sutured to normal posterior leaflet directly opposite, ensuring coaptation and preventing prolapse. Sutures are taken several millimeters deep into the leaflet and span the entire region of prolapse. The stitch should normally not exceed 1 cm in length. Of note, the edge-to-edge technique can also be employed to manage posterior prolapse and bileaflet prolapse; however, it is rarely our primary repair technique.

**Commissural prolapse**

Commissuroplasty is a simple and reproducible solution for management of commissural prolapse involving the anterior leaflet, posterior leaflet, or both leaflets. The edge of the prolapsing segment is sutured to the free edge of the opposite leaflet. A relatively large annuloplasty device is employed to avoid mitral stenosis.

**Bileaflet prolapse**

Bileaflet prolapse is often a consequence of Barlow’s disease. Management of this entity depends upon valve pathology. Nearly all of these patients have excessive leaflet tissue
and annular dilatation. In selected patients with symmetric bileaflet prolapse, a central jet of MR, and no flail, repair can frequently be accomplished by insertion of a large annuloplasty device alone (typically labeled size 36 or greater); this reduces annular diameter and increases leaflet coaptation. In many patients with bileaflet prolapse, prolapse is asymmetric, and the predominant lesion is prolapse of the middle scallop of the posterior leaflet, producing an anteriorly directed jet of MR. In such cases, mitral valve repair is most often achieved by resection of the middle scallop of the posterior leaflet (folding repair, sliding repair, or triangular resection, depending upon leaflet height and extent of resection). A relatively large annuloplasty is applied in order to reduce the risk of SAM. In patients with severe bileaflet prolapse and obvious pathology of chordae to both leaflets, it is necessary to perform repair of both the anterior and posterior leaflets. This generally necessitates a combination of repair techniques, frequently incorporating resection and sliding repair for the posterior leaflet, artificial chordae for the anterior leaflet, and annuloplasty to increase leaflet coaptation.

**Special situations**

**Annular calcium**

Mitral annular calcification complicates mitral valve repair. The calcium tends to be along the posterior annulus. If the valve is to be repaired, it is nearly always necessary to remove the calcium. In most cases, the primary problem is posterior leaflet prolapse. The posterior leaflet is detached from the annulus as for a sliding repair, and the prolapsing segment is resected. The annular calcium is then removed. Although the calcium occasionally comes out as a single bar, the more common situation is that the calcium is resected piecemeal. Great care must be taken not to allow calcium to fall into the ventricle or atrium. If the resection has been particularly deep or extensive, an autologous pericardial patch is sewn to the ventricle and the atrium, excluding the area of resection and preventing rupture of the atrioventricular groove. The posterior leaflet tissue is then reattached to the annulus (or pericardial patch) and an annuloplasty is placed.

**Atrial fibrillation**

In patients with AF, surgical ablation is performed before the mitral valve procedure. We favor a biatrial lesion set in most patients, replicating the lesions of the classic Maze III procedure with alternate energy sources. In the left atrium, this includes a pulmonary vein encircling lesion and connecting lesions to the mitral annulus and to the left atrial appendage. A cryolesion is created on the epicardial aspect of the coronary sinus, corresponding to the endocardial connection to the mitral annulus. The left atrial appendage is excised, or, in a reoperative setting, oversewn from inside the left atrium. Right atrial lesions include incisions in the body of the right atrium and the right atrial appendage, with connecting lesions to the tricuspid annulus and a lesion from the superior vena cava to the inferior vena cava.
The only instance in which we would perform pulmonary vein isolation alone is in the patient with recent onset paroxysmal AF and normal left atrial size.

**Recommendations**

When faced with the need for mitral valve surgery, patients tend to focus on (1) valve repair (vs. replacement) and (2) minimally invasive approaches. It is the surgeon’s responsibility to deliver the highest probability of repair with the safest approach. While minimally invasive procedures are certainly desirable, patient characteristics, as already outlined, may dictate a sternotomy as the approach of choice. Less invasive approaches should be considered only after the surgeon has mastered standard repair techniques via sternotomy.

**References**


History

In 1996 Cosgrove and Cohn demonstrated that either a parasternal incision or a partial sternotomy could be used to perform MV operations safely.\(^1\)\(^-\)\(^3\) Carpentier first used videoscopic assistance and cold ventricular fibrillation to repair a mitral valve (MV) via a right mini-thoracotomy.\(^4\) Shortly thereafter, Mohr and Chitwood reported independently their experiences with minimally invasive mitral valve surgery (MIMVS) at their respective institutions.\(^5\)\(^-\)\(^7\) Since then, the logical trend has moved toward less invasive techniques using robotic assistance. Initially, the main robotic component was the AESOP 3000 voice-activated camera manipulator\(^8\) and more recently the da Vinci™ Surgical System (Intuitive Surgical, Sunnyvale, CA). The use of the Zeus robotic system was short lived with only a few MV cases performed.\(^9\)\(^,\)\(^10\)

In 1999 Carpentier reported the first MV operation using true robotic assistance.\(^11\) In May 2000, our center performed the first da Vinci™ robotic-assisted MV repair in the United States, which consisted of a leaflet resection with a repair and a band annuloplasty. Since then many international centers have establish different levels of MIMVS program sophistication but few have used the da Vinci™ robotic-assisted approach consistently. Recently, Gammie et al. reviewed less invasive MV operative trends in the United States.\(^12\) They identified 28,143 patients, archived in the Society of Thoracic Surgeons (STS) Adult Surgical Database that had undergone an isolated MV operation between 2004 and 2008. During that period, adoption of MIMVS increased from 12% to 20%, with 35% of the latter having been performed using robotic techniques. These data demonstrate that cardiac surgeons are increasingly embracing MIMVS techniques, and this trend has been mirrored in many international centers. Nevertheless, adoption of a MIMVS strategy has been much slower than that in other surgical disciplines. It is not surprising that robotic cardiac surgery, and especially MIMVS, would have a significant penetration phase lag, as the complexity is much greater than in extirpative operations.

Outcomes

Cardiac surgeons have moved toward less invasive MV surgery as these operations result in less morbidity than traditional sternotomy operations. Less invasive approaches often result in faster recovery, shorter hospitalizations, and more rapid return to normal
activities and productivity, compared to patients undergoing a full sternotomy. Although several reports have addressed these issues, sufficient statistical power has not been present to accurately compare MIMVS to sternotomy-based MV surgery in a prospective randomized manner. Thus, definitive evidence has not arisen to support many surgeons’ belief that MIMVS is superior, or at least equivalent to traditional MV surgery. Despite our desire to prove superiority, patients and referring physicians now consider MIMVS very beneficial and, therefore, prefer not to participate in randomized trials. To this end, we are forced to rely on large published series for direction, knowing that many have limitations. Moreover, it is important for surgeons adopting MIMVS to keep detailed databases so that they can provide accurate information to their patients.

Different reports have demonstrated that MIMVS is associated with decreased bleeding, transfusions, and re-explorations for bleeding when compared to traditional approaches. Moreover, these studies suggest that patients have less wound infections, better pain control, improved quality of life, shorter hospitalizations, and faster return to normal activities. In addition, most patients are very satisfied with the cosmetic results associated with a right mini-thoracotomy incision. At the same time, however, MIMVS has been associated with longer cardiopulmonary and cross-clamp times, as well a slight increase in perioperative strokes.

Recently, Modi et al. published a meta-analysis of many MIMVS publications. They identified 43 reports, of which two were from randomized trials, 17 were from case control studies, and 24 from were cohort studies. Of 2,827 cohort patients, 1,358 were in the MIMVS group and 1,469 were in the sternotomy group. The operative mortality was equivalent. The MIMVS cohort had less bleeding, and there was a trend toward shorter hospitalizations. These benefits were demonstrated despite longer cardiopulmonary perfusion and cardiac arrest times. Moreover, these studies consistently showed that after both primary MIMVS and reoperations, patients had less pain and had a more rapid recovery.

Cohn et al. published a comprehensive review that analyzed the recent MIMVS literature. He concluded that in both approaches mortality and valve quality were similar. However, in MIMVS, femoral perfusion may potentially cause complications. Moreover, cardiopulmonary and cross-clamp times are longer, despite the learning curve improvements even in high volume centers. Interestingly, when compared to patients having a full sternotomy, MIMVS was shown to be safer for obese patients and equal in safety for patients over 70 years old. Prior publications also showed beneficial MIMVS outcomes for older patients (>70 years) when compared to traditional mitral operations.

Today, the da Vinci™ robotic system facilitates the least invasive MV operations with the best visualization and instrument ergonomics. Surgeon adoption is increasing steadily and several centers in the United States now have reported excellent results. To date, at the East Carolina Heart Institute, we have performed over 650 robotic MV repairs, either singularly or in combination with other cardiac procedures. Between May of 2000 and January of 2010, 530 patients with either moderately severe or severe preoperative mitral insufficiency had an isolated robotic MV repair. Specific repair techniques included: (1) leaflet resection with an annuloplasty (LRA); (2) a LRA plus a sliding-plasty
and/or chordal procedure (CP); (3) a CP with an annuloplasty; (4) a LRA with CP; and (5) an annuloplasty alone (N = 99, 18.4%; N = 130, 24.5%; N = 64, 12.1%; N = 144, 27.0%, N = 58, 11.2%, respectively). Other techniques were used in 34 (6.6%) patients. Every patient had an annuloplasty band implanted. The mean age was 57.2 ± 0.9 years (mean ± SEM) and 329 (62.1%) were men. Cardiopulmonary bypass, cross-clamp, and total robot repair times were 162.0 ± 2.3, 126.0 ± 3.0 and 90.0 ± 2.0 minutes, respectively. For the group, the mean operating room time was 285.5 ± 3.0 minutes. The overall mortality was 1.5% (N = 8) and average length of hospitalization was 4.8 ± 0.2 days. Complex repairs were done in 82% of patients, and 96.5% had either mild or less MR by follow-up transesophageal echocardiography.

Other recent publications also have suggested that robotic MV surgery is safe and efficacious. Murphy et al. reported 127 robotic mitral operations, in which five patients were converted to a median sternotomy and one had a thoracotomy. Seven patients had prosthetic replacements and 114 had a repair. There was one in-hospital death, one late death, two strokes, and 22 patients developed new postoperative atrial fibrillation. Blood product transfusions were required in 31% with re-explorations for bleeding in two patients (1.7%). Post-discharge echocardiograms were available in 98 patients with no more than mild residual MR in 96.2% at a mean follow-up of 8.4 months.

Chitwood et al. reported results from their first 300 robotic MV repairs that were operated upon between May 2000 and November 2006. This series was strengthened by 100% patient follow-up and interval echocardiographic studies in 93%. Overall there were two (0.7%) early deaths (30 days), six (2.0%) late mortalities, and no conversions to a sternotomy. Immediate post-repair transesophageal echo studies revealed the following levels of mitral regurgitation: none/trivial, 294 (98%); mild, three (1.0%); moderate, three (1.0%); and severe, 0 (0.0%). Operative complications included two (0.7%) strokes, two transient ischemic attacks, three (1.0%) myocardial infarctions, and seven (2.3%) reoperations for bleeding. The mean hospital length of stay was 5.2 +/- 4.2 (+/-SD) days. Sixteen (5.3%) patients required a reoperation for recurrent MV regurgitation. Interval follow-up transthoracic echocardiograms showed the following amounts of mitral insufficiency: none/trivial, 192 (68.8%); mild, 66 (23.6%); moderate, 15 (5.4%); and severe, six (2.2%).

Mihaljevic et al. reported outcomes from 759 patients who had a posterior leaflet mitral repair at the Cleveland Clinic between 2006 and 2009. They compared patients having a complete sternotomy (n = 114), a partial sternotomy (n = 270), a right mini-thoracotomy (n = 114), or a right mini-thoracotomy with robot assistance (n = 261). There were no in-hospital deaths and both cardiopulmonary bypass and cardiac arrest times were longest in the robotic group and shortest in the sternotomy group. There were no group differences in quality of the mitral repairs. The robotic group had the lowest occurrence of postoperative atrial fibrillation and the shortest hospitalization (median 4.2 days). Neurological, pulmonary, and renal complications were similar between groups. Folliguet et al. compared robot-assisted MV repair patients to a matched sternotomy cohort (N = 25 each group). The robotic group had a shorter hospital stay (7 days vs. 9 days, P = 0.05) with no other differences between groups. Lastly, Woo et al. showed in a non-randomized single
surgeon experience that robotic surgery patients had a significant reduction in blood transfusions and hospitalization compared to their sternotomy patients.\textsuperscript{15}

In summary, the outcomes reported for MIMVS have been excellent and in many ways appear to be better that those for conventional sternotomy surgery. Our series and those of others suggest that results from robot-assisted mitral repairs are as good as those performed via sternotomy and are associated with less transfusions, rapid recovery, and better cosmetic effects. We believe that patient selection and preoperative vascular screening will decrease the number of perioperative strokes, as peripheral cannulation with retrograde perfusion may be responsible for some of these events. We believe that both central and axillary cannulation continue to be the best perfusion routes for higher-risk patients (older, previous strokes, and significant peripheral and/or aortic vascular disease). Lastly, completed learning curves for operating surgeons and surgical teams, as well as higher patient volumes, will foist robotic programs toward excellent outcomes in these patients. At the same time, other MIMVS methods provide patients with most of the modern benefits of a less invasive operation. No doubt evolving technology in preoperative planning, echocardiographic modeling, instrumentation, and perfusion will bring surgeons asymptotic to “non-invasive” mitral repairs having structural perfection.

**Operative approach: MIMVS**

**Patient selection**

For our early mini-thoracotomy video-assisted (1996) and da Vinci\textsuperscript{TM} robot-assisted (2000) mitral valve operations, patient selection criteria were very stringent. However, after subsequent experience, the exclusion criteria for isolated MV and/or atrial fibrillation operations have been modified to include: (1) a previous right thoracotomy; (2) significant pulmonary dysfunction and/or severe pulmonary hypertension; and (3) a highly calcified mitral annulus. Some of our earlier contraindications, such as older patients and reoperations, have been abandoned as we have determined that MIMVS often provides better outcomes in the circumstances than a conventional sternotomy.

**Preoperative planning**

Today, patient evaluations are similar to standard ones for those undergoing sternotomy MV surgery. However, a major evaluation criterion is related to cannulation and perfusion strategies for individual patients. Computed tomography (CT) scanning and/or MRI studies best evaluate the descending aorta and peripheral vasculature. As endoballoon aortic occlusion with retrograde perfusion may be dangerous in the presence of mobile aortic atheroma and/or diseased ilio-femoral arteries, preoperative imaging is essential in suspect patients.\textsuperscript{33}

Intraoperative transesophageal echocardiography (TEE) now has become standard for planning of any MV repair. Over the past few years we have relied on intraoperative 3D-TEE to determine detailed valve and annular structure and pathology. This modality has enhanced our planning of all MV repairs. By TEE we always measure $P_1$, $P_2$, and $P_3$ leaflet scallop lengths as well as that of the anterior leaflet. We also define the location
and direction of all regurgitant jets to determine which MV segments needs a repair. Also, ideal post-repair leaflet lengths that will provide optimal coaptation can be predicted. In addition, preoperative topographic MV models can be synthesized and help us define leaflet regions that need reconstruction. Recently, we have paired this precise imaging with simple repair techniques. By defining precisely abnormal leaflet coaptation sites from dynamic echo studies, surgeons have been able to abandon many complex repair techniques of the past. Simplified techniques now include limited triangular and posterior leaflet “haircut” resections,\textsuperscript{34} the “American Correction,”\textsuperscript{35} folding plasties, and chordal replacements with polytetrafluoroethylene (PTFE) neochords.\textsuperscript{36}

**Anesthesia and patient position**

After positioning the patient supine, intubation is performed using a double lumen endotracheal tube. Alternatively, a single lumen tube with a bronchial blocker can be used to deflate the right lung. Thereafter, the TEE probe is passed to the level of the left atrium. For superior vena caval drainage a 15 or 17 Fr thin-walled Bio-Medicus cannula (Medtronic, Minneapolis, MN) is passed into the right internal jugular vein via the Seldinger technique and under TEE guidance. Thereafter, a Swan-Ganz pulmonary artery catheter is inserted either into the subclavian or internal jugular vein (using a “double-puncture” method) (Figure 8.1). To monitor adequate limb perfusion during cardiopulmonary perfusion, oxygen saturation sensors are placed on each leg and levels measured using the

![Figure 8.1](image)  
*Figure 8.1* Neck cannulation using double-puncture technique. SGC, Swan-Ganz catheter.
Invos’ System (Somanetics Inc., Troy, MI). When arterial oxygen saturations fall significantly in the cannulated leg, we pass either a 5 Fr catheter or 14-gauge angiocatheter over a guidewire into the distal femoral artery. Thereafter, it is attached to an arterial shunt that originates from the perfusion circuit. For the remainder of the operation, patients are rotated into a semi-left lateral decubitus position (30°) as shown in Figure 8.2.

**Cardiopulmonary perfusion and myocardial protection**

Typically, the right femoral artery and vein are used for peripheral cannulation. To facilitate arterial cannulation, diagnostic catheterizations should be performed via the left femoral artery. A 2-cm oblique incision is made over the femoral vessels. To minimize lymphocele formation, only the anterior vessel surface is exposed after minimal dissection. Adventitial purse-string sutures (4-0 Prolene, Johnson & Johnson, Piscataway, NJ) are placed in each vessel near the inguinal ligament. After adequate heparinization, 17–19 Fr arterial and 21 Fr venous Bio-Medicus cannulas (Medtronic, Minneapolis, MN) are positioned using the guidewire technique under TEE guidance. In corpulent patients, cannulas can be tunneled through the subcutaneous tissue to allow vessel entrance at a 45° angle. If the angle is too acute, entry is difficult and the potential for vessel disruption or dissection of the posterior wall is increased. After appropriate positioning of the cannulas, cardiopulmonary perfusion can be instituted. For patients with severe peripheral vascular disease, either axillary arterial or direct ascending aortic cannulation (second intercostal space) should be used to maintain antegrade perfusion. For axillary cannulation, a 10-mm woven graft is anastomosed to the artery using a 5-0 Prolene suture (Figure 8.3). For cardiac protection, cold blood cardioplegia is infused into the ascending aorta every 15 minutes through a long dual-lumen cardioplegia/root vent catheter. This is
positioned in the proximal ascending aorta through the access incision and secured with a pledgeted 4-0 PTFE suture.

For cardiac arrest, we most often use the Chitwood transthoracic aortic cross-clamp (Scanlan International, Minneapolis, MN). This clamp is passed into the thorax through a small second intercostal space incision placed near the posterior axillary line. The posterior tine of the clamp is passed through the transverse sinus and behind the aorta. Care must be taken to avoid injury to the right pulmonary artery, the left atrial appendage, or left main coronary artery. Alternatively, the balloon Endoclamp™ system can be used (Edwards Lifesciences, Irvine, CA). This device obviates the need for placement of an aortic cardioplegia catheter and avoids conflicts between a transverse sinus cross-clamp and robot left instrument arms. This method is a very good option for reoperations. It avoids the need for aortic exposure and possible injury to pre-existing bypass grafts. However, it is an expensive technology and requires detailed vascular CT/MRI imaging prior to surgery. For retrograde administration of cardioplegia, a percutaneous EndoPlege™ coronary sinus catheter (Edwards Lifesciences, Irvine, CA) can be inserted via the internal jugular vein.

**Incision and port placement**

Our standard MIMVS access is via a 4-cm right mini-incision, placed in the inframammary fold with the chest entered most often through the fourth intercostal space. The right superior pulmonary vein is the landmark for the best intra-atrial access. Thus, chest
entrance may need to be higher or lower than the fourth interspace. If in doubt pre-
operative imaging will help to establish the best entry point. The pericardium should be
opened 3–4 cm anterior to the phrenic nerve after beginning cardiopulmonary bypass
(CPB). Transthoracic traction sutures are placed through the pericardial edges under
tension to distract the heart toward the incision. Care must be taken not to stretch the
phrenic nerve with this maneuver. The interatrial groove does not have to be developed
as much as in conventional sternotomy mitral surgery. However, fat surrounding both
pulmonary veins should be displaced medially to reveal the left atrial margin. To dis-
place intercardiac air, 14-gauge transthoracic angiocath is inserted for continuous CO₂
thoracic insufflation.

The planning of non-robot-assisted MIMVS is very similar to our robotic operation.
However, for da Vinci™ robotic operations, the instrument arms are deployed through
ports placed in the second and fifth interspaces most frequently. The HD-3D endoscope
can be placed either through the access incision, or through a separate port placed in the
same interspace as the access incision. For left atrial retractor deployment, a fourth port
should be introduced at a point over the right pulmonary veins in the third intercostal
space (Figure 8.4).

Figure 8.4 Da Vinci™ robotic surgical system deployed.
Mitral operation

Using either long-shafted or da Vinci™ robotic instruments, mitral operations are performed using similar techniques as traditional operations. However, suture placement and management are different and new skills to manage these issues must be acquired. Repair techniques have been simplified as already described here. The use of PTFE neochords and limited leaflet resections has both facilitated and made MIMVS more reproducible. After incomplete left atriotomy closure, limiting pump venous return while ventilating both lungs expels air. The atrial closure is completed as the last air is removed. With aortic root vent maintained on suction and the right coronary origin compressed, the cross-clamp is removed. Some prefer to leave a left ventricular vent across the MV until all cardiac air absence is confirmed by TEE. Before weaning from CPB, a temporary bipolar right ventricular pacing wire should be placed on the diaphragmatic surface of the heart. After separation from CPB, a complete TEE study should be done to evaluate prosthetic implantation and/or repair integrity. We routinely return to CPB to remove the aortic root vent and secure the purse-string suture. Once satisfied both with the operative result and hemodynamic stability, protamine is given and is followed by cannula removal. Two small chest tubes are placed through port incisions, and the access incision closed.

References


Chapter 9

Surgical therapy for heart failure

Stephen Westaby

Introduction

The clinical syndrome of congestive heart failure affects 23 million people worldwide, 5 million in North America and 7 million in Europe. Heart failure is the final pathway for many diseases that affect the myocardium. Successful intervention in acute coronary syndromes, together with improved management of idiopathic dilated cardiomyopathy and dysrhythmia provide an ever-increasing number of advanced heart failure patients spread over a wide age range. Young adults with surgically palliated congenital heart disease enter the lower end of the spectrum. In Western countries coronary artery disease is responsible for about 70% of patients with idiopathic dilated cardiomyopathy and valvular heart disease accounting for 15%. The remainder have hypertension-related restrictive cardiomyopathy. Since 10% of patients older than 65 years suffer systolic left ventricular dysfunction, the numbers with heart failure will double within the next 25 years. The major component of healthcare costs is generated by repeated hospital admissions to escalate medical treatment and palliate intolerable levels of breathlessness and fatigue. This amounts to 2% of the healthcare budget in Western countries.

Ten percent (10%) of heart failure patients are categorized as Stage D (New York Heart Association (NYHA) Class IV) with advanced structural heart disease and marked symptoms at rest despite detailed medical or cardiac resynchronization therapy. The symptoms result from two pathological processes: raised left ventricular end diastolic pressure (LVEDP) results in pulmonary congestion and breathlessness, while decreased systemic blood flow triggers numerous cytokine and humoral responses causing salt and water retention and fatigue. The patients become progressively more dependent on hospital admissions for symptomatic stabilization and outpatient nursing for palliative care. Currently there are more than 300,000 Stage D patients in the USA, 60,000 in the UK, and 2.2 million worldwide. Twenty percent are under 65 years of age. Stage D heart failure carries a grim prognosis. In the CONSENSUS Trial, half of the patients in the control arm had died within 6 months. In the REMATCH study, only 8% of patients in the medically treated group were alive at 2 years.

For end-stage patients, cardiac transplantation provides the benchmark for increased longevity and symptomatic relief. However, the vast majority of Stage D patients are over 65 years of age or are referred with established comorbidity which precludes
transplantation. For those patients less than 65 years of age (60,000 in the USA and 12,000 in the UK) there are only around 2,500 and 190 donor hearts per year, respectively. In his paper “The Evolving Challenge of Heart Failure Management” Adamson describes heart transplantation as an “epidemiologically insignificant intervention.” Thus in the global context, transplantation is recognized as irrelevant. Accordingly, the development of non-transplant surgical options is a clear priority.

**Pathology-based heart failure surgery**

Non-transplant surgery is a specialty in itself. The goal of both medical and surgical treatment is to arrest or reverse progression of the adverse cardiac remodeling process. Left ventricular shape and volume are important predictors of survival. In both ischemic and idiopathic-dilated cardiomyopathy, increased chamber sphericity and the onset of mitral regurgitation are markers of worse prognosis (one-year mortality 54–70%). Mitral regurgitation occurs secondary to altered left ventricular geometry, papillary muscle dysfunction, and annular dilatation. Volume overload causes progressive left ventricular dilatation, worsening mitral regurgitation, and decreased survival. Patients with a left ventricular ejection fraction (LVEF) of less than 30% have a 5-year survival of only 54% when left ventricular end systolic volume index (LVESVI) exceeds 150 mL/m². An evidence-based approach to treatment is achieved using detailed investigation to identify the cause of heart failure and the extent of structural and functional abnormalities. The team must then establish whether there is a lesion amenable for surgical repair, whether dysfunctional myocardium is recoverable, or in the event of neither of these, whether complete cardiac replacement or mechanical left ventricular assist are feasible.

It is always preferable to repair rather than replace the diseased heart. All Stage C and D patients should be jointly assessed by a multidisciplinary heart failure team including the surgeon. Significant comorbidity, particularly renal and hepatic status, must be taken into consideration before embarking on a particular procedure. The surgeon’s role is to determine which operation or combination of surgical procedures best suits an individual and whether the operation can be undertaken with acceptable risk.

**Ischemic cardiomyopathy**

The ischemic cardiomyopathy ventricle contains microenvironments of necrosis or scar tissue together with viable myocardial cells in varying proportions. When dyskinetic myocardial scar occupies more than 20% of the total left ventricular mass (as occurs in 40% of transmural myocardial infarctions), the left ventricle progressively enlarges with the onset of symptomatic heart failure. When more than 50% of the myocardium is impaired, increased wall tension causes subendocardial ischemia, which precipitates left ventricular failure. The relationship between the extent of myocardial infarction, degree of left ventricular dysfunction, and late mortality was defined by Yoshida and Gould. They showed that a myocardial infarction more than 23% of left ventricular circumference reduced LVEF less than 45% with a 3-year mortality rate exceeding 40%. This
contrasted with less extensive myocardial infarction where 3-year mortality was only 5%. Patients with an LVEF of more than 40% have modest annual mortality rate (<10%) whereas those with an LVEF of more than 30% have annual mortality rates more than 25%. In patients with an LVEF of 15–40%, there is an almost linear relationship between LVEF and annual mortality. However, LVEF alone is a poor predictor of mortality in patients with hibernating myocardium. The presence of viable myocardium is an independent predictor of survival and a marker for those with impaired LVEF who are most likely to benefit from coronary revascularization (CABG). The 3-year mortality rate in patients with an LVEF less than 45% and no viable myocardium was 63%, in contrast to 13% for those revascularized with viable myocardium.

Exercise capacity has a poor relationship with LVEF measured by echocardiography at rest. Stress- or exercise-related myocardial ischemia and stunning often result in left ventricular systolic and diastolic dysfunction, elevated LVEDP, and dyspnea with or without angina. If stunning occurs frequently with incomplete recovery of contractile function, this triggers the development of hibernation. Eventually the myocardium may progress from structurally normal recoverable hibernation to the development of abnormal contractile proteins, where recovery is unlikely after CABG. Some patients have moderately increased LVEDP at rest with considerably reduced exercise capacity but only mildly increased heart size on chest X-ray. These patients often have marked ischemic dysfunction in non-scarred parts of the ventricles, which can be helped by revascularization. Others have moderate or severe cardiomegaly, reduced cardiac index, and substantial elevation of right atrial pressure with hepatomegaly and fluid retention. This latter group usually has extensive myocardial scarring, which will not improve with CABG alone.

**Coronary bypass or transplantation?**

The vast majority of patients with ischemic cardiomyopathy are older than 65 years, are smokers with chronic obstructive airways disease, and have peripheral vasculopathy. They often have renal impairment and will never be considered for transplantation. In turn, less than 10% of potential heart transplant candidates (referred as opposed to selected for the waiting list) will eventually receive a donor organ. So which patients benefit from CABG as an alternative?

Studies suggest that as many as 50% of ischemic cardiomyopathy patients referred for cardiac transplantation have hibernating myocardium. It is impossible on the basis of echocardiography or coronary angiography alone to determine which areas of myocardium might benefit from improved perfusion. An indication that segmental and global LVEF will improve after CABG is obtained using imaging methods to provide evidence for myocardial viability. These include contrast enhanced MRI and single photon emission tomography (SPECT) with thallium-210 or technicium-99M perfusion tracers. MRI has the benefit of providing very accurate information about left ventricular volume indices, myocardial wall thickness, and mitral valve function. Heart failure patients who benefit from viability testing include those with suspected coronary disease or dilated
cardiomyopathy under consideration for cardiac transplantation, and those with coronary disease and left ventricular (LV) dysfunction (LVEF <35%) who are asymptomatic or have breathlessness with only mild angina. Viability testing is redundant in patients with unstable angina, post infarction angina, and severe chronic stable angina because CABG is indicated for symptomatic relief.

For ischemic heart failure patients without angina, the combination of good target vessels and more than 25% myocardial viability suggests the potential to benefit from CABG. For those with less than 25% viability, poor target vessels, or in reoperative candidates CABG is unlikely to produce improvement. Other unfavorable patient characteristics include advanced age, female gender, severity of coronary disease, presence of dysrhythmias, and renal impairment.

Useful information regarding patient selection for high-risk revascularization has emerged from transplant centers where many candidates have been diverted for CABG instead. Transplant recipients tended to have longer duration of symptoms, concomitant right heart failure, and a greater incidence of previous CABG. Operative risk in CABG patients was significantly higher for those with LVEDP more than 24 mmHg, low preoperative cardiac output (<2.0 L/min/m²), and for NYHA IV patients. Hospital mortality was 7.1% for CABG patients versus 18.2% in the transplant cohort. Survival for CABG patients was 79% at 6 years versus 69% for the transplant group. Reinvestigation of CABG patients showed a significant decrease in mean pulmonary artery and left atrial pressures. LVEF improved from a mean of 24% to 39% (P <0.001). Others have reported similar findings. Symptomatic relief, quality of life benefit, and improved survival have been reported in these patients.

The value of viability testing was confirmed by Haas in a series of patients with three vessel disease and LVEF less than 35%. Half were operated on the basis of angiographic findings alone while the remainder underwent viability testing. Patients with hibernating myocardium had lower hospital mortality (0% vs. 11.4%), fewer postoperative complications (33% vs. 67%), and rarely experienced low cardiac output syndrome (3% vs. 17%). One-year survival was better (97 ± 8% vs. 79 ± 8%). The LVEF increased from 26% to 35% in those with myocardial viability but was unchanged in those without. Myocardial viability index was the only independent predictor of event free survival. Though CABG may provide better short-term outcome than transplantation, the benefits may be time limited. Luciani showed only 47% of patients with poor left ventricular function (LVEF <20%) to be free from heart failure symptoms 5 years after CABG despite 75% survival at this time.

Despite symptomatic and survival benefit after CABG, the myocardial functional response is unpredictable. Using detailed studies of regional perfusion and contractility, Bax showed improvement in only 70% of stunned segments and 31% of hibernating segments by 3 months after CABG. Haas used intraoperative myocardial biopsy to investigate the time course of functional recovery in ischemic segments. Positron emission tomography was used to distinguish stunned from hibernating myocardium. Hibernation was associated with more severe depression of contractility and incomplete recovery. Disappointingly by one year after CABG only 31% of stunned and 18% of hibernating
segments showed complete functional recovery.\textsuperscript{15} Failure to improve was associated with more severe ultra-structural degeneration in the myocyte. Stunning was present more frequently than hibernation and myocardial morphology determined the degree of functional improvement.

**The role of mitral valve repair and surgical ventricular reconstruction**

Functional ischemic mitral regurgitation follows myocardial infarction with degenerative changes in valve–ventricular interaction. Usually there is no structural disease in the valve leaflets or chordae. Mitral regurgitation affects survival. The Duke University Cardiovascular database reports 3-year post CABG survival rates of 78%, 57%, and 54% for patients with 1+, 2+ and 3 to 4+ mitral regurgitation, respectively.\textsuperscript{16} Mitral valve repair is reserved for patients with grade III or IV mitral regurgitation which causes breathlessness on exertion, orthopnea, and fatigue. The principle indication for mitral repair in ischemic cardiomyopathy is a calculated regurgitant fraction of more than 50% of the forward LVEF. Those with a lesser degree usually respond to CABG alone. There are three main clinical problems which cause mitral regurgitation. First, exercise-induced ischemia may impair papillary muscle function causing mitral regurgitation, pulmonary congestion, and dyspnea. Second, acute myocardial infarction located inferobasally (right coronary or dominant circumflex distribution) can cause sudden posteromedial papillary muscle dysfunction and mitral regurgitation. Acute catastrophic pulmonary edema occur if the papillary muscle tears away from the LV wall. The third, and largest, group comprises those with progressive left ventricular dilatation, chronic mitral regurgitation, and pulmonary hypertension. Though valve surgery has been widely advocated for these patients, the long-term outcome is not as satisfactory as once thought.

Ventricular reconstructive surgery is the successor to left ventricular aneurysmectomy (for full-thickness scar), now that thrombolysis or primary coronary angioplasty limits myocardial infarction before the transmural stage. The scar is then limited to the endocardial surface while the epicardium appears normal through a rim of reperfused muscle. This contrasts with the leather-like appearance of an expanding full thickness scar in a dyskinetic left ventricular aneurysm. As LV size increases, the progressively elevated systolic wall stress accounts for worsening symptoms. Stroke volume and global LVEF gradually decline. When more than 40% of the LV circumference becomes dyskinetic the normal left ventricular end systolic diameter index of 25 mL/m² increases beyond 60 mL/m², a level predictive of cardiac mortality. Once decompensation begins, functional impairment progresses rapidly as does the risk of surgical mortality. For this reason, left ventricular reconstruction surgery should be considered for patients with LVEF less than 30%, mean pulmonary artery pressure more than 25 mmHg, left ventricular akinesia or dyskinesia more than 60%, and left ventricular end diastolic volume more than 250 mL. Most of these patients are already NYHA Class III or IV, despite cardiac resynchronization therapy and maximum drug treatment.
The aim is to reduce LV chamber size by around 30% below baseline, restore the natural elliptic LV shape, and decrease wall stress.\textsuperscript{17} At surgery, the ischemic cardiomyopathy ventricle has a globular shape with a veneer of normal epicardium on the anterolateral surface. The surgeon incises through the akinetic muscle to access and excise the scar. The reconstruction is then begun using a continuous suture passed along the border between endocardial scar and healthy septal and lateral myocardium. The suture is tied in such a way as to restore the curvature of the anterolateral LV wall. A small patch of Dacron is used to close the residual defect. By excluding the scar, progressive (adverse) ventricular remodeling is stopped and LV ejection fraction improves by 10–15%. The procedure is supplemented by CABG and mitral valve repair where necessary.

In contrast to the slow and unpredictable improvement in contractility after CABG, left ventricular reconstruction (± mitral repair) produces an immediate result. In a large series by Dor, LVEF improved from 17% to 37%.\textsuperscript{17} Hospital mortality saw a 19% improvement with LVEF, and this was maintained with a late mortality of only 10% at 5 years. Following Dor’s lead, an international cooperative study investigated the outcomes following LV reconstruction on a multicenter basis. Again, the baseline LVEF of 28% ± 10% and mean LVESVI of 110 mL/m\textsuperscript{2} improved to an LVEF of 39% ± 12% with a reduction in LVESVI to 68 mL/m\textsuperscript{2}.\textsuperscript{18} In addition to reconstruction of the ventricle, 96% of the patients underwent CABG and 23% mitral valve repair.

Whether LV reconstruction ± mitral repair adds to CABG alone can only be answered by a large randomized trial in ischemic cardiomyopathy patients. The Surgical Treatment of Ischemic Heart Failure (STICH) was performed on a multicenter international basis but surprisingly did not demonstrate survival or quality of life benefit over and above that achieved by CABG alone.\textsuperscript{19} Those already convinced of the benefits of LV reconstruction criticized the conduct of the trial and the efficacy of the operations performed by low volume surgical centers. The benchmark for LV volume reduction is 30%, whereas the mean for STICH was only 19%. Nevertheless, it is possible that even adequate LV volume reduction may not produce symptomatic or survival benefit because the operation disturbs the three-dimensional architecture of the LV. Loss of the heart’s coordinated helical structure may disturb diastolic function (LV filling) and offset the improvement in systolic function.

Significant doubt has been cast about the efficacy of both mitral valve repair and left ventricular remodeling surgery in ischemic cardiomyopathy. A landmark paper from the Cleveland Clinic provides the best aid to decision-making using prognostic factors for the individual patient.\textsuperscript{20} A 10-year cohort of 1,468 patients subject to the operations described earlier or listed for transplantation had the following outcomes. One-, five-, and nine-year survival rates were as follows: CABG alone 92%, 72%, and 53%; CABG with mitral repair 88%, 57%, and 34%; CABG with ventricular reconstruction 93%, 76%, and 55%; and listing for cardiac transplantation 79%, 66%, and 54%. Coronary bypass alone and listing for transplantation appeared to maximize 5-year survival.\textsuperscript{20} This appears to support the skepticism surrounding other procedures.
Cardiac transplantation

Clinical cardiac transplantation began with Barnard’s landmark operation in 1967 then almost disappeared through limitations in early immunosuppression. With persistence and refinement of antirejection therapy, this compelling procedure emerged as an effective solution for a few highly selected patients without significant comorbidity. Hospital survival has improved from around 75% in the early 1980s to 85% by 2000. Ten-year survival is around 50%. Currently the number of donor hearts is around 2,500 per annum in the United States and 190 in the UK. This contrasts with approximately 100,000 and 12,000 end-stage heart failure patients, respectively, under the age of 65 in these countries. Clearly the scarce donor hearts should be reserved for those most likely to benefit in life expectancy and quality of life. Young patients with congenital heart disease or idiopathic dilated cardiomyopathy fit this category. While arteriopathies with ischemic heart disease comprise the largest cohort of potential candidates, most prove ineligible through heart failure comorbidity or advanced age.

Left ventricular assist devices

Ventricular assist devices were introduced by DeBakey in the late 1960s in an attempt to salvage surgical patients who could not be weaned from cardiopulmonary bypass (CPB). With increasingly sophisticated bioengineering, the original temporary external pneumatic blood pumps have evolved into miniaturized fully implantable electrical devices suitable for the long-term treatment of chronic heart failure. Experimental evidence showing that pulse pressure is not necessary in the systemic circulation of large mammals allowed the development of small continuous flow devices. Mechanical blood pumps are now capable of sustaining full systemic or pulmonary blood flow against physiological and, in some cases, pathological levels of vascular resistance. While left (LVAD), right (RVAD), and biventricular (BIVAD) assist devices are possible options, 85% of acute and 99% of chronic heart failure patients receive only an LVAD. Currently, total artificial hearts (biventricular) are still used in a small number of cardiac transplant candidates.

Temporary mechanical circulatory support

Temporary extracorporeal ventricular assist devices (VADs) are used for “bridge to recovery” and for bridge to transplantation when the blood type suggests that the waiting time will be short (days to weeks). Recovery is followed by weaning from, and removal of the device. Typically, the patient has acute cardiogenic shock after cardiac surgery, acute inflammatory cardiomyopathies, or myocardial infarction. Criteria for beginning temporary circulatory support include a cardiac index less than 2.0 L/min/m², systolic blood pressure less than 90 mmHg, and pulmonary capillary wedge pressure more than 20 mmHg together with biochemical evidence of poor tissue perfusion (increasing serum creatinine and liver transaminases). The patient is oliguric and acidic with cool extremities and obtunded mental state. When receiving maximum medical treatment, these are indices of impending death.
Evidence-based patient selection is crucial and numerous ethical considerations influence the decision to implant the VAD.\textsuperscript{24} The most important of these is the likelihood of a successful outcome in the face of device costs and need for prolonged intensive care. The presence of irremediable renal, hepatic, or respiratory failure is an absolute contraindication to initiating support. Established stroke and sepsis are relative contraindications. Patients older than 70 years have decreased survival, though the potential for weaning is not affected by age. Risk stratification models show preimplantation mechanical ventilation, urine output less than 30 mL/hour, preoperative central venous pressure more than 16 mmHg, hepatic dysfunction (prothrombin time >16 seconds) and increasing serum creatinine and bilirubin levels to be adverse prognostic risk factors. Experience shows extracorporeal pulsatile versus non-pulsatile VADs, and extracorporeal membrane oxygenation to provide similar outcomes.

In cardiac surgical patients the time of beginning VAD support has an important effect on outcome. Early deployment based on predictive models (derived from hemodynamic parameters and level of intraoperative inotropic support) provides improved likelihood of survival to hospital discharge.\textsuperscript{25} When VAD insertion occurs within 3 hours of the first attempt to wean from CPB, then 60% of patients can be separated from VAD support with 45% hospital discharge rate. This contrasts with 27% VAD separation and 7% discharge rate when VAD deployment is delayed more than 3 hours after CPB. Delay also increases the need for biventricular support. An episode of cardiac arrest before VAD insertion decreases survival from around 45–7%. If the patient was weaned from CPB on two high dose inotropes, hospital mortality is 42% versus 80% when three high dose inotropes were required.

**Long-term circulatory support**

“Destination therapy” is an increasingly realistic alternative to cardiac transplantation and a lifeline for the vast majority of heart failure patients rendered ineligible for transplantation through common heart failure comorbidities. The aims of long-term mechanical support are clear. The first is to provide symptomatic relief for the severely debilitated heart failure patient. The second is to extend survival, aiming for at least 5 years of good-quality life. The third objective is cost-effectiveness, by reducing the need for recurrent hospital admissions. The clinical objectives have already been achieved by the new miniaturized rotary blood pumps, but economic considerations delay the final aim of making LVAD technology available to the target population. Three developments have set the scene for long-term support.

First, considerable knowledge and expertise was gained from prolonged bridging to transplantation because of limited donor heart availability. The LVAD gradually reverses the chronic heart failure syndrome, relieves breathlessness, and fatigue and in most cases restores the patient to NYHA Class I. Mechanical unloading improves native heart function, particularly in idiopathic dilated and inflammatory cardiomyopathies.

Second, the REMATCH trial demonstrated improved survival with LVAD use compared with medical management of advanced heart failure. The first-generation pulsatile
HeartMate I LVAD dramatically reduced mortality by 48% over 2 years in non-transplant eligible patients. LVADs were subsequently approved for destination therapy by the Food and Drug Administration in 2002. Nevertheless, survival remained suboptimal in LVAD patients due to deaths from mechanical failure or infection.

Third, the new axial flow and centrifugal pumps (providing continuous as opposed to pulsatile blood flow) have now been shown to be as effective but safer than the large first-generation devices which provide stroke volume and pulse pressure. These miniaturized LVADs are silent, less obtrusive, easier to implant, and more user-friendly. Patients are discharged from hospital within a few weeks and pursue an active life in the community.

**Improvement in native heart contractility**

The failing heart beats more than 120,000 times a day pumping around 7,000 L of blood against an increasing afterload. As the heart dilates ventricular wall tension, myocardial energy, and oxygen consumption (MVO$_2$) increase, while subendocardial blood flow decreases. LVAD deployment has two principal benefits. First the failing ventricle is unloaded thereby promoting functional improvement or rarely recovery in dilated cardiomyopathy patients. Second systemic blood flow is sustained at physiological levels to preserve vital organ perfusion.

Our own clinical experience suggests that rotary blood pump patients experience better survival when native heart contractility improves. There are several potential explanations for this. Cardiac output is boosted by the native heart and there is less propensity for intraventricular thrombus formation when contractility and segmental wall motion improves. Pulsatility generated by the native left ventricle improves coronary blood flow and there is less risk of coronary thrombosis in obstructed vessels.

For many years it has been recognized that ventricular unloading with a blood pump eliminates left ventricular wall stress triggering reversal of the heart failure remodeling process at cellular and molecular level. Reverse remodeling encompasses regression of myocyte hypertrophy, improvement in left ventricle geometry, and resolution of many genetic and molecular mechanisms responsible for heart failure. While complete functional recovery and LVAD removal are rare, early studies showed around 50% of patients with idiopathic dilated cardiomyopathy and 17% with ischemic cardiomyopathy to manifest substantial improvement in cardiac function. The shorter the duration of heart failure, the greater the likelihood of improvement. Others have shown initial improvement in LVEF over 30 days but subsequent deterioration virtually to baseline by 120 days in both idiopathic dilated cardiomyopathy and ischemic cardiomyopathy patients. The shorter the duration of heart failure, the greater the likelihood of improvement. Left ventricular dimensions followed the same pattern with evidence for mild ventricular redilatation during longer periods of support. In contrast to the changes in LV function, right ventricular function improves continuously presumably because the right ventricle is indirectly unloaded through reduction in pulmonary artery pressure and right ventricular recovery occurs over a longer time trajectory than LV recovery.
In ischemic cardiomyopathy the potential for functional improvement is limited by impaired myocardial perfusion and areas of scar, hibernation, and stunning. Without substantial improvement in myocardial blood flow, functional recovery is unlikely. This is the group where an LVAD together with myocardial cell therapy holds the greatest promise. Mesenchymal stem cells appear to convey reparative processes by angiogenesis, extracellular matrix stabilization, and endogenous stem cell recruitment. The objective is to improve capillary growth and vascularity in hibernating myocardium and thereby boost contractility. Meanwhile LVAD unloading promotes the genetic and cellular mechanisms of reverse remodeling in the ventricle as a whole.

Current evidence suggests that intramyocardial injection of bone marrow stem cells is a more effective method of delivery than intracoronary infusion. We have therefore undertaken a dual approach by implanting the LVAD to remove wall stress and injecting autologous bone marrow stem cells to areas of carefully delineated hibernating myocardium. In two innovative ongoing studies, the University of Minnesota and the University of Michigan are employing direct intramyocardial delivery of bone marrow derived mononuclear cells in patients undergoing bridge to cardiac transplantation. Tagged bone marrow stem cells or placebo are injected directly into the territory of the left anterior descending coronary artery and marked with titanium surgical clips. Myocardium from the core of the left ventricle obtained at the time of LVAD implantation will then be compared with myocardium marked with clips from the explanted heart after the transplant. Both ischemic and non-ischemic patients are included in this study.

**Maximizing survival in high-risk cardiac surgery**

The mean age and risk profile of patients referred for cardiac surgery is constantly increasing. Surgeons are now inclined to accept high-risk patients because interventional cardiology provides less invasive alternatives for an overlapping patient cohort. As risk profile increases, so does hospital mortality. A survey of 8,641 patients who underwent coronary artery bypass operations in New England showed an overall mortality of 4.48% of which 65% could be directly attributed to postcardiotomy myocardial failure. In the PURSUIT trial which randomized coronary bypass patients with unstable angina to a glycoprotein IIb/IIIa inhibitor or placebo, the 7-day mortality or myocardial infarction rate was 22.3% in almost 700 patients in the control arm. A collective review of 279 dialysis dependent coronary bypass patients reported a 12.2% hospital mortality. Similarly, the Mayo Clinic Group reported a 14% perioperative mortality for aortic valve replacement patients with a LVEF less than 35% and a borderline transvalvular gradient. Intraoperative myocardial injury remains prevalent in the increasingly elderly surgical population because tolerance to ischemia is reduced in aged myocardium.

Patients who are difficult to wean from CPB and those who subsequently deteriorate into a low cardiac output state have mortality rates of between 50% and 80%. In established cardiogenic shock, conventional treatment with inotropes, the intra-aortic balloon pump (IABP) or temporary circulatory support devices has not substantially improved
survival. In an analysis of risk factors and outcomes for postcardiotomy mechanical support in 19,985 Cleveland Clinic patients, 0.5% received circulatory support with overall survival of 35%. Included were patients who were converted to the HeartMate I implantable system and bridged to transplantation with 72% survival. In the absence of the transplant option, more innovative circulatory support strategies are required to improve survival in the postcardiotomy setting.

**Prediction of postoperative low cardiac output syndrome**

Coronary and valve patients with very poor ventricular function often have the most to gain from a successful operation. This is also the group at greatest risk from post-ischemic myocardial dysfunction. Because risk-scoring systems provide insufficient weight to very poor ventricular function, some patients may be declined surgery on the grounds of elevated risk. Paradoxically, refined operative techniques and myocardial protection should widen the availability of surgical repair to high-risk groups. Improved processes are needed to identify very high-risk patients and improve their survival.

Poor LVEF is the most important index of mortality because these patients have less margin for recovery from postoperative stunning.

**Management of patients at risk from low cardiac output syndrome**

Three categories of patient are at substantial risk. First are those who present urgently for surgery, already in cardiogenic shock, often with a complication of myocardial infarction or infective endocarditis. Second is the group submitted for high-risk non-transplant heart failure surgery with LVEF less than 20% together with renal impairment or aortoiliac disease, which precludes the use of an IABP. The third category includes patients who sustain an unanticipated negative event during surgery, which may prejudice separation from CPB.

Conventional postcardiotomy supportive treatment begins with inotropic drugs though prolonged use may augment perioperative ischemic injury. Drugs commonly employed are dopamine, dobutamine, milrinone, and epinephrine. These agents increase stroke work, left ventricular wall tension, and myocardial oxygen consumption, thus depleting energy reserves. High doses may cause endocardial necrosis and impaired diastolic function with an overall negative effect on myocardial recovery. Because of this an IABP or circulatory support system are preferable for patients with moderate to severe hemodynamic compromise.

The principal effects of the IABP are to reduce left ventricular afterload (and MVO₂), improve diastolic coronary blood flow and thereby enhance subendocardial perfusion in patients with elevated LVEDP. The IABP itself does not substantially increase systemic blood flow. Transoesophageal echocardiography indicates that peak diastolic coronary flow velocity increases by a mean of 117% with an increase in mean flow velocity integral of 87%. Blood flow velocities of × 1.5 to × 2.0 baseline have been measured in
the stenosed left anterior descending coronary arteries of patients supported by an IABP. Factors that determine the effectiveness of IABP support include balloon volume, location in the aorta, rate of inflation, and deflation and synchrony relative to the events of the cardiac cycle. The optimal inflation timing has been shown to be slightly preceding the diastolic notch with deflation bordering on isovolumetric systole. Modern IABP controllers are designed to optimize timing during sinus rhythm and in the presence of cardiac arrhythmias. The IABP also has the capacity to improve right heart function through ventricular interdependence mechanisms and augmentation of right coronary blood flow.

In a large series of IABP patients from the Massachusetts General Hospital, multivariate predictors of death in medical and surgical patients included: (a) IABP insertion in the operating room or intensive care unit; (b) transthoracic insertion; (c) advanced age; (d) procedures other than coronary bypass grafting; or (e) percutaneous transluminal coronary angioplasty and insertion for cardiogenic shock. In this series predictors of death were great age, mitral valve replacement, prolonged CPB, urgent or emergency operation, preoperative renal dysfunction, complex ventricular dysrhythmias, right ventricular failure, and emergency resumption of CPB. In the Benchmark Registry and Society of Thoracic Surgeons (USA) National Databases IABP procedures were initiated preoperatively in 52.4% and 63.5%, respectively, of all IABP procedures. Preoperative insertion was associated with a mortality of 18.8–19.6%, intraoperative insertion 27.6–32.3%, and postoperative insertion 39–40.5%. Thus, there is a consensus of opinion that preemptive use of the IABP reduces mortality. The absolute risk reduction is around 7%.

Vascular complications are the most frequent cause of morbidity for IABP patients with rates between 9% and 36%. Femoral cannulation may be complicated by leg ischemia caused by mechanical occlusion, thrombosis, or embolism. Factors predisposing to leg ischemia include female gender, diabetes mellitus, and pre-existing peripheral vascular disease. Possible injuries to the aorta include intramural hematoma, dissection, arterial perforation, and arterial thrombus and embolism. The IABP may also cause mesenteric ischemia or acute pancreatitis probably as a result of athero-emboli in the celiac axis. Neurological complications are much less frequent than vascular complications but paraplegia can occur secondary to aortic dissection or adventitial hematoma producing spinal cord infarction. Stroke has occurred after balloon rupture and cerebral helium embolization. Rupture may result in balloon entrapment because blood leaks into the system and forms clots, which block full deflation.

**Outcome after circulatory support for postcardiotomy cardiogenic shock**

Pae and colleagues from the Pennsylvania State University reviewed combined registry data on the use of first-generation temporary LVADs between 1985 and 1990. Nine hundred and sixty-five patients were treated for postcardiogenic shock, of which 45% were weaned from the system and 25% were discharged from hospital. Notably, 90% of patients who survived to leave hospital were weaned from the pump within one week. Those
requiring univentricular support alone fared better irrespective of whether pulsatile pneumatic or non-pulsatile centrifugal pumps were used. The patient age group of over 70 years was the principal determinant of mortality. Irrespective of multiple complications including bleeding, stroke and renal failure, patients who left hospital had 2-year actuarial survival of 82% and 86% were in NYHA Functional Class I or II. In rare incidences of device dependency (4.5%), those patients without contraindications to transplantation were sustained until a donor organ became available. Of the transplanted patients, 62% were discharged from hospital.

Golding and colleagues from the Cleveland Clinic reported a 12-year experience of 91 patients supported with a centrifugal blood pump after failure to wean from CPB.\textsuperscript{53} The mean age of postcardiotomy patients was 54.8 years and mean duration of support 3.56 days (range 1 hour to 19 days). Sixty-two percent (62%) of the patients were successfully weaned, but only 25% survived to leave hospital. Patients with biventricular failure and renal failure had worse late outcomes.

DeRose and colleagues from the Columbia Presbyterian Medical Center, New York adopted a policy of early implantation of the ThermoCardioSystems HeartMate XVE LV AD for patients who developed circulatory failure after high-risk cardiac surgery.\textsuperscript{54} In a 4-year period, 12 patients received this LVAD for postcardiotomy cardiogenic shock following coronary artery bypass grafting. Of the 12 patients included in the report, one recovered sufficiently for device explantation, while 9 of the remaining 11 patients (82%) survived to undergo transplantation with successful hospital discharge in each case.

From these and other reports, it is clear that less than one third of patients who suffer postcardiotomy heart failure, refractory to the use of the IABP can be salvaged after the onset of cardiogenic shock. Device-related adverse events, particularly bleeding and infection, have so far precluded widespread prophylactic deployment of temporary LVADs for high-risk patients in order to prevent cardiogenic shock.

**Elective transfer from cardiopulmonary bypass to centrifugal blood pump support**

The decision to pre-emptively deploy an LVAD must balance safety with efficacy. In order to improve outcome in borderline survival situations following high-risk cardiac surgery, the Oxford Group decided to wean directly from CPB to a new temporary centrifugal blood pump designed to reduce bleeding and thromboembolic complications.\textsuperscript{55}

The Levitronix Centrimag short-term VAD is an extracorporeal system composed of a single use centrifugal blood pump, a motor, a console, a flow probe, and a tubing circuit. The device is comprised of a bearingless motor, which combines the drive, the magnetic bearing, and the rotor function in a single unit. This device can produce flows up to 10 L/minute under normal physiological conditions with a priming volume of 31 mL. Initial European clinical trials in postcardiotomy cardiogenic shock have been encouraging over mean support periods of 2 weeks, with the longest at 64 days. Overall 30-day mortality was 50%, which compares favorably with that reported for other devices. The
system is reliable and versatile so that it can be quickly implemented in situations of rapid deterioration. Device mechanical reliability and relatively low complication rates make the Levitronix pump safe to use for patients who need time for evaluation for cardiac transplantation or a longer-term device.

For elective transfer from CPB to centrifugal blood pump support, the patients at highest risk of postcardiotomy cardiogenic shock are selected before surgery. Candidates may have chronic left ventricular dysfunction with LVEF less than 20%, recent acute myocardial infarction, impaired renal function, or aortoiliac disease precluding IABP use. LVAD implantation is undertaken during a 30-minute reperfusion time before discontinuation of CPB. Conduits for the inflow and outflow cannulas are used to improve the safety of decannulation. A tube of descending aortic homograft (8 cm × 10 mm diameter) is sewn to an incision at the junction of the superior pulmonary vein with the left atrium. Through this conduit is introduced the 32 F right-angled wire reinforced venous cannula into the center of the left atrium. Ligatures are placed around the homograft tube to retain the inflow cannula in position. The distal end of the venous cannula is brought through the skin below the sternotomy wound and then filled by raising left atrial pressure. A Dacron polyester fabric graft (8 mm) is then sewn to the ascending aorta with a side clamp. The straight 22 F arterial inflow cannula is inserted through this graft, secured into place by ligatures and brought out through the skin adjacent to the venous cannula. The system is filled during reperfusion and de-airing of the native heart. The patient is then weaned directly from CPB onto LVAD flow to provide between 3 and 4 liters per minute. Antegrade cardiac ejection continues to provide systemic pulsatility. Combined output from the device and the native left ventricle is around 3.0 L/min/m².

Transoesophageal echocardiography is used to confirm the position of the inflow cannula and the efficacy of de-airing.

After protamine administration, the sternotomy wound is closed to allow extubation during support. To minimize bleeding, no anticoagulation is given for 12 hours. Once the chest tube drainage is less than 50 mL/hour heparin infusion is given to provide an activated partial thromboplastin time ratio of 1.5–2.5. For recovery after ischemic arrest the support duration is usually less than 7 days. In this time frame, the Levitronix pump is reliable, safe, and effective. It is readily managed by nursing staff and easily portable. Reoperation for bleeding and decannulation problems are avoided by the use of the conduits.

With a view to explant, myocardial function is assessed daily with the pump flow turned down to 2.0 L/min/m². After sustainable improvement in myocardial function has been achieved, the patient is returned to the operating room, the pump is switched off and the cannulas are withdrawn. The grafts are ligated close to their insertion to prevent thrombus formation. As part of the step-down process, an IABP is used for a further 24–48 hours.

To date the Levitronix Centrimag pump has been used in thousands of patients, of whom around 45% of cases have been salvage postcardiotomy support with a mean of 9 days and 53% survival. It is likely that the 47% mortality could have been reduced substantially by anticipating postoperative deterioration and using the blood pump electively to prevent cardiogenic shock during the duration of reversible post-ischemic stunning.
References


Introduction

Atrial fibrillation (AF) is the most common of all cardiac arrhythmias and accounts for nearly one-third of all hospital admissions due to heart rhythm irregularities. \(^1\) AF affects nearly 4.5 million people in the European Union and 2.2 million people in the United States. The prevalence of AF increases with age, afflicting 4% of the population over 60 years old and nearly 9% of persons 80 years and older. The most serious complication of AF is thromboembolism and resultant stroke; however, significant morbidity and mortality also result from hemodynamic compromise due to loss of atrial contraction, exacerbations of congestive heart failure from atrioventricular asynchrony, and tachycardia-induced cardiomyopathy. As a result, atrial fibrillation has an enormous socioeconomic impact,\(^3\) and with the aging population in the United States, AF is expected to become an even larger public health burden in the future. A recent study predicted that the number of Americans diagnosed with AF will grow to over 10 million by the year 2050.\(^4\)

The available medical treatments for atrial fibrillation have many shortcomings. Antiarrhythmic drug therapy is complicated by significant side effects and may necessitate warfarin for anticoagulation.\(^1,5\) Moreover, these drugs have limited efficacy. Rate control strategies, conversely, leave the patient in AF and therefore do not address the impaired hemodynamics seen with this arrhythmia.

The Cox-Maze procedure

The first effective surgical procedure for atrial fibrillation was introduced clinically at Washington University in St. Louis in 1987 by Dr. James Cox.\(^6-8\) This operation, now known as the Cox-Maze procedure, was originally developed to interrupt the multiple macro-reentrant circuits that were felt to develop in the atria, thereby precluding the ability of the atrium to flutter or fibrillate. Unlike previous procedures, the Cox-Maze procedure successfully restored both aortic valve (AV) synchrony and sinus rhythm, thereby significantly reducing the risk of thromboembolism, stroke, and hemodynamic compromise.\(^9\) The operation was comprised of a pattern of surgical incisions across both the right and left atria, which were placed so that the sinoatrial node could still direct the propagation of the sinus impulse (Figure 10.1). This allowed for most of the atrial
myocardium to be activated, resulting in preservation of atrial transport function in most patients.\textsuperscript{10}

The first versions of the Cox-Maze procedure were complicated by late chronotropic incompetence resulting in a high incidence of pacemaker implantation, as well as significant surgical complexity. The Cox-Maze III, the third design iteration, became the gold standard for the surgical treatment of AF (Figure 10.2).\textsuperscript{7,11} Although the Cox-Maze III procedure was effective in eliminating AF, it did not gain widespread acceptance because it was still technically difficult, and it significantly prolonged time on cardiopulmonary bypass. During the last decade, most groups have replaced the traditional “cut-and-sew” lesions with ablation lines created using various energy sources in an attempt to make the operation simpler and faster to perform.\textsuperscript{12} In 2002, our group introduced the Cox-Maze IV operation, which uses a combination of bipolar radiofrequency ablation and cryoablation to effectively replace the majority of lesions that comprise the Cox-Maze III (Figure 10.3).

These ablation-assisted procedures have resulted in widespread adoption of the Cox-Maze and a significant increase in the number of operations that are performed annually for atrial fibrillation.\textsuperscript{13} Nationally, as reported in the Society of Thoracic Surgery National Database,
representing over 700 institutions, 12,737 patients (5% of cardiac surgery patients) had a surgical procedure performed for AF in 2005, whereas only 3,987 patients had AF surgery in 2004. Prior to 2004, the volume was so low that the operation was not reported.

**Surgical ablation technology**

The development of surgical ablation technology has transformed a difficult and time-consuming operation into a procedure that is technically easier, shorter, and less invasive. However, incorporation of many new technologies has led to confusion in the literature as to what is the best energy source. It is imperative that the relative advantages and disadvantages of each of the available ablation technologies are understood. Several early energy sources that were clinically available, such as microwave and laser technology, have been removed from the market and will therefore not be discussed further.

The ideal device would meet the following criteria. First, it must reliably produce bidirectional conduction block across the line of ablation. This requires a transmural lesion, as even small gaps in ablation lines can conduct both sinus and fibrillatory wavefronts. Second, the ablation device must be safe. This requires a precise definition of dose-response curves to limit excessive or inadequate ablation and potential hazards.
to surrounding vital cardiac structures, such as the coronary sinus, coronary arteries, and valvular structures. Third, the ablation device should make AF surgery simpler and require less time to perform. This would require the device to create lesions rapidly, be intuitive to use, and have adequate length and flexibility. Finally, the device should be adaptable to a minimally invasive approach. This would include the ability to insert the device through minimal access incisions or ports. For the treatment of lone AF, there is a further requirement of the device to be able to create a transmural lesion on the beating heart without the need for cardiopulmonary bypass. Failure in this regard has proven to be the biggest shortcoming of unipolar energy sources. As of the present time, no device has met all of these criteria. The following sections will briefly summarize the currently available ablation technologies.

**Cryoablation**

Cryoablation is unique in that it destroys myocardial tissue by freezing rather than heating. Ice crystals caused by cryoablation cause acute disruption of cell membranes, and microvascular damage leads to chronic local tissue ischemia. This has the benefit of
preserving the myocardial fibrous skeleton and collagen structure and is thus safe for use around valvular tissue.\textsuperscript{17,18} There is also evidence that the induction of apoptosis plays a role in late lesion expansion.\textsuperscript{19} Lesion size and depth depend on the probe temperature, the duration of the ablation, the thermal conductivity and temperature of the tissue, and the choice of cooling agent.\textsuperscript{17}

Commercially available sources of cryothermal energy employ nitrous oxide (AtriCure, Cincinnati, OH), or Argon (Medtronic, Minneapolis, MN). At one atmosphere of pressure, nitrous oxide is capable of achieving a temperature of $-89.5 \degree C$, whereas argon has a minimum temperature of $-185.7 \degree C$. The nitrous oxide technology has a well-defined efficacy and safety profile and is generally safe except around the coronary arteries, where studies have shown late intimal hyperplasia after cryoablation.\textsuperscript{18,20} Potential disadvantages of cryoablation are the relatively long time it requires to create lesions (1–3 minutes), and the difficulty encountered in creating transmural lesions on the beating heart. Furthermore, if blood is frozen during epicardial ablation on the beating heart, it may coagulate, creating a potential source for thromboembolism.

**Radiofrequency energy**

Radiofrequency (RF) energy uses an alternating current at a frequency that is high enough to prevent rapid myocardial depolarization and induction of ventricular fibrillation, yet low enough to prevent tissue vaporization and perforation, ultimately using thermal energy to create a lesion.\textsuperscript{21} The lesion size depends on electrode tissue contact area, the interface temperature, the current and voltage (power), and the duration of delivery. Accordingly, the depth of the lesion can be limited by char formation, epicardial fat, myocardial and endocardial blood flow, and tissue thickness. Irrigated devices have been designed to reduce charring.

There have been numerous unipolar RF devices developed for ablation, and some have been modified to use irrigation and suction. Although dry unipolar RF devices have been shown to create transmural lesions on the arrested heart in animals with sufficiently long ablation times, they have not been consistently successful in humans. After 2-minute endocardial ablations during mitral valve surgery, only 20% of the \textit{in vivo} lesions were transmural.\textsuperscript{22} Epicardial ablation on the beating heart has been even more problematic. Animal studies have consistently shown that unipolar RF is incapable of creating epicardial transmural lesions on the beating heart,\textsuperscript{23} and epicardial RF ablation in humans resulted in only 10% of the lesions being transmural.\textsuperscript{24}

To overcome this problem, bipolar RF clamps were developed. With bipolar RF, the electrodes are embedded in the jaws of a clamp to focus the delivery of energy. Shielding the electrodes from the circulating blood pool improves and shortens lesion formation and limits collateral injury. Bipolar ablation has been shown to be capable of creating transmural lesions on the beating heart both in animals and humans with ablation times typically less than 20 seconds.\textsuperscript{25–27}

Another advantage of bipolar RF energy over unipolar RF is its safety profile. Several clinical complications of unipolar RF devices have been reported, including coronary
artery injuries, cerebrovascular accidents, and esophageal perforation. Bipolar RF technology has eliminated this collateral damage by confining the energy within the jaws of the clamp. Moreover, devices by AtriCure and Medtronic employ algorithms capable of predicting lesion transmurality by measuring the tissue conductance between electrodes, whereas the Estech device uses a temperature-controlled algorithm—thus tailoring the energy delivery to the physiological characteristics of tissue. There have been no injuries described with these devices despite extensive clinical use. One drawback of bipolar RF devices is the requirement for the tissue to be clamped. This has limited the potential lesion sets, particularly on the beating heart, and has required the use of adjunctive unipolar technology to create a complete Cox-Maze lesion set.

**High-intensity focused ultrasound**

High-intensity focused ultrasound, or HIFU, is another modality being applied clinically for surgical ablation (St. Jude Medical, St. Paul, MN). In these devices, ultrasound waves travel through the tissue causing compression, refraction, and particle movement, which are translated into kinetic energy, ultimately creating thermal coagulative tissue necrosis. HIFU is the one unipolar source that produces high-concentration energy in a focused area at a defined distance from the probe, and it is reportedly able to create transmural epicardial lesions through epicardial fat in less than 2 seconds without affecting intervening and surrounding tissue. There is a steep temperature gradient between the focus of energy and collateral tissue with the targeted tissue rapidly raised to 80ºC.

An advantage of HIFU technology is its mechanism of thermal ablation. Unlike other energy sources that heat or cool tissue by thermal conduction, which creates a graded response dependent on the distance from the energy source and is susceptible to cooling near blood vessels, HIFU ablates tissue by directly heating it in the acoustic focal volume. It is, therefore, much less vulnerable to this heat sink effect.

A few clinical studies using HIFU have shown good results. However, there has been no independent experimental verification of the efficacy of HIFU devices to reliably create transmural lesions, and more recent clinical experience has been much less encouraging. Additionally, the fixed depth of penetration of these devices can be problematic because of the variability of atrial wall thickness in pathological states.

In summary, each ablation technology has its own advantages and disadvantages. It has been the inability of some devices to create reliable linear lesions on the beating heart that has primarily limited their clinical applicability and the development of more minimally invasive procedures for lone AF. Continued research investigating the effects of each surgical ablation technology on atrial hemodynamics, function, and electrophysiology will allow for more appropriate use in the operating room.

**Indications for surgical ablation**

While there remains controversy over the relative roles of catheter-based ablation and the Cox-Maze procedure in the management of patients with medically refractory, lone AF,
there are many patients who are presently undergoing cardiac surgery who have concomitant AF and would benefit from treatment. In a review of our experience at Washington University from 1996 to 2005, the incidence of preoperative AF was 22% in patients referred for valvular surgery and 24% in patients referred for combined valvular/coronary surgery. The role of surgery for AF has been recently clarified and endorsed in a consensus statement.\textsuperscript{37} It stated that surgical ablation for atrial fibrillation is indicated for: (1) all symptomatic AF patients undergoing other cardiac surgery; (2) selected asymptomatic AF patients undergoing cardiac surgery in which the ablation can be performed with minimal additional risk; and (3) symptomatic AF patients who prefer a surgical approach, have failed one or more attempts at catheter ablation, or are not candidates for catheter ablation. Thus, surgery is a complimentary, rather than a competitive, approach to catheter ablation.

There are also relative indications for surgery that were not included in the consensus statement. The first is the presence of a contraindication to long-term anticoagulation in patients with persistent AF and a high risk for stroke (CHADS score ≥2). Up to one-third of patients with AF who were screened for participation in clinical trials of warfarin were deemed ineligible for chronic anticoagulation due to a high perceived risk for bleeding complications.\textsuperscript{38–40} In one study, the annual rate of intracranial hemorrhage in anticoagulated patients with AF was 0.9% per year, and the overall rate of major bleeding complications was 2.3% per year.\textsuperscript{41} In contrast, the stroke rate following the Cox-Maze procedure off anticoagulation has been remarkably low, even in high-risk patients. After a mean follow-up of 6.9 ± 5.1 years, only 5 of 450 patients had a stroke at our institution, and there was no difference in stroke rate between patients with CHADS scores above or below 2.\textsuperscript{42} This low risk of stroke after the Cox-Maze procedure has been noted in other series, as well.\textsuperscript{9,43} In patients undergoing concomitant valve surgery, studies have shown that adding the Cox-Maze procedure can decrease the late risk of cardiac- and stroke-related deaths.\textsuperscript{44,45} However, there have been no prospective, randomized studies demonstrating survival or other benefits in this population.

Finally, surgical treatment for AF with amputation of the left atrial appendage should also be considered in patients with persistent AF who have suffered a cerebrovascular accident despite adequate anticoagulation, as these patients are at high risk for repeat neurologic events. Anticoagulation with warfarin reduces the risk of ischemic and hemorrhagic strokes by more than 60% in patients with AF but does not completely eliminate this serious complication.\textsuperscript{2,46} At our institution, 19% of patients who underwent the Cox-Maze III procedure had experienced at least one episode of significant cerebral thromboembolism before undergoing the operation.\textsuperscript{47} Less than 1% of patients (2 of 306) had a late stroke after a mean follow-up of 3.8 ± 3.0 years, even with 90% of patients off anticoagulation at last follow-up.\textsuperscript{9} Furthermore, a series from Japan has demonstrated a 10% increase in incidence of stroke at 8-year follow-up for patients with chronic AF who underwent mitral valve replacement alone when compared to similar patients who had mitral valve replacement with concomitant Cox-Maze.\textsuperscript{48}
Surgical results

The Cox-Maze procedure

The Cox-Maze III procedure has had excellent long-term results. In our series at Washington University, 97% of 198 consecutive patients that underwent the procedure were free from symptomatic AF at a mean follow-up of 5.4 years. There was no difference in the cure rates between patients undergoing a stand-alone Cox-Maze procedure and those undergoing concomitant procedures. Similar results have been obtained from other institutions around the world with the traditional “cut-and-sew” method. Our results using a combination of bipolar RF ablation and cryoablation (the Cox-Maze IV operation) have been encouraging, as well.12,52 A recent prospective, single-center trial from our institution followed 100 consecutive patients with lone AF between January 2002 and May 2010.52 The mean follow-up was 17 ± 10 months, and enrolled patients had paroxysmal (31%), persistent (6%) and longstanding persistent (63%) AF. This study demonstrated postoperative freedom from AF of 93%, 90%, and 90% at 6, 12, and 24 months, respectively. Freedom from AF off antiarrhythmic drugs was 82%, 82%, and 84% at the same time points. In a group of 282 patients at our institution, the majority of whom had a Cox-Maze IV procedure with concomitant cardiac surgery, the results were similar with a freedom from AF of 89%, 93%, and 89% at 3, 6, and 12 months, respectively.53 However, these studies are difficult to compare to the prior Cox-Maze III results due to the more stringent follow-up and endpoints in the present studies. Holter monitor readings were taken at three time points, and AF recurrence was defined as any episode lasting over 30 seconds. A separate propensity analysis performed by our group has shown that there was no significant difference in the freedom from AF at 3, 6, or 12 months between the Cox-Maze III and IV groups.54

Interestingly, our group has shown that isolating the entire posterior left atrium by creating a “box” is preferable to isolating the left and right pulmonary veins separately with or without a connecting lesion between the pulmonary veins (Figure 10.4).52,55 In the Weimer et al. study, 78 patients underwent a “box” lesion, and those patients had higher

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Figure 10.4 Schematic illustration of the methods used to isolate the pulmonary veins, either separately (a), with a connecting lesion (b), or as a “box” isolation of the entire posterior left atrium (c).
freedom from AF (96% vs. 86%) and freedom from AF off antiarrhythmic drugs (79% vs. 47%) compared to patients that underwent different methods of pulmonary vein isolation. Postoperatively, 7% of patients required a pacemaker for chronotropic incompetence or for slow junction rhythms, and there were zero late strokes. There was only one postoperative death within 30 days (1%).

The Cox-Maze IV procedure has also significantly shortened the mean cross-clamp times for a lone Cox-Maze from 93 ± 34 minutes for the Cox-Maze III to 41 ± 13 minutes for the Cox-Maze IV \( (P < 0.001) \) and from 122 ± 37 minutes for a concomitant Cox-Maze III procedure to 92 ± 37 minutes \( (P < 0.005) \) in those undergoing the Cox-Maze IV procedure concomitantly with another cardiac operation.\(^{25}\)

Risk factors for late recurrence of AF at 1-year include: enlarged left atrial diameter, failure to isolate the entire posterior left atrium, and early atrial tachyarrhythmias.\(^{53}\) Increasing left atrial size has been related to operative failure in several studies,\(^{43,56}\) and our group has clearly demonstrated that the probability of recurrence exceeds 50% once left atrial size is greater than 8 cm.\(^{53}\) Early atrial tachyarrhythmias were associated with an odds ratio of 3.020 \( (P = 0.01) \), and it is thought that these might be a marker of more advanced pathology of the atrial substrate in patients with AF of long duration.

**Left atrial lesion sets**

Several centers have suggested performing lesion sets confined to only the left atrium to cure AF. Denke and colleagues have provided some evidence in a prospective analysis that suggests a left atrial lesion set is as effective as a biatrial lesion set in patients with chronic AF undergoing concomitant open heart surgical procedures.\(^{57}\) This concept is supported by the fact that the majority of paroxysmal AF appears to originate around the pulmonary veins and the posterior left atrium. A left atrial lesion set typically involves pulmonary vein isolation with a lesion to the mitral annulus, as well as removal of the left atrial appendage. Many ablation technologies have been used to create these lesion sets with varied degrees of success.\(^{30,58–65}\)

There have been no randomized trials of biatrial versus left atrial ablation in the surgical population. As a result, the importance of the right atrial lesions of the traditional Cox-Maze procedure has been difficult to define. A meta-analysis of the published literature by Ad and colleagues revealed that a biatrial lesion set resulted in a significantly higher late freedom from AF when compared with a left atrial lesion set alone (87% vs. 73%, \( P = 0.05)\).\(^{56}\) Moreover, a randomized trial of patients with persistent atrial fibrillation undergoing mitral valve surgery and radiofrequency ablation (RFA) of the left atrium versus mitral valve surgery alone demonstrated that sinus rhythm was only present in 44.4% of RFA patients at one year follow-up (compared to 4.5% in the patients in the valve surgery alone group).\(^{67}\) However, it is important to note that lesions were created using a monopolar RF device applied from the endocardial surface, which may not have provided transmural ablation. Regardless, it is not surprising that left atrial lesions alone would have lower success rates considering that results of intraoperative mapping of patients with atrial fibrillation from our
group, and others have shown that AF originates from the left atrium in approximately 30% of cases.\textsuperscript{68–70}

Of the specific left atrial lesions of the Cox-Maze procedure, it is difficult to determine the precise importance of each particular ablation. All surgeons agree on the importance of isolating the pulmonary veins. Work from Gillinov \textit{et al.} has shown the importance of the left atrial isthmus in a retrospective study.\textsuperscript{71} In a rare randomized trial, Gaita and coauthors examined pulmonary vein isolation alone versus two alternate lesion sets that both included ablation of the left atrial isthmus. In this study, normal sinus rhythm at 2-year follow-up was only seen in 20% in the PVI group versus 57% in the other groups (\(P <0.006\)).\textsuperscript{60} Moreover, as just discussed, we have demonstrated the importance of a “box” lesion around the pulmonary veins. Therefore, most of the left atrial Cox-Maze lesion set is likely needed to ensure a high success rate; however, there has been no randomized trial to conclusively demonstrate the correct left atrial lesion set. It must also be kept in mind that recurrent atrial flutter or tachycardia is a well-known complication of performing only the left atrial lesions, and it has been reported in as many as 13–21% of patients undergoing the procedure.\textsuperscript{61,72}

\textbf{Pulmonary vein isolation}

The results of pulmonary vein isolation (PVI) alone have been variable. While most of the triggers for paroxysmal AF originate around the pulmonary veins,\textsuperscript{73} over 30% of triggers originate elsewhere.\textsuperscript{74} However, PVI is an attractive therapeutic option due to the fact that it can be performed off cardiopulmonary bypass through small or endoscopic incisions. In the first report of surgical PVI, Wolf and colleagues reported that 91% of patients undergoing a video-assisted bilateral PVI and left atrial appendage exclusion were free from AF at three months follow-up.\textsuperscript{75} Edgerton \textit{et al.} reported on 57 patients undergoing PVI with ganglionated plexus (GP) ablation with more thorough follow-up and found 82% of their patients with paroxysmal AF were free from AF at 6 months, with 74% off antiarrhythmic drugs.\textsuperscript{76} Subsequent studies have shown encouraging results in patients with paroxysmal AF. McClelland \textit{et al.} reported 88% freedom from AF at one year without antiarrhythmic drugs in a study involving 21 patients with paroxysmal AF undergoing PVI with GP ablation.\textsuperscript{77} A larger, single-center trial recently reported a 65% single procedure success at one year in a series of 45 patients undergoing PVI with GP ablation, including patients with persistent and paroxysmal AF. A multicenter trial reported 87% normal sinus rhythm rate in a more diverse patient population, including some patients with longstanding persistent AF; however, those patients with longstanding persistent AF only had a 71% incidence of normal sinus rhythm.\textsuperscript{78}

The success of PVI is highly dependent on patient selection, as results are consistently worse in patients with longstanding persistent AF. In a study from Edgerton and his group, only 56% of patients were free from AF at 6 months (35% off antiarrhythmic drugs).\textsuperscript{79} With concomitant procedures, the success rate of PVI is even lower. Of 23 patients undergoing cardiac surgery with concomitant PVI, only 59% of patients were free from AF at their last follow-up (23 ± 15 months).\textsuperscript{12} When broken down for patients with
paroxysmal versus persistent AF, the percentages were 70% and 43%, respectively. In the setting of mitral valve disease, Tada and colleagues report 61% freedom from AF and only 17% freedom from antiarrhythmic drugs in their series of 66 patients undergoing PVI. These results highlight the need to fully understand the electrophysiological substrate of AF in order to perform an optimal operation for any individual patient.

**Ganglionated plexus ablation**

Electrophysiologic studies have demonstrated that local autonomic ganglia in ganglionated plexi clustered in the epicardial fat pads play a role in the initiation and maintenance of AF. Both pulmonary vein myocardial sleeves and adjacent atrial muscle are innervated by these plexi. As a result, some surgeons have added GP ablation to PVI in hopes of increasing procedural efficacy. Some of the initial surgical results have been encouraging. In 2005, Scherlag and colleagues reported a study of GP ablation combined with catheter PVI in 74 patients with lone AF. After a relatively short median follow-up of 5 months, 91% of patients were free from AF. However, there have not been any direct comparisons as part of randomized clinical trials.

Moreover, the effects of vagal denervation and the long-term efficacy of GP ablation have not been clearly defined. Experimental evidence in our laboratory and others has demonstrated recovery of autonomic function in as few as 4 weeks after GP ablation. It is worrisome that the reinnervation may not be homogeneous and could result in a more arrhythmogenic substrate. In a more recent report, Katritsis and colleagues used left atrial GP ablation alone to treat 19 patients with paroxysmal AF. Fourteen of these patients (74%) had recurrent AF during 1-year follow-up. Due to these suboptimal results and the lack of any long-term follow-up of the effects of GP ablation, our practice is not to perform GP ablation to treat AF. GP ablation should be reserved for centers participating in clinical trials.

**Surgical techniques**

The three categories of surgical procedures currently used in the surgical management of AF are the Cox-Maze procedure, left atrial lesion sets, and pulmonary vein isolation. The important technical details surrounding each of these surgical approaches are discussed in this section.

**The Cox-Maze IV procedure**

Most centers have replaced the surgical incisions described in the original “cut-and-sew” Cox-Maze III procedure with lines of ablation created by a variety of different energy sources. At our institution, we have successfully used bipolar RF energy to replace most of the surgical incisions of the Cox-Maze III procedure in an operation termed the Cox-Maze IV (Figure 10.3). The Cox-Maze IV procedure is performed on cardiopulmonary bypass using either a median sternotomy or a less invasive right mini-thoracotomy. Both the right and left
pulmonary veins (PVs) are bluntly dissected. If the patient is in AF at the time of surgery, amiodarone is administered and the patient is electrically cardioverted before proceeding with the operation. Pacing thresholds are obtained from each pulmonary vein. The PVs are then isolated using a bipolar RF ablation device, such that a linear line of ablation surrounds a cuff of atrial tissue encompassing the right and left PVs, respectively. The adequacy of electrical isolation is demonstrated by confirming exit and/or entrance block from each PV.

The right atrial lesion set is performed on the beating heart through a small purse-string suture at the base of the right atrial appendage and a single vertical atriotomy (Figure 10.5). A bipolar RF device is used to create most of the lesions. Due to the difficulty in using the bipolar RF clamp in the area of the tricuspid annulus, a unipolar device utilizing either cryoablation or RF energy is used to complete the endocardial ablation lines in this area.

The heart is then arrested by cold cardioplegia. The left atrial appendage is amputated, and bipolar RF ablation is performed through the amputation site into one of the left pulmonary veins. The remaining ablation lines are then created using the bipolar clamp through a standard left atriotomy that extends from the dome of the left atrium to the

Figure 10.5 Illustration of the right atrial lesion set. Bipolar radiofrequency ablation is indicated by the white lines. Cryoablation is used to complete the ablation lines at the tricuspid valve annulus. Reproduced from J. Interv. Card. Electrophysiol., The Cox-maze IV procedure for lone atrial fibrillation: a single center experience in 100 consecutive patients 31(1), 2011, pages 47–54, Weimar T. et al. with permission of Springer
right inferior PV (Figure 10.6). Connecting lesions into the left superior and inferior pulmonary veins effectively isolate the entire posterior left atrium, and a linear line of ablation is created toward the mitral annulus. Unipolar energy, usually cryoablation, is then used to connect the RF lesion to the mitral annulus and to complete the left atrial isthmus line. An epicardial ablation of the coronary sinus is also performed, typically with a cryoprobe, in line with the endocardial mitral isthmus ablation. In patients undergoing a right mini-thoracotomy, cryoablation is more extensively applied to complete the posterior left atrial isolation.

**Left atrial lesion sets**

Over the last decade, several left atrial procedures have been introduced in an attempt to find a surgical cure for AF. The individual lesion sets themselves vary widely, and results have been dependent on multiple variables, including the type of ablation device used, the lesion set, and the patient population. \(^{30,63,65,88,89}\)

From a technical standpoint, all of these procedures have incorporated at least some subset of the left atrial lesion set of the Cox-Maze procedure, and have attempted to electrically isolate the pulmonary veins. A typical left atrial lesion set involves PVI, which can
be performed around the right and left PVs individually, with a connecting lesion, or as a “box” isolation of the entire posterior left atrium, along with a lesion to the mitral annulus and removal of the left atrial appendage. Left atrial lesion sets have been performed from both an endocardial and epicardial approach, and have utilized all available ablation technologies. 58–60,62,64,90,91

**Pulmonary vein isolation**

Pulmonary vein isolation is an attractive treatment option since the procedure can be added to other open-heart surgeries with minimal impact on operative time, can be performed using minimally invasive techniques, and does not require cardiopulmonary bypass. As previously mentioned, electrical isolation of the pulmonary veins can be performed around the right and left PVs individually, with a connecting lesion, or as a box isolation of the entire posterior left atrium (Figure 10.4). In lone AF, the procedure can be performed via either a mini-thoracotomy or an endoscopic, port-based approach. Although a variety of energy sources have been used successfully in PVI, our institution favors bipolar RF clamps for this procedure.34,92,93

Prior to initiating the operation, the patient is intubated using a double-lumen endotracheal tube, and external defibrillator pads are placed. A transesophageal echocardiogram is performed to confirm the absence of thrombus in the left atrial appendage. If thrombus is identified, the procedure is either aborted or converted to an open procedure in order to minimize the risk of systemic thromboembolism. The patient is positioned in a modified left lateral decubitus position, at a 45- to 60-degree angle, with the right arm extended over the head in order to expose the right axilla.

For the more common thoracoscopic approach, a camera port is placed in the sixth intercostal space, and a smaller working port is placed under direct vision in either the third or fourth intercostal space at the mid-axillary line. Upon entering the chest, the right phrenic nerve is identified and a pericardotomy is performed from the superior vena cava to the diaphragm. Care is taken to open the pericardium anterior and parallel to the phrenic nerve in order to protect it from injury. The space above and below the right PVs, including the opening into the oblique sinus and the space between the right superior PV and the right pulmonary artery, is then dissected free. A specialized thoracoscopic dissector and guiding sheath are introduced through a second port, either lateral or medial to the scope port, and the space between the right superior PV and the right pulmonary artery, is then dissected free. A specialized thoracoscopic dissector and guiding sheath are introduced through a second port, either lateral or medial to the scope port, and the space between the right superior PV and the right pulmonary artery is further dissected. The dissector is removed from the chest, leaving the sheath in place, and the patient is cardioverted into sinus rhythm. Pacing thresholds are obtained for each pulmonary vein in order to ensure appropriate electrical isolation at the end of the procedure. At this point, some surgeons take advantage of the surgical exposure afforded by PVI and also ablate the ganglionated plexi.

A bipolar RF clamp is then introduced into the chest using the previously placed sheath as a guide. The left atrium surrounding the pulmonary veins is clamped and ablated as previously described. Electrical isolation is confirmed with pacing, the instruments are removed, and the right chest is closed.
The patient is repositioned to expose the left chest in the same fashion as the right. A port for the thoracoscopic camera is placed in the sixth intercostal space, slightly posterior to the site on the right chest. The other working ports are introduced into the left chest in the same positions used for the right chest. In a similar fashion, the left phrenic nerve is identified and a pericardotomy is performed, this time parallel and posterior to the structure. The Ligament of Marshall is identified and divided prior to introducing the sheath and dissector. The left PVs are then isolated using a bipolar RF clamp, and exit block is confirmed in identical fashion to the right side. Prior to closing the left chest, the left atrial appendage is typically excluded by either stapling across the base with an endoscopic stapler or using a clip. Clip devices are currently favored to address left atrial appendage exclusion since the stapler poses a significant risk of tears and bleeding. While left atrial appendage exclusion is performed to eliminate a potential source of thromboemboli, data is mixed on the effectiveness of the practice.

**Future directions in atrial fibrillation surgery**

The advent of surgical ablation technology has made the Cox-Maze IV procedure easier and faster to perform while preserving the high success rates of the original lesion set. However, it remains an invasive procedure that requires cardiopulmonary bypass, and there are certain populations, such as patients with enlarged atria, that have high postoperative failure rates. Further modifications based on the most current theoretical mechanisms of AF will be best developed using patient-specific and minimally invasive approaches. Such refinements should preserve normal atrial physiology, incur minimal morbidity, and achieve high success rates in curing AF.

**Critical mass hypothesis**

In the decades since the introduction of the Cox-Maze procedure, it has been proposed that a “critical mass” of tissue is requisite for fibrillation. The critical mass hypothesis proposes that a certain minimal size of atrial tissue is required for the induction and maintenance of AF, owing to the idea that this area represents the minimum path length necessary for re-entry in sustained AF. The minimum path length, or wavelength, has been quantitatively defined as the product of conduction velocity (CV) and effective refractory period (ERP). In *vitro* studies from our laboratory supporting this model have shown that the probability of sustained AF is dependent on increasing atrial surface area, widths, and weights, as well as the length of the ERP and CV of the tissue. Concordantly, it has been shown that patients with large left atrial surface areas are at disproportionate risk of failing to convert to normal sinus rhythm and of suffering recurrent AF after a Cox-Maze procedure, presumably because the procedure fails to divide the atria into small enough sections to prevent sustained AF. Based on these data and clinical results, it has been hypothesized that certain patients may benefit from either atrial reduction or additional ablative lines that further subdivide the atria. The initial lesions of a novel AF procedure
could be determined by a calculation of the critical area needed to maintain AF in the individual patient.⁹⁸

**Electrocardiographic imaging**

To calculate the critical mass required to sustain AF in the individual patient, one must be able to derive the minimum wavelength; however, determining CV and ERP, as well as the atrial activation sequence and mechanistic information, has presented a challenge in the past. Because epicardial activation mapping, the traditional gold standard for mapping of AF, is both invasive and time-consuming, a new method of multipoint mapping known as electrocardiographic imaging (ECGI) is currently being evaluated at our institution.¹⁰⁰ When combined with computed tomography (CT) scanning, ECGI uses body surface potential mapping with 250 electrodes representing over 800 epicardial sites to obtain patient-specific heart-torso geometry to create maps of cardiac electrophysiologic activation, which can then be superimposed onto the heart surface.¹⁰¹–¹⁰⁶ This technique has been well-described in patients with AF, and allows activation times to be calculated and displayed as either static or dynamic activation maps on a 3D surface model of an individual patient’s atria.¹⁰⁰,¹⁰⁷ Previous studies have demonstrated that substrate information can be extracted from this data, allowing ERP to be estimated from the activation intervals calculated at each electrode site, and CV to be calculated from the activation maps.¹⁰⁸,¹⁰⁹ Data derived from this technology, which take into account the patient’s atrial geometry, electrophysiology, and arrhythmogenic mechanism, may allow a surgeon to design a patient-specific optimal lesion set, thereby leaving the atria unable to sustain AF but able to conduct a normal sinus beat. Additionally, focal trigger mechanisms could be identified using this technique, potentially allowing for targeted ablation strategies in either the electrophysiologic laboratory or operating room.

**Minimally invasive techniques**

The development of ablation devices not only simplified the formerly complex and technically demanding Cox-Maze procedure, but also introduced the possibility of minimally invasive surgery for AF. Using new ablation technologies, simpler procedures are being developed that can be performed through small incisions without the need for cardiopulmonary bypass.

As discussed previously, there is strong evidence that PVI performed on the beating heart may be effective in the subset of patients with paroxysmal AF.⁷⁵ Using minimal access techniques, Edgerton et al. have achieved excellent visualization through the transverse sinus in order to develop a new linear lesion set that uses RF ablation to electrophysiologically mimic all of the left atrial lesions of the Cox-Maze procedure on the epicardial surface. This new lesion set, termed the Dallas Lesion Set, uses PVI in combination with connecting lesions created on the dome of the left atrium, and has shown promising results at both 6 and 12 months.¹¹⁰,¹¹¹ Two-stage hybrid procedures that combine PVI and resection of the left atrial appendage via a minimally invasive surgery approach with delayed electrophysiology ablation in the area of the biatrial isthmus lines are
being performed at some institutions. Similarly, procedures that combine simultaneous epicardial and endocardial ablation have also been performed.\textsuperscript{112}

Unfortunately, although new technology has led to advances in the field, the limitations of current ablation devices have impeded the development of a truly minimally invasive procedure. Future advances may be anticipated with new devices and techniques that allow surgeons and electrophysiologists to obtain reproducible complete lines of block.

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Chapter 11

Mechanical circulatory support

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Introduction

Over the last half-century, mechanical circulatory support (MCS) for the failing heart has provided a compelling, and often dramatic, story of engineering achievement, pioneering physicians, and brave patients (Table 11.1). The 1950s, 1960s, and 1970s saw the transition of MCS from the necessary extension of cardiopulmonary bypass to the development of durable devices. This era was defined by the occasional case followed by design readjustment. In the late 1980s and moving into the 1990s, the surgical principles as well as improved technology allowed wider adoption by major centers. Within the last 20 years, enhanced pumps as well as surgical and medical experience have allowed MCS to become a routine part of the armamentarium for treating heart failure (HF) patients. Most recently, within the last 10 years, there has been a dramatic shift from the use of large, pulsatile left ventricular assist devices (LVADs) to smaller continuous flow (CF) devices. In fact, the Thoratec XVE, one of the most widely used pulsatile devices, is no longer available or supported. Conversely, several CF LVADs are now available to the heart failure community. In this chapter, we will review the current state of MCS for treating advanced heart failure, as well as detail many of the surgically related issues with LVADs.

General indications

Mechanical circulatory support can be used to salvage the cardiogenic shock patient, bridge a suitable patient for transplant (BTT), or device explantation for myocardial recovery (BTR), and provide lifetime use or destination therapy (DT). In addition, there is a gray zone category of patients that have durable LVADs implanted to determine their eligibility for transplant, also called bridge to eligibility or decision (BTD). Although there is some enthusiasm to investigate the role of durable LVADs in a less sick population, most patients receiving durable LVADs are functional New York Heart Association (NYHA) Class IV or patients in Stage D HF. Classic indications for DT, versus BTT, include—but are not limited to—advanced age and significant comorbidities such as advanced diabetes, pulmonary hypertension, renal dysfunction, and recent malignancy.

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) follows all FDA-approved pump implants and has created a system to define patient
The algorithm for the acute cardiogenic shock patient often involves insertion of non-durable pumps (INTERMACS Profile 1). The majority of LVAD patients are those in progressive decline (INTERMACS Profile 2—i nto trope dependent with continuing deterioration) and those stable but inotropic dependent (INTERMACS Profile 3). Recent analysis demonstrates a relative flat rate of implants of Profile 1 patients (~15%).
but also a progressive decrease in implants for Profile 2 (41–33%), reflecting the poor outcomes associated with ventricular assist device (VAD) implantation with the most ill patients.²

**Bridge to recovery**

Using mechanical circulatory devices to achieve myocardial recovery is best described by the urgency and length of support needed for a given condition. Most commonly, recovery refers to short-term mechanical support, designed specifically to support patients in postcardiotomy shock, large myocardial infarctions with hemodynamic instability, or cardiogenic shock related to myocarditis. In general, these are INTERMACS Level 1 patients that require urgent/emergent support. Ideally, as the acute insult resolves, the heart recovers, and the pump is removed. This category is markedly different than patients with longstanding HF that have durable pumps implanted, are treated medically, and ultimately are able to have sustained recovery with pump removal.

**Short-term recovery**—Historically, the first line of defense for most patients requiring mechanical support is the intra-aortic balloon pump (IABP). First described in 1968,³ the IABP has since undergone numerous improvements that facilitate ease of use, including sensing of the cardiac cycle through both pressure transduction and electrocardiogram (EKG) monitoring. The IABP functions specifically to improve coronary blood flow in diastole and to offload the left ventricle during systole. Several studies have used surrogate measures to evaluate the efficacy of IABP counterpulsation versus pharmacologic therapy alone: for example, in the Kaiser Permanente healthcare system in California, hospitals that were more liberal with IABP therapy had lower mortality for myocardial infarction even when controlling for patient characteristics and other procedures like percutaneous coronary intervention (PCI).⁴

The first randomized trial addressing questions regarding the efficacy and safety of the IABP in addition to early revascularization in patients with cardiogenic shock complicating myocardial infarction, the IABP-SHOCK II trial, was conducted between 2009 and 2012 at 40 centers in Germany.⁵,⁶ Six hundred patients were randomized 1:1 to revascularization by PCI with an IABP and optimal medical therapy (Group 1, 300 patients) and to revascularization by PCI with optimal medical management (Group 2, 300 patients). The primary endpoint was 30-day all-cause mortality. At 30 days, mortality was similar among patients in the IABP group and those in the control group. In addition, there was no significant difference in mortality between the group of patients in whom the balloon pump was inserted before revascularization and the group in whom it was inserted after revascularization. The modest effect on cardiac output and the lack of reducing the infarct size could contribute to those findings. The 6-month and 12 month follow-ups showed that the IABP support did not increase survival compared to the control group, supporting the short-term 30-day follow-up data.⁷ Importantly, the functional status and the quality of life for survivors of cardiogenic shock were good at 6 and 12 months. Despite early revascularization and optimal medical therapy in both groups,
the mortality of cardiogenic shock complicating myocardial infarction is still higher than 50% at 1-year follow-up.

Patients with chronic systolic heart failure who develop cardiogenic shock are physiologically different than patients who develop cardiogenic shock as a complication of an acute myocardial infarction. In chronic heart failure, the ventricular remodeling has taken place. The IABP increases the coronary blood flow and diastolic blood pressure and reduces isovolumetric contraction and ventricular afterload. As such, any increase in stroke volume is a result of better ventricular performance and not augmentation from the device. In chronic heart failure, IABP reduces arterial impedance and the resultant increase in stroke volume may be enough to rescue patients from severe shock. In this patient population, the IABP inserted through the femoral artery or, in the more recent years, through the axillary artery can provide significant support, hemodynamic improvement, and end-organ recovery in the majority of patients with chronic heart failure who develop heart failure exacerbation or cardiogenic shock. If the patient is unable to be weaned from the device, they can safely be bridged to a durable LVAD or heart transplantation.

Newer percutaneous devices seek to provide support above and beyond balloon counterpulsation. In 2008, the FDA-approved the Impella 2.5 (Abiomed, Danvers, MA). This percutaneously placed, 9 French device spans the aortic valve, drawing blood from the left ventricle and ejecting it into the ascending aorta. The device is capable of providing a theoretical maximum flow of 2.5 lpm. It has been widely used to support high-risk PCI after favorable outcomes in the Protect I and Protect II trials. For the treatment of cardiogenic shock, the Impella 2.5 appears comparable to IABP in efficacy. In 2009 the company gained approval for the Impella 5.0. This device provided reasonable support for postcardiotomy shock patients in the RECOVER I study. The primary limitation is a 21 French deployment system, and therefore it is frequently placed intraoperatively through a graft on the ascending aorta. Most recently, in 2012, Abiomed launched the Impella CP, capable of up to 4 lpm of flow, but able to deployed on the same system as the 2.5.

The Tandem Heart Percutaneous Ventricular Assist Device (pVAD, Cardiac Assist, Inc., Pittsburgh, PA) is another commonly utilized percutaneous device. One cannula is placed through the femoral vein crossing the interatrial septum to drain the left atrium and the return 17 Fr cannula perfuses the aortoiliac system. A centrifugal flow device capable of pumping up to 5 L/min is strapped to the patient’s thigh. Early results with this device have been reported by Texas Heart Institute. In their series of 117 patients, all had failed therapy with high-dose inotropes, and 80% had inadequate perfusion with both inotrope and IABP. Nearly half the patients were undergoing cardiopulmonary resuscitation (CPR) at the time the devices were placed. The average duration of therapy was 6 days, and survival was 60% at 30 days, and 55% at 6 months. This led the group to conclude that the pVAD was more effective than the combination of IABP and high-dose inotrope therapy.

Operative placement of a temporary ventricular support device allows for optimal positioning of cannulas, with the opportunity for excellent decompression of the heart and high
flow rates that are important in larger patients. Standard approaches for postcardiotomy support include full extracorporeal membrane oxygenation (ECMO) support driven by a centrifugal pump such as the CentriMag (Thoratec, Pleasanton, CA) or the Rotaflow (Maquet, Rastatt, Germany). Either pump can alternately be configured for left, right, or biventricular support. The CentriMag was initially FDA approved as a frictionless pump for cardiopulmonary bypass, but its versatility, compact size, and ease of use paved the way for a transition to temporary extracorporeal support. The CentriMag features a magnetically levitated centrifugal rotor that pumps blood through a device without seals, bearings, vents, or valves. The only connections are the inflow and outflow tubing. The CentriMag is currently FDA 510(k) cleared for use in the US in an investigational capacity for short-term left-sided or biventricular support, and is FDA approved for use as a right ventricular assist device for periods of up to 14 days. Results of an initial safety and efficacy study—the CentriMag ventricular assist system (VAS) Pivotal Trial—revealed a favorable survival profile for cardiogenic shock patients. The three arms of the trial included 12 patients treated with the CentriMag as a temporary right ventricular assist device (RVAD) during permanent LVAD placement, 12 patients with postcardiotomy cardiogenic shock, and 14 patients with postmyocardial infarction cardiogenic shock. In this group of 38, nearly half of the patients were alive 30 days after device explant, with a median duration of support of 15 days. The infection rate was 21%, bleeding 5%, and neurologic dysfunction 11%. Although there was concern for hemolysis given the nature of the pump, the observed rate of significant hemolysis was only 5%. Since this initial trial, the CentriMag has been widely adopted and numerous centers have reported success with this system.

One particular advantage to the CentriMag configuration is the ability to align an oxygenator within the circuit to provide full ECMO support. Indeed, ECMO has long been used to provide cardiopulmonary support for both pediatric and adult patients. Using the femoral vessels, either by cut-down or percutaneously, this approach can be readily accomplished for patients in extremis without having to open the chest. As many of the post-MI patients are on multiple anticoagulants and antiplatelet agents, avoiding bleeding issues with sternotomy can be advantageous. If the patient’s end-organ function can be reversed and they demonstrate neurologic recovery, the circulation can either be explanted or transitioned to a more durable device. Alternative access involves cannulating the axillary artery by a graft, and the right atrium through the right internal jugular vein. In this fashion, patients can be on full ECMO support, and have ambulatory potential.

**Long-term recovery**—Use of durable devices to promote recovery of chronic HF patients is often considered the “holy grail” of the advanced HF field. Although frequently discussed, this is a very rare phenomenon. In the first 1,000 LVADs reported to the INTERMACS database, only 63 (2%) were ultimately explanted. Missing, however, in many of the competing outcomes associated with VAD therapy is the fact that few centers actively look for evidence of myocardial recovery. While one can argue about the pathophysiologic semantics of reverse remodeling, remission of heart failure, and myocardial recovery, the fundamental issue is that the advanced heart failure provider has to look for recovery to see it.
The two centers with the largest experience are from Berlin and Harefield. The former group has followed over 100 patients that have had pumps removed. Successful pump removal (freedom from reinsertion and transplant for 5 years) is predicted by off-pump echocardiography demonstrating an ejection fraction more than 45% and an end-diastolic dimension less than 55 mm, as well as patients with shorter duration of HF. The Harefield group has reported a two-phase approach to chronic recovery by first reversing pathologic hypertrophy and remodeling with standard HF meds including high-doses of lisinopril, carvedilol, losartan, spironolactone, and digoxin. When weaning, echocardiography demonstrated an LVIDd less than 60 mm, then the second phase of promoting physiologic hypertrophy was initiated by changing the carvedilol to a beta-1 selective agent and adding clenbuterol, a beta-2 agonist. In their latest report using the CF HeartMate II LVAD, 12 of 20 patients met criteria for explantation with 80% of those free from HF at 3 years. Unfortunately, the promising results from this single center have not been able to be reproduced in a more recent multicenter trial using the Harefield protocol where only 1 out of 17 patients were able to have their LVAD explanted. While the reasons for this disparity in results are unclear, differences related to demographics, chronicity of HF, and medication up-titration point to the difficulty of expanding these demanding studies. That said, when a single institution actively engages in intense medical therapy—with biweekly neurohormonal titration—return of left ventricular (LV) function may be present in a larger proportion of patients.

Hence, LVAD-induced cardiac recovery is a real but underrecognized phenomenon. Heart failure teams focusing on this group of patients need to look for it, to adopt a “bridge to recovery strategy,” and identify the features of the group of patients amenable to cardiac recovery. The University of Utah recovery program identified six independent predictors of cardiac recovery: age less than 50 years; non-ischemic cardiomyopathy; time from cardiac diagnosis less than 2 years; absence of an implantable cardioverter defibrillators (ICD); serum creatinine level 1.2 mg/dL or less; and left ventricular end diastolic diameter (LVEDD) less than 6.5 cm. On the basis of these results, a prognostic score they labeled the INTERMACS Cardiac Recovery Score (I-CARS) was derived. The score ranged from 0 to 9 and three groups with significantly different prognosis were identified: a low probability group (0 to 3); an intermediate probability group (4 to 6); and a high probability group (7 to 9). The cardiac recovery rates applying I-CARS to a bridge to recovery strategy group and in the non-bridge to recovery group yielded cardiac recovery rates of 0%, 4.9%, and 25.4% for patients in the low, intermediate, and high probability categories, respectively.

The remission from Stage D Heart Failure study (RESTART-HF, ClinicalTrials.gov NCT01774656) has since been designed to investigate the influence of aggressive medical intervention, including regular testing of underlying function, on selected patients receiving HeartMate II LVADs. The primary outcome is the proportion of patients in whom their LVADs can be removed and remain free from additional mechanical support or transplant for at least 3 years. Importantly, these patients will be rigorously followed with serial imaging to not only better define predictors of explantation, but to also chart
the course of durable recovery after LVAD removal. Forty patients have been enrolled and have finished their initial follow-up. The results of the RESTAGE-HF clinical trial are to be published the spring of 2018, and will offer significant insight on this interesting group of patients.

A discussion of medical therapy would be incomplete without mentioning the vast potential of adjuvant biologic therapy to both enhance reverse remodeling and augment contractile function. Several previous attempts at investigating the role of stem cells in LVAD patients have been abandoned by the National Heart, Lung, and Blood Institute (NHLBI) for administrative reasons. That said, individual centers are injecting both autologous (University of Minnesota, ClinicalTrials.gov NCT00869024) and allogeneic mesenchymal stem cells (MSC) in LVAD patients (AHEPA University Hospital, Greece, ClinicalTrials.gov NCT01759212). The NIH-sponsored Cardiothoracic Surgery Network (CTSN) recently reported a 30-patient pilot trial of intramyocardial MSC injection at the time of LVAD placement. There were no safety issues and potential efficacy signals were observed. A follow-up trial with more centers and a recruitment goal of 169 patients is currently in follow-up (CTSN LVAD MPC-II). Adjuvant therapy studies are not limited to stem cells, but also include growth factor (e.g., SDF) and gene (e.g., SERCA2a) based therapies. Cumulatively, the LVAD patient provides a platform that allows for a multitude of creative, biologic interventions that will provide a robust opportunity for future advances in the field.

**Bridge to transplant (BTT)**

Although the number of adults with end-stage heart disease continues to increase, the number of heart transplants performed annually remains static. In the United States, there have been roughly 2,400 annual transplants for almost 20 years. To help address deaths on the waiting list, the United Network of Organ Sharing adjusted its allocation strategy in 2006, giving higher priority to patients with a poorer prognosis. This change in the allocation formula, together with improving LVAD therapy for patients in end-stage HF, has helped to significantly reduce wait list deaths in recent years.

LVAD therapy has long offered a way for patients to help survive the wait for a suitable donor heart. Even with the nascent LVAD technology available in the early nineties, Frazier and other investigators demonstrated a doubling in survival to transplant for patients treated with LVADs. The device in the study was the pneumatically driven HeartMate IP (Implantable Pusher Plate). The success of the trial mandated that future BTT LVAD trials could no longer be ethically conducted with a medical treatment arm. This study was followed up in 2001 with the next generation pulsatile device—the HeartMate VE, or vented electric assist device. In this group of 280 patients, 71% survived to either transplant or elective device removal. Although the average creatinine and total bilirubin improved significantly for the population as a whole, hepatic and renal dysfunction were two of the most common complications, with bleeding, infection, neurologic dysfunction, and thrombosis following closely behind. Of these complications, infection and bleeding...
were the most commonly associated with the device itself. Notably, this was one of the first large-scale papers to report on LVAD patients that were able to live with their LVAD outside of the hospital. Of the 280 patients treated with LVAD, 160 met criteria to participate in a “release program,” with 115 achieving full outpatient status. All 160 patients in the release program had improved from an NYHA functional class of III or IV to I or II.20

Concurrently, improvements to the HeartMate VE were consolidated and integrated in a newer device, the HeartMate XVE. Mechanistically similar, the XVE incorporated numerous engineering refinements to address issues that had led to mechanical failure. The HeartMate Investigators group published their experience after the XVE became widely available. They observed significantly fewer percutaneous lead fractures, fewer inlet valve failures, and fewer bearing fractures. Trends toward less outflow graft kinking and accidental disconnects were also observed.30 Overall, freedom from major device malfunction improved from 76% at one year for the VE to 97% for the XVE. This durability and reliability helped establish the HeartMate XVE as the dominant device in the US for much of the early twenty-first century.

Continuous flow devices—At the turn of the century, the next generation of device was just beginning preclinical and clinical trials. These axial flow devices included the Jarvik 2000, HeartMate II, Micromed, and the Berlin devices. The HeartMate II first entered clinical use in 2001,31 and within a few years, a large scale multicenter trial in BTT patients was initiated. In 2007, the HeartMate II Clinical Investigators published the results of the landmark study investigating this device in status I patients as a BTT.32 Over 130 patients were enrolled, all of whom were on inotropic therapy and/or IABP. By 180 days, 100 patients had reached the principal outcomes of heart transplantation, cardiac recovery, or survival on device. Twenty-five patients died within the 180-day period, five became ineligible for transplantation, and the last three patients had their device replaced with a different device. Actual survival for patients that continued to receive LVAD therapy was 89% at 1 month, 75% at 6 months, and 68% at 1 year. Although the patients could not be randomized with a medical therapy group for reasons of equipoise, it is likely that this survival pattern was considerably better than that which could have been achieved with medical therapy alone. Additionally, most patients reported an improvement of 2–3 NYHA functional classes at the three-month interval. The six-minute walk, Minnesota Living with Heart Failure score, and the Kansas City Cardiomyopathy score were all significantly better in patients receiving LVAD therapy. Moreover, end-organ perfusion was demonstrably improved on LVAD therapy; the average blood urea nitrogen (BUN) and creatinine decreased from 30 to 18 mg/dL, and 1.4 to 1.1 mcg/dL, respectively. The most common complication was perioperative bleeding, followed by stroke. Eight patients had an ischemic stroke and three had a hemorrhagic stroke. Twenty-eight percent (28%) of patients experienced a localized infection, approximately half of these being driveline infections. Unlike in prior LVAD studies, there were no pump pocket infections. Although not compared directly with the HeartMate XVE, the results of this study were powerful enough to establish axial flow as the new standard in mechanical support.
The HeartMate II Investigator group published again in 2009 with greater patient numbers and extended follow-up. At 18 months, 222 of 281 patients that had been listed status 1A or 1B for heart transplant had either undergone transplantation, LVAD removal for cardiac recovery, or had ongoing VAD support. Survival was 72% at 18 months, and 83% of patients had recovered from NYHA Stage IV to Stage I or II. Complication profiles were consistent with those previously reported, including death from sepsis in 4% of patients, stroke in 6% of patients, and right heart failure in 3% of patients. Deaths directly attributable to the LVAD totaled 3%, including pump thrombosis, kinking of the inflow graft in implantation, disconnect of the outflow graft, and driveline fracture with power loss. This study helped further cement axial or CF as the new standard in left ventricular assist technology.

One of the criticisms of the axial flow devices is that they contain bearings, and this is a potential source of thrombosis, device wear, and shearing of blood components like the von Willebrand factor (vWF) multimer. To address these design issues, the newest generation of devices are centrifugal flow, using a magnetically levitated impeller—conceptually identical to the CentriMag. This allows for a bearingless device with zero wear and possibly less thrombosis risk. The two most commonly implanted centrifugal pumps to date include the DuraHeart (Terumo Heart, Inc, Ann Arbor, MI), and the HeartWare HVAD (HeartWare Intl, Framingham, MA). European centers have achieved greater experience with the DuraHeart, and have published their trial experience and early postmarket surveillance data. The study population included 68 patients with heart failure that had been listed for heart transplant; the first 33 patients were part of the European multicenter clinical trial and the next 35 were from the postmarket launch surveillance. Adverse event rates were comparable to those of axial flow devices. Bleeding requiring surgery was less than expected in axial flow support, while driveline and pocket infection were comparable. Overall neurological events were higher than expected for axial flow devices at 0.56 per patient year of support, with a high rate of fatal hemorrhagic stroke. This was recognized early in the trial and the anticoagulation regimen was reduced.

The HeartWare HVAD gained rapid popularity in part because of its small size. Although it uses the same blood acceleration principle as the DuraHeart, its overall displacement is small enough to allow the body of the pump to be placed intrapericardially, thus avoiding the need for a preperitoneal pocket. The ADVANCE BTT trial, published in 2012, enrolled 140 patients in 30 centers. ADVANCE demonstrated that 92% of the patients successfully made it to transplant or survived to 6 months. The adverse event profile was favorable compared to an INTERMACS propensity matched cohort. Patients had a marked improvement in functional capacity and quality of life that matched those obtained with heart transplant. Initial concerns with stroke incidence were addressed halfway through recruitment in the trial with an improved ventricular coring device and a sintered inflow cannula. This decreased ischemic strokes with permanent deficits by nearly half. FDA approval of the HVAD for BTT in 2012 allowed widespread use of both the HVAD and the HeartMate II in North American BTT patients.
The adverse clinical events related to mechanical circulatory support, infection, neurologic complications, and pump thrombosis are pushing the field toward innovation and engineering improvements. The HeartMate 3 is a new centrifugal flow pump engineered to optimize fluid dynamics. It involves a magnetically levitated rotor and wide blood-flow passages that are designed with the intent to reduce blood shear stress exposure. In addition, the wide blood-flow passages facilitate rapid rotor speed changes, allowing for the introduction of an artificial pulse with intent to disrupt regions of stasis within the pump and provide a degree of native pulsatility. Initial studies in Europe allowed for CE Mark approval. In the United States, The Multicenter Study of MagLev Technology in patients undergoing mechanical circulatory support therapy with HeartMate3 (MOMENTUM 3) trial began in September 2014. It has as primary objective to evaluate the safety and effectiveness of the HM3 Left Ventricular Assist System by demonstrating non-inferiority to the HeartMate II. Secondary objective includes the assessment of adverse events, quality of life, functional status, device malfunction rates. The study population includes a short-term cohort (6-month follow-up) and a long-term cohort of a total of 1,028 patients for evaluation of the secondary end-points of pump replacement at 2 years.

The 6-month report demonstrated that the HeartMate 3 was associated with a higher rate of survival free of disabling stroke or survival free of reoperation to replace or remove the device. The hemocompatibility profile of the HeartMate 3 was superior and was associated with the absence of medically or surgically managed pump thrombosis and marked reduction in non-disabling strokes. In 289 patients, survival free of any hemocompatibility related clinical adverse events was achieved in 69% of the HM3 group and in 55% of the HMII group \( (P = 0.012) \). There was no difference between the two left ventricular assist system (LVAS) in disabling strokes, which typically represent a devastating non-surgical bleeding complication. The results of two-year follow-up will be published in 2018.

**Biventricular support**—Patients requiring biventricular support can be categorized in two classes: those requiring temporary support during the placement of a durable LVAD and those requiring long-term biventricular support. The former group often utilizes an extracorporal pump (i.e., CentriMag or Thoratec percutaneous ventricular assist device (PVAD)) in the hope that LVAD support will satisfactorily unload the pulmonary circulation and thus allow the RVAD to be removed within a relatively short-period of time (days–weeks). In an INTERMACS report of 10,542 patients, 579 patients required biventricular support. Although it is difficult to discern if some of these patients only required short-term RVADs, it is thought that 5–10% of HF patients will require this level of support. The Thoratec paracorporeal or intracorporeal VADs are the most commonly used devices for this situation. More recently, use of tandem CF devices—one for the RV, the other for the LV—has been successfully reported with both the HeartWare and Jarvik devices.

In the latest INTERMACS report, 396 total artificial hearts (TAH) were reportedly implanted with a 12-month survival less than 60%. Although used somewhat rarely, the TAH—its development and use—has played a vital role in the history of mechanical
support (Table 11.1). The most complete set of data on the Cardiowest comes from Copeland and his colleagues from University of Arizona. Five centers enrolled 130 patients in a prospective, non-randomized study from 1993 to 2002. Nearly 80% of patients receiving the Cardiowest survived to transplant compared with only 46% in the control group. The overall one-year survival rate of patients receiving TAH was 70% compared to 31% of controls. In comparing the 1- and 5-year survival rates in patients who received an organic transplant, those bridged to transplant with the TAH group had 86% and 64% survival rates, respectively, while the controls were 69% and 34%, respectively. As would be expected, infection and bleeding were the most common adverse early events. However, only two patients died secondary to these complications. Ultimately, this study provides reassuring evidence for the potential use and standardization of the TAH as a successful means to bridge patients to transplantation with improved survival rates and improved outcomes in quality of life. This latter point has become even less of an issue, as a portable driver is now available.

**Destination therapy (DT)**

Fundamentally, destination therapy is an evolution of bridge to transplant. BTT was designed to provide life-sustaining support for patients awaiting transplantation. To even consider a device as a permanent therapy for a patient, a device must enable a patient to be discharged from the hospital. At minimum, it must be implantable, it must grant the patient mobility, and must be reasonably straightforward to care for and manage. Device requirements are further complicated by the nature of the DT patient population. Because they are not transplant candidates, they are either older than, or have more comorbidities than, the BTT population. In the mid to late 1990s, device technology matured to the point where clinical trials of devices for DT could begin. With the publication of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) in 2001, DT therapy began in earnest.

From 1998 to 2001, 129 patients with NYHA Stage IV heart disease that were not eligible for transplantation were randomized to either optimal medical management or LVAD therapy with the HeartMate VE vented electrical device. The survival benefit of LVAD therapy was both statistically significant and clinically relevant: LVAD patients had a 48% reduction in the risk of death from any cause compared to optimal medical therapy. Quality of life was also assessed with numerous measures, with most demonstrating a significant improvement over medical therapy. Perhaps most importantly, those patients treated with LVAD achieved on average a NYHA level II, while those treated medically remained level IV. Despite this incredible survival advantage, LVAD therapy was associated with several major limitations including an infection rate of 28% by 3 months and a bleeding rate of 42% at 6 months. Device failure among patients that lived 24 months was 35%. The neurologic dysfunction rate, including stroke, TIA, and encephalopathy, was 0.39 events per patient year, approximately 4.35 times that of the medical group. Summarily, REMATCH was the first major study to demonstrate the viability of LVADs
as a meaningful therapeutic option for severe heart failure patients, and in doing so, set
the minimum criteria for DT VAD therapy (Figure 11.1).

In 2005, the four largest centers from the Thoratec DT registry pooled their results from
2003 and 2004 and reported significantly improved results relative to REMATCH, using
the HeartMate XVE device. They demonstrated less neurologic dysfunction, fewer infec-
tions, less bleeding, and overall improved survival, reporting a 40% reduction in mortality
relative to the REMATCH LVAD therapy group. These improvements were likely related
to the institutional experience at these high-volume centers, as well as some technical
modifications to the HeartMate device.

By establishing a clear superiority of LVAD over optimal medical management for end-
stage heart failure patients, REMATCH has redefined the way in which new devices are
trialed for DT. Most recently, the CF HeartMate II was compared to its predecessor in
a 2:1 head-to-head trial for DT. Similar 1- and 2-year survival with the XVE during
REMATCH was observed (55% and 24%, respectively). Comparatively, HM II survival at
1 and 2 years was markedly improved (68% and 58%, respectively). Of the patients sur-
viving 2 years in the pulsatile flow group, 18 had had their device changed to a HeartMate
II during the trial for reasons of mechanical failure or infection. Quality of life was also
better in the HMII arm of the trial, with 40 (of 50 surviving) patients achieving a NYHA
functional class of I or II at 24 months. By comparison, only one of the 55 patients im-
planted with the HM XVE was both still alive and still had his device at 2 years. All of the

Figure 11.1 Comparison of survival for destination therapy patients with the HeartMate
I (pulsatile) and HeartMate II (continuous flow) pumps.
Reproduced from Fang JC. Rise of the machines—left ventricular assist devices as permanent therapy for advanced
the Massachusetts Medical Society.
complications reviewed favored patients with the HM II CF device, with significant benefits in pump replacement, infection including sepsis, right heart failure requiring extended inotropic support, arrhythmia, respiratory failure, and renal failure. Thrombosis was the only major comorbidity in which the CF LVAD was worse, with 4% of patients having a thrombosis event, whereas none of the pulsatile flow patients experienced thrombosis. Overall, the HeartMate II has demonstrated a clear benefit over the HeartMate XVE, and has evolved to become the new standard to beat.

The ENDURANCE trial randomized 297 patients ineligible for transplant from 48 US centers to either a centrifugal flow LVAD (HeartWare, study device) or an axial flow LVAD (Heart Mate II, control device). The 2-year follow-up analysis of the primary end point showed that the study device was non-inferior to the control device with respect to survival free from disabling stroke or need for device replacement. There was also a sustained improvement in functional and quality-of-life measures. Importantly, the HVAD had more strokes, predominately hemorrhagic, occurring within the first 6 months, after which the rate of stroke decreased (29.7% vs. 12.1%, $P < 0.001$). Changes in the protocol to mandate strict blood pressure control with a mean arterial pressure of 90 mmHg or lower was accompanied with a subsequent 34% decrease of risk of stroke among those patients. Finally, no significant difference between the two devices in the rate of pump exchange because of device thrombosis was identified. Based on results from the ENDURANCE and ENDURANCE Supplement trials (which enrolled 465 patients to be followed up for a total of 5 years) the FDA approved the HeartWare HVAD system for destination therapy in patients for whom subsequent transplantation is not planned, in September 2017.

Extended survival with the current and newer generation of cardiac assist devices, HeartWare, and HM3, has helped providers to the following terms: bridge to decision (BTD) or bridge to candidacy (BTC). This is a subset of destination therapy patients that are not too old to receive a transplant, but instead are prohibited by comorbidities that are consequences of their heart failure. With the rehabilitation facilitated by their device, and the improved end-organ perfusion they achieve, they are able to reach a state where they may actually be considered for transplant. Most commonly, this has been observed in patients with pulmonary hypertension refractory to inotropic challenge. Several papers have documented regression of pulmonary hypertension with chronic unloading of the left atrium by assist device, to the point where transplant becomes feasible.

### Surgical implantation

Despite the variety of pumps available, issues related to surgical implantation remain the same. That is, most devices use the apex of the left ventricle as the inflow site to the pump that subsequently gives off an outflow graft to the aorta, thus bypassing the ailing left ventricle. Herein, we will describe some of the issues related to implantation of LVADs. Although there are many types of devices currently available, the general approaches are similar.

**Patient selection**—Although most patients listed for transplant are at some level candidates for mechanical circulatory support, there are several compelling issues that might
lead a group to go straight to transplant. These include multiple reoperations, congenital heart anomalies, restrictive heart disease with small ventricles, and other surgical issues (i.e., previous pericardectomy). These are all relative contraindications. The most important contraindication to LVAD therapy is the ability of the right ventricle to support LVAD flows. Although it is not unusual (<10% of implants) to require temporary RVAD support at the time of LVAD, if one has a high suspicion of RV failure (severe dysfunction, low right ventricular stroke work index, high right atrial pressures, low pulmonary artery pulsatility index) then the best options are either biventricular assist devices, total artificial heart, or transplant. The emergence of destination therapy has created a different set of issues as many of these patients are older with end-organ dysfunction and seen as last-option or even heroic implants. Rigorous assessment of their ability to survive and thrive after LVAD needs to be seriously evaluated by a multidisciplinary team.

**Perioperative considerations**—Standard cardiac surgery anesthesia is utilized with LVAD procedures. Although most procedures are done with the use of cardiopulmonary bypass, many centers will maintain low tidal volume ventilation during bypass to theoretically decrease post-pump pulmonary vascular resistance. Antifibrinolytic therapy is usually used and blood products are used as indicated. Some centers rely heavily on thromboelastography and more recently rotational thromboelastometry (ROTEM) for guiding replacement therapy.

Most LVAD procedures can be performed without systemic cooling and routine measures for cardiopulmonary bypass are used. As most of the HF patients are fluid overloaded, perfusionists should utilize ultrafiltration, if possible, and avoid excessive hemodilution. Cell saver should be replaced with concomitant, liberal use of fresh frozen plasma (2–3:1). In patients with heparin-induced thrombocytopenia, successful LVAD implants have been performed, albeit with additional risk, using alternative anticoagulants such as bivalirudin or argatroban. Additional strategies to minimize perioperative bleeding complications include the use of desmopressin acetate (DDAVP), discontinuation of aspirin for elective LVAD placement, a strong focus on a short pump run, synthetic factor replacement, and delayed primary closure, although none of these strategies have been studied explicitly.

Postinsertion attention is focused on decreasing pulmonary vascular resistance and protecting right ventricular function. Some centers will routinely use nitric oxide or inhaled epoprostenol on each case. All efforts are aimed at reducing transfusion requirements as well as avoidance of hypoxia, hypercarbia, and acidosis. Several preoperative risk factors are associated with right ventricular (RV) failure including female sex, non-ischemic cardiomyopathies, elevated central venous pressure, right ventricular stroke work index, and previous cardiac surgery. More sophisticated echocardiographic measurements, including an increased RV-to-LV end-diastolic ratio (>0.72) can also predict postoperative RV failure. Intravenous pulmonary vasodilators are used routinely, including nitrates and phosphodiesterase inhibitors (milrinone). Inotropic support for the right ventricle is also routinely used (milrinone, epinephrine, dobutamine). There is recent enthusiasm to use sildenafil both pre- and perioperatively in these patients. For very sick right ventricles,
it might be necessary to support the RV mechanically for several days (e.g., RVAD with CentriMag device).

**Surgical implantation**—Although individual surgeons and centers have different methods of inserting the device, the fundamental concepts outlined remain true for all. The sequence of implantation can vary also from patient to patient depending on their particular situation.

The majority of LVADs are placed in the supine position standard to any cardiac surgery operation. This standard position can be used for several non-sternotomy approaches as well. For example, some pumps (notably the Jarvik 2000) have been placed through a left subcostal incision with the outflow to the supraceliac aorta. Others have used a left subcostal incision and tunneled the outflow graft to the ascending aorta through a counterincision in the right third interspace or mini upper sternotomy. A left thoracotomy approach can alternatively have the outflow graft anastomosis to the descending thoracic aorta. This latter technique has been most often used with the off-cardiopulmonary bypass approach using the Jarvik 2000 LVAD, but has been successfully used for several other small pumps as well. In these cases, the patient should be positioned in the left lateral position with the hips turned back to give access to the left femoral vessels if needed.

After anesthesia, monitoring lines, and positioning, median sternotomy is performed. In many cases, this will be a redo-sternotomy. If the patient has a hostile mediastinum (multiple surgeries, recent surgery, congenital heart disease, right ventricular enlargement, or substernal grafts), alternative forms of cannulation for cardiopulmonary bypass should be considered. Arterial inflow can be accessed through the subclavian or femoral arteries (we usually sew a side-armed graft on the vessel) and venous return is through a long femoral venous cannula placed under transesophageal echocardiography (TEE) guidance with the tip in the superior vena cava (SVC).

Before full heparinization and sternal re-entry, many will try to develop the LVAD pocket. For the HeartMate 2 device, full creation of the pocket is made easier when the sternum is open. Two schools of thought regarding the pocket creation exist: within the preperitoneal space or between the posterior rectus sheath and the rectus abdominis muscle. The latter was routinely performed with the larger pumps to avoid peritoneal erosion. That said, with the smaller pumps, requiring smaller pockets, many have gone back to the preperitoneal approach just under the diaphragm. Most will take down the anterior slip of diaphragm laterally to allow the inflow cannula to orient correctly. Either electrocautery or a vascular endoscopic stapler can be used to divide this muscle. Be sure to check this transection line prior to closure as it often will have points of bleeding. With the emergence of the HeartWare, Jarvik, HeartMate 3, and other small size pumps, each of which can be placed inside the pericardium, many of the pocket problems will become obsolete.

The pericardium is opened, and the LV apex is identified. One of the nice features of the HeartMate II device is its inflow elbow. Theoretically this allows good placement without having to go as lateral on the pocket. The prospective sight for driveline exit is then identified. This is usually in the typical right upper quadrant position but can vary according to
the patient’s need. A tunneling device is then brought through the rectus sheath. Enough subfascial dissection should be performed on the right side to allow for tension-free closure as well as space for driveline exit.

On the backtable, the pump is prepared according to the device manufacturer. Some outflow grafts need to be prepared. Some devices require some reinforcement as well. Others are taken out of the package and are ready to go. It is beyond the scope of this review to discuss individual pump preparation especially with the excellent training provided by all the respective VAD companies with regards to their specific pump.

Depending on the pump, the outflow anastomosis can either be done before or after the inflow. The outflow graft is stretched and cut to size with a slight bevel. A side-biting aortic cross-clamp is placed and an aortotomy is created. Many will round the two ends of the aortotomy with a 4.5 mm proximal coronary punch. The distal anastomosis is sewn with any number of techniques. Some will place individual pledgeted mattresses or running sutures over felt or pericardium. After removal of the cross clamp, hemostasis is checked, and repair sutures are placed as necessary.

Aortic and right atrial cannulas are placed and, often, an aortic vent needle as well. The patient is placed on cardiopulmonary bypass and maintained at normothermia. As mentioned before, it is possible, even from a sternotomy approach, to perform this without the use of cardiopulmonary bypass.61 That said, most centers perform the remainder of the operation on bypass. The heart is elevated with the assistance of laparotomy packs in the posterior mediastinum. The left anterior descending artery is identified, thus marking the intraventricular groove. With larger ventricles, identification of the apex is fairly straightforward. On smaller ventricles, some will core a little more anterior to provide a reasonable angle. Conversely, with the newer intrapericardial devices, some will take a more inferior and posterior approach. The core is excised, the LV cavity is inspected, and further debridement of trabeculae or thrombus is performed as necessary. The alignment along the interventricular septum is examined. Large pledgeted sutures are then passed full thickness. Sutures are then mattress to get the edge of the epicardium. Usually 12–14 sutures are required, although some use less. These are attached to the sewing ring and tied. Many surgeons will put a very thin layer of BioGlue over the insertion site and pledgets.

The prospective driveline site is cored and the tunneling device is passed subcutaneously and then through the rectus at the inferior margin of the incision. The controller and pump are brought to the table. The driveline is passed and connected to the controller. During this time, we insufflate CO\textsubscript{2} into the LV cavity to evacuate air. The inflow stabilizing ring is removed. The LV cavity is inspected to make sure the inflow is clear. The inflow cannula is inserted and secured with the sewing rings suture. Tie-Bands can also be placed to further secure the cannula. Others will place several large suture ties.

At this point, the anesthesiologist and perfusionist have had ample timing for weaning. Inotropic support is going, full ventilation ensues, calcium is repleted, and the acid-base status is corrected. Some will routinely use nitric oxide or inhaled epoprostenol to assist with reduction of pulmonary vascular resistance. The aortic graft is backbled. Volume is
left in the heart and the outflow cap is loosened to help de-air the ventricle. The unkinked outflow graft is then connected. The patient is weaned off cardiopulmonary bypass or to 1–2 liters/minute of flow. The LVAD is started at its lowest RPM with the aortic clamp on to continue de-airing. With the aortic vent on, the outflow graft clamp is removed. Often there is a small rush of air bubbles visible on the long axis view of the TEE that is air around the clamp. Usually this last for less than 5 seconds and is removed with the aortic vent.

LVAD flows are slowly increased while monitoring right-sided function, pressures, and septal motion. Often no flow will be recorded on the monitor, but the patient will be doing just fine. Avoid the temptation to quickly increase RPMs to get high flows. Most centers will leave the operating room without full decompression as long the hemodynamics are suitable. Often the “final” settings on the pump are often not made for days after the implant. Protamine is administered, and all of the cannulas are removed. Chest and mediastinal tubes are placed.

Final position of the LVAD within the chest, especially without the retractor, should be viewed under TEE. In particular, the inflow cannula should be directed slightly posterior toward the mitral valve. TEE is crucial for this procedure. In addition to evaluating cannula location, TEE can identify valvular problems (see next). Importantly, a bubble study needs to be performed with the LVAD on in order to identify a patent foramen ovale (PFO). With heart failure patients with high left-sided pressures, these defects can be difficult to detect until the left side is decompressed. If identified, the PFO needs to be repaired.

Some centers have advocated an aggressive policy of leaving the chest open for 1 day to allow for stability prior to chest closure. Our approach is to leave the chest open if there are ongoing bleeding concerns or if we are worried about RV functional decline associated with sternal compression. Leaving the sternum open can be an excellent strategy for the marginal patients.

At the beginning of 2011, an increase on the incidence of pump thrombosis with the Heart Mate 2 led to the PREVENTion of Heart Mate II Pump Thrombosis Through Clinical Management (PREVENT) prospective, multicenter, non-randomized study. Strict adherence to surgical recommendations, anticoagulation, and antiplatelet management, pump speed management, and blood pressure control with the Heart Mate II implantation demonstrated lower rate of confirmed pump thrombosis at 3 months post implant (2.9%), lower than what was hypothesized (4%).

For BTT, it is helpful to prepare for the re-entry that will occur with transplant. For starters, attention to spacing of the aortic cannulation site and outflow graft can help leave space for recannulation, aortic cross clamp, and a cuff of sewable aorta. Some will place vessel loops around the SVC and inferior vena cava (IVC) to allow for the identification. We have done this with some reoperative LVAD patients, yet, if possible, we try not to create dissection planes if not necessary. We take a piece of spare graft to cover the outflow graft from the edge of the bend relief to the aorta. We then place a piece of 1 mm GoreTex to the base of the pericardium on the left side where it joins the diaphragm
and use interrupted sutures to reconstruct the pericardium and isolate the LVAD. In particular, we try to separate the left lung from the device as this can be quite traumatic at the time of explant. Other barrier products (CorMatrix) can also be used to help with transplant reentry.

Increasingly, VAD surgeons are tunneling further through the abdomen in order to bury more of the driveline. One approach is to bring the driveline out first through a counterincision in the right upper quadrant and then retunnel to exit in the patient’s left upper quadrant. Alternately, the counterincision can be made in the right lower quadrant, and the driveline then brought back up and out in the right upper quadrant. Thoratec recently presented registry results for patients in which the entire velour component of the driveline is buried, showing an 85% freedom from driveline infection at two years compared to 65% in the HeartMate II DT Trial. At operation, we use two #1 Prolene sutures to provide traction relief around the exit site that are removed 4–6 weeks after surgery.

Other considerations

Several issues require additional commentary that can complicate what often can be a very straightforward operation.

- **Coronary artery disease and prior grafts**: Coronary artery disease for LVAD patients is mostly related to the right ventricle. In a right dominant system with significant right coronary artery (RCA) disease, a bypass graft to that coronary would be advisable. If possible, protect all patent grafts at the time of reentry.

- **Valvular disease**: Many patients have either had prior valve operations or have concomitant and significant valvular disease. The risks and benefits of additional valve procedures remain controversial. Some general, but valve-specific guidelines include:
  - **Aortic stenosis**: Generally, not a problem and can be left alone.
  - **Aortic insufficiency**: Needs to be fixed if anything more than mild. Options include bioprosthetic aortic valve replacement (AVR), oversewing the valve with a Hemashield patch, and approximation of the Nodes of Arantius. The particular option is debatable between multiple centers. Although there is much enthusiasm for the relatively ease of oversewing the valve, this makes the patient completely LVAD dependent for LV ejection.
  - **Prosthetic AVR**: No problem if bioprosthetic; currently no data on what to do with mechanical AVR. Some think it would be best to oversew or replace with a bioprosthetic (especially if DT or BTR). The sandwich plug technique is also a simple, safe, and effective way to close the valve. Others might consider leaving it in place.
  - **Mitral stenosis**: This needs to be repaired to allow for LV inflow. Options include tissue valve replacement or, if amenable, valvuloplasty.
  - **Mitral regurgitation**: Mitral valve repair can be done at the time of implantation either transatrially with placement of a mitral annuloplasty ring, or an Alfieri stitch can be placed through the ventriculotomy. Valve repair has been shown to assist with
decreasing pulmonary vascular resistance, but to date there is no conclusive evidence that overall outcomes are improved with repair. This may be most beneficial in bridge to transplant (or BTC) patients with high pulmonary vascular resistance.

- **Prior mitral valve replacement (MVR):** Can be left in place.
- **Tricuspid regurgitation:** Some centers have demonstrated improved outcomes with tricuspid valve annuloplasty or replacement in the setting of moderate to severe regurgitation and/or annular dilatation (>4.2 cm) at time of LVAD implantation. Other centers have been unable to demonstrate similarly conclusive findings, so the standard of care is yet to be defined.

- **Anticoagulation:** Most centers will administer warfarin when the patient is extubated and taking oral medications with an ultimate goal of 2.0–3.0. If a delay in anticoagulation is anticipated, heparin is administered. Some patients with the HeartMate II LVAD have been successfully managed either off coumadin or with lower target INRs. All patients receive aspirin, either low- or high-dose. Many will add other antiplatelet agents such as dipyridamole or clopidogrel. Some centers will also use outpatient thromboelastography to help drive their therapy. The intensity of anticoagulation has recently come under increased scrutiny in the VAD community. Recently, three major implant centers published findings of dramatically increased pump thrombosis in the HeartMate II device. At 18 months, thrombosis rates increased from 5% in 2011 to 15% in 2013. Until the reasons for this finding are further clarified, clinicians may return to erring on the side of more anticoagulation. More concerning, these findings have led some centers to slow recruitment into trials of early LVAD therapy for Stage IIIB heart failure patients.

- Other circumstances can alter surgical strategies and need to be planned for including previous heart operations, congenital heart disease, and prior ventricular reconstruction.

Importantly, the success of the LVAD implantation is more than the technical performance of the operative procedure. Judicious preoperative evaluation and preparation must be combined with vigilant postoperative management, both for the usual issues in the intensive care unit, as well as those as an outpatient. We cannot overstate the importance of an active and engaged multidisciplinary team.

### Complications

Advances in patient management, as well as technical advances in miniaturization, pump, efficiency, and battery power have made LVAD therapy safer and more applicable to a wider range of patients than ever before. Still, LVAD therapy continues to be associated with significant morbidity and mortality. Table 11.3 lists some of the major adverse events and their general incidence based on the recent HeartMate II and HeartWare CF device data. The operative mortality for these patients ranges between 2% and 30%, mostly dependent on the INTERMACS level of the patient as well as if the device is placed for
BTT or DT. Well-known complications include bleeding requiring reoperation or transfusion, neurologic events including stroke (both ischemic and hemorrhagic), infections (LVAD related, and remote), arrhythmia, respiratory failure, renal failure, hepatic dysfunction, hemolysis, pump thrombosis, and rehospitalization. In addition, many of these patients will be readmitted for heart failure as diuretic and right ventricular dysfunction is managed.

Several particular intraoperative complications should be noted. Foremost is right ventricular failure. There is a trend by many centers to take an aggressive approach for temporary RVAD support. Rather than leave the operative suite on high-doses of multiple inotropes and vasoconstrictors, many would rather place a temporary RVAD to allow for hemodynamics and coagulopathic stabilization. This pump can usually be removed within 5 days. Another potentially catastrophic intraoperative complication is related to air embolism. Although some air is to be expected, especially as pumping is initiated, persistent air entrainment should lead to suspicion for apical disruption of the inflow cannula.

Three particular long-term complications are becoming more problematic as more patients are being supported and for longer periods of time:

1. *Aortic insufficiency*: The native aortic valve is under a different pattern of shear stress with CF valves and is prone to develop leaflet fusion and hemodynamically significant aortic insufficiency. As just discussed, an aggressive approach to aortic valve pathology is important, especially with long-term use patients. Postoperatively, there is evidence to suggest that aggressive blood pressure control and intermittent aortic

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**Table 11.3** Common adverse events associated with LVAD therapy

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infection</strong></td>
<td></td>
</tr>
<tr>
<td>LVAD related</td>
<td>18–35%</td>
</tr>
<tr>
<td>Non-LVAD related</td>
<td>14–46%</td>
</tr>
<tr>
<td><strong>Neurologic dysfunction</strong></td>
<td></td>
</tr>
<tr>
<td>Stroke (ischemic or hemorrhagic)</td>
<td>8–18%</td>
</tr>
<tr>
<td>Other (TIA)</td>
<td>5–17%</td>
</tr>
<tr>
<td><strong>Bleeding requiring reoperation</strong></td>
<td>15%</td>
</tr>
<tr>
<td><strong>Right heart failure</strong></td>
<td></td>
</tr>
<tr>
<td>Prolonged inotropes</td>
<td>20–30%</td>
</tr>
<tr>
<td>RVAD</td>
<td>3–5%</td>
</tr>
<tr>
<td><strong>Pump replacement</strong></td>
<td>7–10%</td>
</tr>
<tr>
<td><strong>Hepatic dysfunction</strong></td>
<td>3%</td>
</tr>
<tr>
<td><strong>Renal dysfunction</strong></td>
<td>8–15%</td>
</tr>
</tbody>
</table>
valve opening may decrease the progression of aortic insufficiency (in addition to decreasing the frequency of neurologic events).\textsuperscript{74} For symptomatic severe aortic insufficiency, reoperation for valve closure, valve replacement, and the use of transcatheter valve replacement have been shown to be reasonable and effective.\textsuperscript{75}

2. \textit{Acquired von Willebrand syndrome:} As mentioned previously, axial flow is associated with the development of acquired von Willebrand syndrome.\textsuperscript{76} The breakdown of the vWF multimers appears to be one of many different factors associated with major bleeding issues including subarachnoid hemorrhages, epistaxis, and importantly, gastrointestinal bleeding.\textsuperscript{77,78} HeartMate 2 and HeartWare have shown the same degree of vWF factor break down and large multimers loss. However, the HeartMate 3 centrifugal pumps demonstrated a significantly lower level of high-molecular-weight multimers degradation compared with the Heart Mate II. This finding did not translate to functional difference in von Willebrand factor (VWF) activity between these devices.\textsuperscript{79} How bleeding and thrombotic complications will be affected by the engineering changes of the HeartMate3 will require further study.

3. \textit{Driveline infections:} As the durability of the actual pump has increased, more attention has focused on issues related to the power source. Driveline infections as well as cable damage are important causes for pump exchange, are associated with worse transplant outcomes, and cause significant psychologic stress on the patients. Transcutaneous energy transfer technology is still actively being investigated. The skull pedestal implant of the Jarvik 2000 LVAD is one novel approach to dealing with driveline issues that has been particularly successful in over 110 European patients.

\textbf{The future}

The evolution of technology, along with the development of dedicated care teams, has allowed LVAD therapy to become an integral and highly effective component of any advanced HF center. Perioperative and long-term medical strategies will continue to be refined. Peripheral components are becoming lighter, and more user-friendly. Removing the driveline component of VADs, as demonstrated by the actively used skull pedestal implant with the Jarvik 2000, or the ongoing development of transcutaneous energy technology will provide even more freedom for patients that require these pumps for lifetime use. The next generation of pumps from multiple different vendors will be smaller and more efficient (i.e., CircuLite, HeartMate 3, HeartWare’s MVAD).\textsuperscript{80} This detail will be important as the field moves to implant mechanical devices in patients that are less ill and perhaps do not require full replacement of their cardiac output. Broadening indications to class III patients will necessitate pumps that can be placed, and potentially removed, less invasively. This latter point is further highlighted in the enthusiasm to promote myocardial recovery. Device technology has progressed so much that providers and patients feel comfortable with its routine use (not to say improvements to the morbidity profile are not needed). As such, less attention will be focused on the study of the pumps, but rather on the study of the heart. Indeed, mechanical circulatory device companies have
traditionally focused on whether or not their pump will work or not; how they handle blood, or how long the pump will last. With newer, smaller devices, physicians will again be able to focus on the biology of the heart and use these pumps to provide pressure/volume relief while simultaneously delivering adjuvant biologic therapies. This latter direction within the field remains in its infancy.

References


Chapter 12

Current status of heart transplantation

Ayyaz Ali and Robert L. Kormos

Introduction

Cardiac transplantation represents one of the major medical advances of the twentieth century. Since its introduction it has extended and improved the lives of patients suffering from severe heart failure. Despite advances in medical therapy, cardiac transplantation remains the definitive treatment for end-stage heart disease. The success of heart transplantation was made possible by prior landmark achievements in the transplantation of other solid organs, primarily renal transplantation. Extensive laboratory research provided the foundation for the development of this procedure. Surgical techniques for organ procurement and implantation, development of appropriate methods for preserving the heart, and understanding the immunological challenges associated with transplantation were among the many areas which required focused investigation. In the current era, heart transplantation is associated with a low operative mortality and excellent long-term survival.\(^1,2\) Furthermore, alleviation of symptoms of heart failure following transplantation has transformed the lives of patients with severely impaired cardiac function.\(^3,4\) A major obstacle to the more widespread application of heart transplantation is a shortage of suitable donor organs.\(^5\) Consequently, strategies aimed at expanding the donor pool have been actively implemented. The use of marginal donor organs describes a policy where criteria used to describe adequate function of the organ are made less stringent. Consequently, organs which may previously have been discarded on the basis of borderline performance or adverse characteristics, such as left ventricular hypertrophy or depressed left ventricular ejection fraction, have been utilized for transplantation.\(^6–8\)

History of cardiac transplantation

Alexis Carrel and Charles Claude Guthrie were responsible for pioneering early techniques for transplantation of the heart, lungs, and other organs. In 1905 Carrel reported the first successful heterotopic heart transplant in a canine model.\(^9,10\) In 1933, Frank C. Mann and James T. Priestley described survival of up to 8 days in a canine model of heterotopic heart transplantation.\(^11\) They observed that explanted hearts were infiltrated with lymphocytes, mononuclear cells, and neutrophils. They correctly suggested that the success of transplantation was limited not by technical factors but by unidentified biological factors, later identified as allograft rejection. The next advance in cardiac
transplantation was made by Vladimir Demikhov who performed the first intrathoracic heterotopic cardiac transplant, once again using a canine model. He reported survival of up to 32 days. In the 1960s Norman Shumway and Richard Lower established a dedicated research program at Stanford University which they aimed to translate into a clinical program of human cardiac transplantation. They reported that the major obstacle to long-term survival of cardiac allografts was rejection and that without immunosuppression, extended graft survival would be impossible. Adrian Kantrowitz and Yoshio Kondo, working at Downstate Medical Center in Brooklyn, New York, demonstrated prolonged survival of up to 112 days after heart transplantation in puppies without any immunosuppressive therapy. The suggestion that newborn animals may possess an immunological advantage encouraged Kantrowitz to later attempt cardiac transplantation in infants.

The first heart transplant operation in a human was performed in 1964 by James Hardy on the background of several years of laboratory research. The donor heart was obtained from a chimpanzee. Their intention had been to use a human heart, but the condition of their recipient did not permit them to wait for a human organ to become available. The decision to use a chimpanzee heart was based on an experience of transplantation of kidneys from chimpanzees into humans. Although the xenograft demonstrated good function within the recipient, it was unable to support the circulation after separation of the recipient from cardiopulmonary bypass.

On December 3, 1967, the first human-to-human heart transplant was performed by Christiaan Barnard in Cape Town, South Africa. The recipient was a 53-year-old male with ischemic cardiomyopathy named Louis Washkansky, suffering from severe biventricular failure. The donor was a 25-year-old female who had suffered severe head injuries after being hit by a speeding car. At that time in South Africa there was no legislation for the designation of brain death as being synonymous with circulatory death. Therefore, cardiac arrest was awaited after withdrawal of life support and was deemed necessary for declaration of death. Immediately after the heart had stopped the donor was placed on cardiopulmonary bypass (CPB) and the coronary circulation was reperfused with oxygenated blood to resuscitate the heart. Hypothermia was established to facilitate preservation and protection of the heart prior to transplantation. The patient survived the operation but died of pneumonia on the eighteenth postoperative day. The transplant attracted the attention of the entire world and was one of the most publicized medical events in history. Three days after the transplant in South Africa, Adrian Kantrowitz performed the second human heart transplant in Brooklyn. This was undertaken in an 18-day-old infant with severe cardiac failure due to congenital heart disease. The donor heart was obtained from an anencephalic infant. The recipient died 5 hours after implantation of the heart due to poor graft function. Toward the end of 1968, 102 heart transplant operations had been performed in 17 different countries around the world. The results of the procedure were disappointing with a 60% early mortality rate and a mean survival of 29 days. By 1970 this had led to a wide-scale abandonment of the procedure with only a few institutions continuing with clinical cardiac transplantation. Dr. Shumway persisted with the procedure with intensive efforts
recipient management

Patients awaiting a cardiac transplant should receive optimal medical therapy for heart failure. Angiotensin-converting enzyme (ACE) inhibitors, beta blockers, and diuretics are used in varying combinations. Patients in severe heart failure can be stabilized hemodynamically with inotrope therapy. The use of an intra-aortic balloon pump can...
further augment hemodynamics in critically ill patients with heart failure. A selected group of patients with severe refractory heart failure may be candidates for mechanical circulatory support with a ventricular assist device (VAD). Such devices are indicated if patients remain unstable despite a period of conventional support. VAD’s are used to stabilize or “bridge” a patient until a suitable donor heart becomes available. In patients with a history of inducible ventricular tachycardia or fibrillation, the placement of an automatic implantable cardioverter-defibrillator may reduce the likelihood of sudden cardiac death. Sudden cardiac death is the commonest cause of death in patients awaiting heart transplantation and is most common in the first 3 months after listing.

**Organ procurement and preservation**

Routine evaluation of the cardiac donor includes a review of biographical data such as height, weight, gender, and blood type. Laboratory tests are taken for serology, hematological, and biochemical analysis. Hemodynamic status of the donor is scrutinized, and specific investigations include an electrocardiogram (EKG), chest X-ray, and echocardiography. Swan-Ganz catheterization can be undertaken for more detailed assessment of hemodynamic function. Coronary angiography is recommended in male donors aged greater than 45 and females older than 50. In donors with risk factors for coronary artery disease or history of cocaine abuse angiography is obtained regardless of age.

Brainstem death results in physiological derangements which culminate in hemodynamic instability. The culprit is an increase in serum catecholamines in response to brainstem ischemia. An initial hyperdynamic phase with hypertension, tachycardia, and subendocardial ischemia is followed by vasodilatation, autonomic dysfunction, and dysrhythmia. The severity of this response is proportional to the extent of brain injury. Aims in management of the donor are to restore stable hemodynamics with a mean arterial pressure greater than 60 mmHg and a central venous pressure in the range of 6–10 mmHg. Swan-Ganz catheterization allows for more accurate assessment, evaluation, and control of hemodynamics. Exogenous catecholamine administration is minimized as it can deplete ATP stores in the donor heart which may impair post-transplant function. Vasopressin is used for maintenance of blood pressure and to treat coexisting diabetes insipidus. Hormonal replacement, with insulin, triiodothyronine, and steroid therapy, is also commonly administered. Volume replacement and maintenance of fluid, electrolyte, and acid-base balance are important in maintaining cardiovascular stability within the organ donor.

Final assessment of the donor heart is undertaken in the operating room. A median sternotomy is performed and visual assessment of cardiac function is undertaken. The superior vena cava (SVC) is dissected and encircled with a tie. The azygos vein is identified and ligated. The inferior vena cava (IVC) can be encircled between finger and thumb which facilitates its separation from the right inferior pulmonary vein. Heparin is administered intravenously (300 units/kg). Prior to the application of a cross-clamp across the
ascending aorta, the SVC is ligated close to its junction with the innominate vein. The donor heart is vented to prevent distension by incising the IVC and left superior pulmonary vein. Alternatively, the left atrial appendage is transected if the lungs are being procured. The aorta is clamped and cardioplegia is infused into the aortic root. Cold saline solution or slushed ice is copiously applied around the donor heart to augment preservation. The donor left atrium is incised; if the lungs are being procured, care is taken to preserve a cuff of left atrial tissue incorporating the pulmonary veins, otherwise the left atrium can be incised at the pulmonary veins. The ascending aorta, pulmonary artery, SVC, and IVC are transected and the donor heart removed and placed into a container with cold preservation solution. Further packaging is undertaken using sterile bags and the organ is surrounded by ice and transported.

Preservation of the donor heart relies on methods of myocardial protection to minimize injury during procurement, storage, transportation, and implantation of the organ. Hypothermia remains the cornerstone of most preservation strategies. Crystalloid cardioplegic solutions (4–10°C) are most commonly utilized for perfusion of the aortic root and their composition can vary widely. These solutions are categorized based on their constituents as either intracellular or extracellular solutions. Intracellular solutions have higher concentrations of potassium and lower sodium content; their purported benefits relate to avoidance of cellular edema. Bretschneider (HTK), University of Wisconsin, and Euro-Collins solutions are commonly used intracellular solutions. Extracellular solutions have higher concentrations of sodium with lower potassium levels due to concerns over cell damage secondary to hyperkalemia. This category includes St. Thomas’s hospital solution, Celsior, and Krebs solutions. Cardiac distension is avoided during administration of the preservative by insuring that both the right and left heart are vented as described just now. The maximal tolerable cold ischemic period is between 4 and 6 hours. Increasing cold ischemic times are associated with a higher incidence of donor organ dysfunction and primary graft failure. After removal from cold storage, the organ is subjected to warm ischemia as it is exposed to room temperature. Cardioplegic solutions are often administered into the aortic root immediately following removal of the organ from its storage container. Further doses can be administered intermittently during the course of implantation.

Machine perfusion and continuous delivery of preservative solutions have been advocated as a means of improving myocardial preservation. Such methods may allow an extension of the maximum period of cold ischemia to which the donor organ can be exposed. Concerns remain over the development of myocardial edema due to the large volumes of perfusate that may be infused. More recently, the development of devices that allow for continuous warm perfusion of the donor heart with oxygenated blood has been suggested as a means to improve organ preservation. These devices may also offer the potential for resuscitation and biochemical and functional assessment prior to implantation. The use of machine perfusion remains largely experimental and substantial clinical experience is lacking. However, it is feasible that this technology may play an important role in the future of organ preservation.
Surgical procedure

Recipient operation

Standard antiseptic preparation and draping is undertaken and the thoracic cavity is accessed via a median sternotomy. A proportion of patients will have had a prior sternotomy for previous cardiac surgical procedures such as coronary artery bypass grafting. Increasingly, patients with left ventricular assist devices are being bridged to heart transplantation. In both of these patient groups and particularly in the latter, dissection of the heart and institution of cardiopulmonary bypass can be difficult (CPB). Peripheral CPB can be used as an alternative if there are concerns about being able to safely institute extracorporeal circulation. Bicaval cannulation is necessary with separate drainage of the SVC and IVC. Ascending aortic cannulation is most commonly used for CPB inflow. Following the initiation of bypass, core temperature is often reduced to achieve moderate hypothermia (28°C). Both vena cavae are snared and a cross-clamp is applied across the ascending aorta. The recipient cardiectomy is then performed. An incision is made into the right atrium (RA) close to the aortic valve (AV) groove and continued along the AV groove toward the coronary sinus. The classical biatrial technique described by Lower and Shumway is less commonly performed and has been replaced by the bicaval technique, where the recipient RA is incised circumferentially to create a cuff for the IVC anastomosis. The SVC is also dissected and mobilized and divided from the recipient RA to allow for a separate SVC anastomosis. An incision is made across the atrial septum and the left atrium (LA) is incised along the AV groove leaving a cuff for anastomosis to the donor LA. Both the pulmonary artery and ascending aorta are divided above the commissures of their respective semi-lunar valves. Both vessels are separated from one another proximally to facilitate anastomosis to the donor great vessels. It is important to ensure that the recipient and donor cardiotomies are coordinated in a manner to minimize allograft ischemic time. The donor heart is removed from cold storage and prepared for implantation. Prior to this, cardioplegia can be administered to the donor heart via the aortic root. If the pulmonary vein orifices are intact, incisions are made to connect them to open the LA. Excess atrial tissue is trimmed to create a cuff for anastomosis to the recipient LA. If an RA anastomosis is undertaken as opposed to separate caval anastomoses an incision is made from the IVC toward the RA appendage. If a patent foramen ovale is identified it should be oversewn.

Implantation

The LA anastomosis is constructed with a 3-0 Prolene suture and is commenced near the left superior pulmonary vein of the recipient. The suture is passed through the corresponding area of the donor LA and the donor heart is parachuted into the pericardial cavity. Both left atria are aligned via retraction of the donor heart to facilitate the anastomosis. The suture line is continued inferiorly toward the left inferior pulmonary vein, then medially toward the septum. The second arm of the suture is used to complete the superior aspect of the anastomosis. A vent can be inserted at this time into the left ventricular (LV) via the right superior pulmonary vein to drain collateral blood entering the
LV via the pulmonary veins. The pulmonary artery anastomosis is constructed next in an end-to-end fashion using a continuous 4-0 Prolene suture. The donor pulmonary artery can be trimmed to a point about 1 cm above the pulmonary valve. If the pulmonary artery is left too long it can predispose to kinking in the region of the anastomosis. The donor and recipient aorta are anastomosed to one another using 3-0 or 4-0 Prolene, prior to tying this suture the heart is initially deaired through this anastomosis. Prior to releasing the cross-clamp warm blood “hot shot” cardioplegia may be administered to promote recovery of anerobic myocardial metabolism. An aortic root vent can be inserted to further facilitate the de-airing process after the cross-clamp is released. After the aortic cross-clamp is removed the allograft is reperfused. Using the batrial technique, a continuous 3-0 Prolene suture is used to anastomose the donor and recipient right atria. Currently the bicaval technique is preferred as it is associated with a lower incidence of arrhythmias, atrioventricular valve insufficiency, and conduction disturbances. Also, it has been associated with less right ventricular (RV) failure, shorter hospital stay, and improved 1-year survival. The IVC and SVC are anastomosed separately to the recipient cavae in an end-to-end fashion. The implantation procedure can vary significantly depending upon surgeon preference. Some prefer to complete the RA or IVC anastomosis prior to anastomosing the great vessels. Releasing the cross-clamp prior to the caval/RA connections minimizes warm ischemic time and allows time for reperfusion of the donor heart while implantation is completed. Ischemic time can further be minimized by undertaking the pulmonary artery anastomosis and even the LA anastomosis after the aortic anastomosis, although these maneuvers are technically more challenging.

Heterotopic heart transplantation

This technique of implantation is less commonly used in the current era. Recipient cardiectomy is not performed and the donor heart is anastomosed to the recipient heart with the two organs working in tandem. The principal indications for this procedure are when the donor heart is judged to be too small to support the circulation in isolation or in patients with fixed pulmonary hypertension. A left atriotomy is made in the Sondergaards groove in the recipient. A corresponding incision is made in the donor LA to connect the left inferior and superior pulmonary veins. The donor and recipient atriotomies are anastomosed such that the allograft lies to the right of the native heart. Both the donor aorta and pulmonary artery are anastomosed to the recipient great vessels in an end-to-side fashion. An interposition graft may be required to connect the donor and recipient pulmonary arteries. The donor SVC is then connected to the RA. Despite its infrequent application, heterotopic transplantation is associated with satisfactory outcomes which are comparable to those of orthotopic transplantation.

Postoperative management

Inotropic support is usually required in the postoperative period due to impaired myocardial contractility. Myocardial dysfunction in this setting is often transient and secondary
to injury sustained prior to procurement, during cold storage, and in association with warm ischemia during implantation. The RV is particularly susceptible to injury and this can result in RV failure, especially in the presence of elevated PVR. Inotropic support with beta-agonists and phosphodiesterase inhibitors is often utilized and is gradually discontinued after hemodynamic stability and satisfactory cardiac function are confirmed. Nitric oxide can be introduced to ameliorate RV dysfunction by reducing the PVR. As the donor heart is denervated due to transection of its autonomic nerve fibers, it has an intrinsic resting heart rate of between 90 and 110 beats per minute. The absence of reflex control of heart rate can interfere with normal cardiovascular physiology and can result in adverse effects such as orthostatic hypotension and an increased sensitivity to inotropic and chronotopic agents.

Primary allograft dysfunction is one of the commonest causes of perioperative mortality. The underlying cause for severe donor organ dysfunction is not always easily identified and is often multifactorial. Common causes include ischemic myocardial injury due to inadequate preservation, acute rejection, or pulmonary hypertension with severe RV failure. After maximal inotropic support has been instituted, ongoing donor organ dysfunction requires mechanical support. An intra-aortic balloon pump can be used to support cardiac function. More aggressive forms of mechanical circulatory support include extracorporeal membrane oxygenation (ECMO) and the use of VAD to support the failing heart. Retransplantation can be considered in rare circumstances but is often not feasible due to limited availability of donor organs. Irrespective of the different treatment options, the mortality associated with early allograft failure is high and accounts for one-fifth of perioperative deaths following heart transplantation. As mentioned earlier, RV failure is an important cause of mortality early after cardiac transplantation and is due to inability of the RV to function in the presence of an elevated PVR. The RV can be supported by administering agents that reduce the PVR such as prostaglandin E1, prostacyclin, inhaled nitric oxide, and nitroglycerin. If pharmacological therapy is insufficient, mechanical support of the RV can be instituted using a right ventricular assist device.

Antiarrhythmic therapy should be initiated if clinically indicated to reduce rhythm-related complications. Hypertension should be controlled with medical therapy to reduce afterload. Patients should be followed up in the outpatient clinic and echocardiography can be used to evaluate cardiac structure and function. Endomyocardial biopsies are performed for the detection of acute rejection.

**Immunosuppression**

**Induction therapy**

Immunization of animals with human lymphocytes leads to the production of polyclonal antibodies that can destroy immune cells. They are potent agents which can markedly reduce the number of circulating T cells. Thymoglobulin is comprised of purified IgG immunoglobulins derived from rabbits after exposure to human thymocytes. Polyclonal antibodies have been utilized for induction of immunosuppression in the perioperative
period as prophylaxis against rejection and evidence indicates that they reduce early acute rejection.\(^{34,35}\) They are also used for the treatment of acute rejection which is unresponsive to steroid therapy. Monoclonal antibodies have also been developed and are also used for induction therapy and treatment of refractory rejection.\(^{36}\) OKT3 is a murine monoclonal antibody, which was the first to be used in clinical practice. By interacting with the T-cell recognition complex it inhibits the function of naïve as well as cytotoxic T cells. Its use for induction therapy has decreased significantly due to an increased incidence of infection and post-transplant lymphoproliferative disorders.\(^{37,38}\) Administration can also lead to the development of human antimouse antibodies which reduce its efficacy. IL-2 receptor blockers such as basiliximab and daclizumab confer more selective immune suppression as they target only activated T cells which express CD25 antigen. These chimeric antibodies have a greater human component reducing the production of antimouse antibodies after exposure. Doses given at induction produce a protracted effect which markedly reduces the rates of acute rejection early after heart transplantation. This has been confirmed in randomized studies,\(^{39}\) although concerns have been raised over a possible increased risk of infection and graft dysfunction. Alemtuzumab is a rat-derived chimeric monoclonal antibody directed against CD52 on mature lymphocytes. We currently use this agent for induction therapy in cardiac transplantation at our center and its potent activity against T cells has allowed us to withdraw corticosteroids from our immunosuppression regimen.\(^{40}\)

**Perioperative and maintenance therapy**

Cyclosporine inhibits the calcium-calcineurin pathway which is involved in the activation of transcription factors that lead to the expression of important molecules involved in the immune response, such as IL-2, CD154, and CD25. Inhibition of this signal transduction pathway impairs proliferation of cytotoxic T-lymphocytes. Other components of the immune response are less affected conferring a degree of selectivity. Its introduction is responsible for the improvement in long-term survival following heart transplantation observed over the last three decades, attributed largely to an associated reduction in infective complications. Renal insufficiency is the major adverse effect associated with its use. Its evolution into a microemulsion formulation has improved its pharmacokinetics and therapeutic index. Tacrolimus (FK506) is a macrolide antibiotic that binds to FK506-binding protein. This complex is a more potent inhibitor of the calcineurin pathway than cyclosporine. Tacrolimus has been demonstrated to produce less hyperlipidemia and hypertension compared to cyclosporine, although the incidence of rejection and death after heart transplantation has been similar.\(^{41,42}\) Recent reports indicate that tacrolimus is now the most commonly used calcineurin inhibitor in the current era. Antiproliferative agents interfere with cell replication and lymphocyte proliferation in response to antigen. Mycophenolate mofetil (MMF) is an ester prodrug of mycophenolic acid which interferes with purine synthesis. Azathioprine impairs DNA synthesis. Randomized trials of the two agents have demonstrated that the former reduces mortality and rejection and is therefore more commonly administered.\(^{43}\) Sirolimus and everolimus prevent T-cell proliferation
by interfering with signal transduction following IL-2 receptor activation. Similar to tacrolimus, these agents bind to FK-506-binding protein but in contrast do not inhibit calcineurin; alternatively, they inhibit cytoplasmic proteins necessary for normal progression of the cell cycle. Both agents may also attenuate the development and progression of coronary allograft vasculopathy. Corticosteroids have been used since the early era of transplantation and are powerful inhibitors of the immune response. They are used for induction and maintenance therapy as well as being the most common first-line agents for treatment of acute rejection. Side effects associated with steroid use have been the impetus for using reduced doses or even withdrawing these agents from current regimens. However, most centers continue to use steroids for long-term maintenance therapy.

**Acute rejection**

Rejection of the allograft remains a significant cause of morbidity and mortality after heart transplantation.\(^4\) Cell-mediated immune responses are primarily responsible for this process but antibody mediated rejection can also occur. In the modern era, acute rejection can be reliably diagnosed and adequately treated in most patients.

Constitutional symptoms include lethargy, malaise, and low-grade pyrexia. Cardiac dysfunction can result in low cardiac output and congestive heart failure. Arrhythmias are also a manifestation of acute rejection. However, patients may remain asymptomatic despite advanced rejection, particularly with current immunosuppressive regimens. Endomyocardial biopsies from the RV are routinely obtained to identify rejection.\(^45\) Right heart catheterization also allows assessment of hemodynamic function. In patients with hemodynamic compromise inotropic agents may be necessary and occasionally mechanical circulatory support is required for extreme situations. Biopsies are performed frequently in the initial few weeks after transplantation and then less often after the first postoperative year.

Grading of rejection from biopsy specimens is undertaken by examining the extent of lymphocyte infiltration and the presence of myocyte necrosis. Gene expression profiling from peripheral blood samples may allow for non-invasive identification of acute rejection in the future. Rejection episodes within the first 3 months are treated with 1 gram of intravenous methylprednisolone administered daily for 3 days. Later episodes are treated with high doses of oral prednisone. Response to therapy is assessed by biopsy approximately a week after completion of treatment. Refractory rejection can be treated with a second steroid pulse. Polyclonal or monoclonal antibody therapy is reserved for severe steroid-resistant rejection associated with hemodynamic instability. If rejection is mild in severity it can be monitored with repeat biopsies as in most instances it does not progress. Myocyte necrosis is an indicator of severe rejection and requires aggressive treatment.

Humoral immune responses are associated with vascular rejection and often result in severe cardiac dysfunction.\(^46\) The diagnosis can be made by light microscopy and immunoflourescence of biopsy specimens. Treatment involves the use of plasmapheresis, high dose corticosteroid therapy, heparin, immunoglobulins, and cyclophosphamide. The mortality is high despite aggressive treatment. Repeated and recurrent episodes predispose to the development of coronary allograft vasculopathy.
**Allograft vasculopathy**

The coronary arteries of the transplanted heart develop cardiac allograft vasculopathy (CAV). This process is characterized by intimal proliferation with stenosis of the epicardial coronary arteries and occlusion of smaller vessels leading to myocardial ischemia. The onset of CAV is variable and it can develop early after heart transplantation. CAV reduces long-term survival and is the primary cause of death after the first post-transplant year. Approximately 50% of patients have evidence of CAV on angiography within 5 years. In contrast to conventional atherosclerosis, luminal narrowing is concentric and diffuse as opposed to eccentric and proximal. Both immunologic and non-immunologic factors contribute to its development. The presence of circulating anti-HLA antibodies and episodes of acute rejection are associated with CAV. Additional risk factors include advanced donor age and recipient hypertension, hyperlipidemia, and diabetes. Inflammation of the endothelium following injury may be an early trigger for CAV. Myocardial ischemia associated with CAV is silent due to cardiac denervation and consequently the disease often manifests as congestive cardiac failure, arrhythmias, or sudden cardiac death. Surveillance and screening can be achieved with either coronary angiography or intravascular ultrasound (IVUS). Percutaneous or surgical interventions are difficult due to the diffuse pattern of disease. Minimizing cold ischemia, optimizing cardiac preservation, and modifying risk factors for atherosclerosis can attenuate its development and progression. Calcium channel blockers, ACE inhibitors, and statin therapy have been demonstrated to decrease the incidence of CAV. The only definitive treatment for established CAV is retransplantation.

**Infection**

Infection is a major cause of morbidity and mortality following heart transplantation. Prophylactic treatment with antimicrobial agents is instituted to minimize infectious complications. Although a variety of pathogens can produce infection, cytomegalovirus (CMV) is the predominant cause of infection related mortality and morbidity in cardiac transplant recipients. In addition CMV has been implicated in allograft vasculopathy and post-transplant lymphoproliferative disease (PTLD). Infection can result from reactivation of latent infection in the recipient or due to transmission from the donor. Patients who are seropositive for CMV may also become reinfected by a different viral strain. Ganciclovir is used for prophylaxis, as well as for treatment of symptomatic CMV infections. Valganciclovir has greater bioavailability than ganciclovir and has also been demonstrated to be effective for both prophylaxis and treatment of active infection. Fungal infections can result from species such as candida and aspergillus, the latter being associated with a high mortality. Aspergillus pneumonia develops in up to 10% of patients early after heart transplantation. Pneumonia can also be caused by protozoal organisms such as Pneumocystis carinii. Toxoplasmosis can result from reactivation of latent disease, with toxoplasma gondii often implicated.
Late complications

Renal insufficiency is common among late survivors of heart transplantation. Nephrotoxicity associated with the use of calcineurin inhibitors such as cyclosporine is the most important predisposing factor. Modification of immunosuppressive regimens aimed at minimizing or avoiding calcineurin inhibitors may reduce renal dysfunction. Hypertension is also extremely common among cardiac transplant recipients. Altered activity of the sympathetic nervous system and cyclosporine nephrotoxicity are implicated in its progression. Pharmacological therapy includes the use of calcium channel blockers, diuretics, and beta blockers. Hyperlipidemia is also prevalent and is controlled through dietary modification and lipid-lowering therapy. The incidence of malignancy among heart transplant patients is 100-fold greater than that of the general population. Its incidence is rising, and it represents an increasingly important obstacle to long-term survival. Lymphoproliferative disorders and skin cancers are the most common malignant processes. Treatment can be undertaken with chemotherapy, radiotherapy, and surgery, however mortality remains high despite intervention.

Clinical outcome following cardiac transplantation

Since its inception 40 years ago heart transplantation has become an established treatment for severe heart failure. The evolution and success of this procedure over this time period can be appreciated in a recent report of the 1,446 heart transplant operations performed at Stanford University between 1968 and 2007. Over this time the 1-year survival of patients undergoing heart transplantation has increased from 43.1% to 90.2%. Very long-term survival (20 years) was achieved in 12.5% of patients transplanted before 1988. The commonest causes of death in heart transplant patients were identified as allograft vasculopathy (56.3%) and malignancy (25.0%). Since 1983 approximately 85,000 heart transplants performed worldwide have been reported to the registry of the International Society for Heart and Lung Transplantation (ISHLT). There has been a steady decline in the number of procedures performed over the last 15 years. The number of procedures performed worldwide peaked in 1994 at 4,460, following which there has been a steady decline toward just over 3,000 heart transplants per year over the last 3 years. This decline is largely due to a decrease in the number of brainstem-dead organ donors.

The primary indication for adult heart transplantation over the past decade has been divided equally between ischemic and non-ischemic cardiomyopathy. Recently patients with non-ischemic cardiomyopathy have become the predominant group presenting for transplantation. The mean age of adults currently undergoing heart transplantation is 51.1 years. The average recipient age continues to increase, with patients over the age of 60 representing 25% of all patients receiving heart transplants over the last 5 years. There has also been a 10-fold increase in the number of patients aged 70 and older undergoing heart transplantation. Consequently, with continued refinement of the procedure of heart transplantation and its associated pre- and postoperative management, the number of individuals to whom this treatment can be offered is expanding. This further magnifies the
relative shortage of donor organs in the face of increasing demand. Accordingly, criteria used for selection of organ donors have been made less stringent in order to accommodate for the reduction in organ supply. The mean age of donors for heart transplantation has increased from 23 years in 1983 to 33.6 years in 2009. Donors aged 50 or greater were exceedingly rare prior to 1986. Currently this age group accounts for 12% of donors, with donors over the age of 60 representing 1.4% of all donors.\(^2\)

The transplant half-time is the time at which 50% of transplanted patients remain alive (median survival). For patients transplanted between 1982 and 2007, the transplant half-time for all patients having undergone adult and pediatric heart transplantation is currently 10 years. For patients who survived the first postoperative year the transplant half-life is 13 years. Survival for adult recipients has improved successively for each 5–10-year era. This increase in survival during each progressive era has been observed during the first postoperative year. The attrition of transplant recipients over the longer term has remained relatively unchanged over the entire history of heart transplantation. The transplant half-life for recipients transplanted between the year 2000 and 2007 is approximately 11 years. This increase in long-term survival has occurred despite more frequent utilization of marginal organs from “higher risk” organ donors and despite performing transplantation in recipients with a higher preoperative risk. In a risk-adjusted analysis undertaken by the ISHLT registry there was a 5% increase in 1-year predicted survival between patients transplanted in 1998 and in 2002 and a 9% increase observed in the 5-year survival.

A range of risk factors are associated with increased 1-year mortality following heart transplantation. These include the need for temporary circulatory support prior to transplantation, congenital heart disease as the indication, preoperative mechanical ventilation, or hemodialysis, female sex, recent treatment for infection with intravenous antibiotics, and ischemic cardiomyopathy. Increasing recipient age, body mass index (BMI), serum creatinine, and PVR are associated with reduced 1-year survival.\(^2\) With regards to donor characteristics, increasing age and organ ischemic time along with decreasing BMI were predictive of an increase in 1-year mortality.\(^2\) The mortality during the first year following heart transplantation is greater than the next 4 years combined. Accordingly, risk factors for 1-year mortality are also important predictors of longer-term outcome. In those patients surviving the first postoperative year, risk factors for subsequent 5-year mortality include the development of CAV within the first postoperative year, the need for retransplantation, mechanical ventilation prior to transplantation and treatment for rejection during the first postoperative year. Recipients with diabetes, increasing age, and a diagnosis of ischemic cardiomyopathy had reduced conditional 5-year survival. An increase in age of the donor also imparted a higher 5-year mortality risk in those patients who had survived for 1 year following transplantation.\(^2\)

The leading cause of death within the first 30 days after heart transplantation is primary graft failure, accounting for 41% of deaths followed by multiorgan failure (13%) and infection (13%). After the first month infection is the predominant risk factor for death during the first year following transplantation, accounting for 30% of deaths during this
period with graft failure being responsible for 18% and acute rejection for 12%. Over the longer-term allograft coronary artery disease was responsible for 32% of deaths 5 years after transplantation, followed by malignancy (23%) and infection (10%). During the most recent era of transplantation, there has been a modest yet significant reduction in the incidence of CAV.

**The future**

Cardiac transplantation remains an established and effective treatment for patients with advanced heart failure. Clinical outcomes after transplantation continue to improve despite an increase in the risk profiles of both recipients and donors. Furthermore, the incidence of CAV, renal dysfunction, malignancy, and other barriers to prolonged survival have been decreasing. Advances in immunosuppression, diagnostic testing, medical management, and mechanical support are likely to have a favorable impact on outcomes after heart transplantation. As mentioned earlier, the major limitation toward increasing the availability of this procedure for patients with heart disease has been the limited numbers of organs available. Donor organ shortage is the most prominent obstacle preventing heart transplantation from being offered to a substantial population of patients who may benefit from this procedure. The number of patients listed for heart transplantation is approximately two times greater than the number of suitable donor hearts. Consequently, approximately 8% of patients die while awaiting a heart transplant.

Despite a more aggressive approach toward the utilization of “borderline” donor organs, a considerable number of organs continue to be declined on the basis of suboptimal function or other unfavorable characteristics related to the organ or donor. The development of more rigorous methods for organ assessment, resuscitation, recuperation, and preservation may allow for such organs to be utilized. New sources of organ donation may also allow for expansion of the donor pool. Donation of organs after circulatory arrest within the organ donor has led to significant increases in the number of organs available for renal, liver, and lung transplantation. Although there are concerns over injury incurred to the donor heart during warm ischemia, historical experience and scientific investigation supports the possibility that cardiac donation from DCD (donation after circulatory death) donors may be possible. Machine perfusion and *ex-vivo* evaluation of donor hearts may represent a means to objectively evaluate the function of such extended criteria donor hearts. The potential for recovering organs initially identified as having inadequate function for transplantation will require robust methods of measurement of cardiac function, and machine perfusion devices may provide the ideal platform to allow repeated assessment and evaluation of donor organ function. Furthermore, there may be scope for the application of therapeutic measures to improve donor heart function in this setting. The potential for eliminating cold ischemia by maintaining perfusion of organs during transportation promises to enhance donor heart viability and favorably influence logistical considerations associated with cardiac transplantation.
The worldwide decline in heart transplant activity since the mid-1990s is a concerning trend. Despite an overall decrease in heart transplant volumes the short and long-term results of heart transplantation continue to be satisfactory, improving the lives of thousands of patients with severe heart failure. The early era of heart transplantation was plagued with poor clinical outcomes, but through persistence and dedication the therapy became an outstanding success. Similar efforts may be necessary in the current era to revitalize heart transplantation, primarily through high-caliber scientific investigation and through the optimal utilization of the existing donor pool and the identification of new donor sources.

References


Introduction

Since the first successful human lung transplant by the Toronto Lung Transplant Group in 1983\(^1\) over 16,000 lung transplants have been performed. Donor shortage and chronic allograft rejection continue to be the biggest hurdles preventing lung transplantation from reaching its full potential.

Recipient selection

General selection criteria are listed in Box 13.1.\(^2\) Patients over age 65 or with failure of another organ system are generally not eligible for transplantation due to an elevated risk of mortality.\(^3\) A history of malignancy within the prior 5 years generally precludes pulmonary transplantation. A potential exception is a patient with bilateral bronchoalveolar carcinoma or a recent extrathoracic malignancy judged to be cured.\(^4,5\) Serious psychological dysfunction, active smoking, and high-dose corticosteroid therapy (≥20 mg prednisone) are other contraindications. Ventilator dependency is also not a contraindication but has been identified as a risk factor for increased mortality.\(^3\)

Patients considered for transplantation participate in a monitored exercise rehabilitation program while awaiting transplantation. Patients experience an improvement in strength and exercise tolerance without any measurable change in pulmonary function thus better enabling patients to withstand the rigors of a transplant procedure and subsequent convalescence.

Prior to 2005, lung allocation in the US was based on time spent on the waiting list, regardless of medical urgency or deterioration in medical condition. This system favored recipients well enough to survive on the transplant list while sicker patients, who may benefit most from the operation, risked death while waiting. An ideal system balances organ allocation based on clinical necessity while selecting recipients able to recover from a transplant operation. The United Network for Organ Sharing (UNOS) Thoracic Organ Committee revised the listing algorithm by assigning each patient a lung allocation score (LAS), based on the need for transplant and the probability of post-transplant survival. Details of the new allocation system are found on the Organ Procurement and Transplantation Network website, https://optn.transplant.hrsa.gov/learn/about-transplantation/how-organ-allocation-works/.\(^6\) The highest scores are listed first for
transplantation. Several recent studies have analyzed data obtained a short-to-moderate
length of time after the LAS implementation. In general, the results have been prom-
ising and have achieved the goals of the change in the allocation system (i.e., a decrease
in waiting list times, decreased waiting list mortality, and an increased number of lung
transplants performed),\textsuperscript{7–11} with an increase in the urgency of those transplanted, which is
particularly reflected in the group of idiopathic pulmonary fibrosis (IPF) patients. Longer
follow-up will be needed to confirm these findings and determine the non-inferiority of
long-term survival of patients.

**Single- versus double-lung transplantation**

Double-lung transplantation is the norm for septic lung disease. A significant number
of patients worldwide receive single-lung transplants for COPD (Chronic Obstructive
Pulmonary Disease) and IPF but registry data indicate that double-lung transplantation
is rising in popularity for these indications.\textsuperscript{12} The advantages of a single-lung transplant
include a technically easier operation, shorter ischemic time, and a societal benefit with
two recipients benefiting from each donor. On the other hand, double-lung transplant re-
cipients have better lung function and better quality of life than single-lung recipients.\textsuperscript{13,14}
The long-term survival of double-lung transplant recipients is also better with median
survival improving from 4.5 to 6.0 years.\textsuperscript{15} Our preference is to perform a bilateral se-
quential lung transplant for all patients if possible.

**Specific indications**

COPD has previously been the most common indication for lung transplantation, accounting
for 46% of the adult lung transplantations reported in the 2007 Registry of the UNOS/
ISHLT.\textsuperscript{3} When evaluating patients with emphysema for surgical therapy, consideration
should be given to lung volume reduction surgery (LVRS) in ideal patients: hyperinflation,
heterogeneous distribution of disease, forced expiratory volume in 1 s (FEV1) of more than

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**Box 13.1 Recipient selection criteria**

- Clinically and physiologically severe disease
- Medical therapy ineffective or unavailable
- Substantial limitations in activities of daily living
- Limited life expectancy
- Adequate cardiac function without significant coronary disease
- Ambulatory with rehabilitation potential
- Acceptable nutritional status
- Satisfactory psychosocial profile and emotional support system

Donor selection

Since many conditions resulting in brain death (trauma, spontaneous intracerebral hemorrhage) also lead to significant pulmonary parenchymal pathologic change because of lung contusion, infection, aspiration, or neurogenic pulmonary edema, only 20% of otherwise multiorgan donors have lungs satisfactory for transplantation by standard criteria (Box 13.2).

Although a significant smoking history (≥30 pack years) in the donor is a concern, it is not an absolute contraindication. Histocompatibility antigen (HLA) matching currently

Box 13.2 Ideal lung donor selection criteria

| Age <55 years |
| No history of pulmonary disease |
| Normal serial chest radiograph |
| Adequate gas exchange—\( \text{PaO}_2 > 300 \text{ mmHg} \); \( \text{FiO}_2 1.0 \); positive end-expiratory pressure 5 cm H\(_2\)O |
| Normal bronchoscopic examination |
| Negative serologic screening for hepatitis B and human immunodeficiency virus (HIV) |
| Recipient matching for ABO blood group |
| Size matching |
is not performed between donor and recipient unless the patient has an elevated panel reactive antibody or known HLA antibodies from prior sensitization.

Size matching between donor and recipient is a significant consideration. The most reliable method of size matching predicts donor and recipient lung volumes using standard nomograms based on age, sex, and height. Implantation of a large allograft is easily achieved in a patient with obstructive lung disease because of the enormous size of the recipient pleural space. Conversely, in patients with pulmonary fibrosis or pulmonary vascular disease, the pleural spaces are reduced or normal in size, respectively. It is therefore inadvisable to oversize these patients. Donor lungs that are larger than the recipient’s chest cavity but are otherwise usable should be accepted. A minor degree of pulmonary infiltrate may be accepted in donor lungs being used for a bilateral transplantation.

Novel techniques to optimize donor usage have been introduced. The first is a split-lung technique that bipartitions the left lung of a large cadaveric donor and uses the two lobes to perform a bilateral lobar transplant in the smaller recipient. It requires significant expertise but has been performed successfully with good outcomes.

Another technique is the use of non-heart-beating donors. Results from this group of DCD donors (donation after cardiac death), where withdrawal of support is under controlled circumstances, have been published in some series over the last 3–4 years. Some series show excellent early results. DCD lung transplantation should continue to be used cautiously at experienced centers.

Steen and colleagues from Sweden have advocated extracorporeal perfusion and ex vivo assessment of donor lung function in non-heart beating donors by reconditioning initially unacceptable lungs. The lungs are perfused ex vivo with Steen solution, mixed with red blood cells to a hematocrit of 15%. An oxygenator maintains a normal mixed venous blood gas level in the perfusate. The lungs are ventilated and evaluated through analyses of pulmonary vascular resistance, oxygenation capacity, and arterial carbon dioxide pressure minus end-tidal carbon dioxide difference. The technique has also been outlined by the Toronto Lung Transplant Group. Since then, a growing body of literature is looking at clinical results from such approaches.

In the living lobar donation strategy, two healthy donors donate one lobe each. Donor right lower lobe and left lower lobe are implanted in the recipient on the respective side. In a large series, the operation provided recipient results comparable to conventional transplantation with no donor mortality but a morbidity rate of 20%. With the new LAS the need for this approach has dropped off dramatically as patients who would benefit most from it, namely decompensated sicker patients, now have much reduced waiting periods for cadaveric organs.

**Donor procurement**

**Brain-dead donor**

Once a donor is determined to be suitable, the procuring team is activated. The procuring surgeon has the ultimate responsibility in making the final assessment of suitability of
lungs and in ensuring the safe and expeditious conduct of the operation. The procuring team ensures appropriate ABO compatibility (including two separate blood group analyses on the donor), cross-checks the declaration of brain death and confirms appropriate permission for lung procurement. A flexible bronchoscopy is performed to assess anatomy and evaluate secretions. Clear communication between the heart and lung procurement teams is important. The sites of left and right heart venting, division of the left atrial cuff and the site of cannulation and division of the main pulmonary artery (PA) should be discussed and agreed upon.

Via a standard median sternotomy, the pericardium and both pleural spaces are widely opened. The lungs are palpated and a compliance check is performed. The pericardium is retracted with heavy sutures. At this point the quality of lungs and any concerns are communicated with the implantation team.

The superior vena cava (SVC) is encircled caudal to the azygous vein with heavy silk suture. The plane between the anterior surface of the right PA and the back of the SVC and the ascending aorta is developed. The aortopulmonary window is dissected and the aorta encircled with an umbilical tape that is useful in placement of the cross-clamp. The SVC and the aorta are gently retracted, posterior pericardium is incised above the right PA, and the plane around the trachea is developed bluntly. After all the procurement teams are ready, the donor is heparinized (250–300 units/kg iv). An aortic cardioplegia cannula is placed if the heart is being procured. A U-stitch is placed just proximal to the bifurcation of the main PA and a Sarns (Sarns, Ann Arbor, MI) 6.5-mm curved metal cannula is placed into the main PA (Figure 13.1)

A 500-microgram bolus of prostaglandin-E1 (PGE1) is injected directly into the PA. Hypotension ensues. Next the SVC is ligated, and the left atrial appendage is incised venting the left side of the heart. The inferior vena cava (IVC) is divided, thus venting the right heart. The aorta is cross-clamped and cardioplegia initiated. The pulmonary preservation solution consisting of several liters (50–75 cc/kg) of cold (4°C) Perfadex (Vitrolife, Goteborg, Sweden) is initiated via the PA cannula. Ice slush is generously used to topically cool the heart and both pleural spaces. We continue gentle ventilation to prevent atelectasis and homogenously distribute the perfusate. Clear perfusate exiting the left atriotomy confirms adequate lung flushing. After completion of the antegrade flush, the cannulae are removed. The IVC is now freed posteriorly and dissected up to the level of the right atrium avoiding injury to the right inferior pulmonary vein. Division of the left atrium ensues with the cooperation of the heart and lung teams. The heart is retracted toward the right and an incision is made in the left atrium midway between the coronary sinus and the left inferior pulmonary vein. The opening is extended superiorly and inferiorly while visualizing the orifices of the left sided pulmonary veins from inside the atrium. The remaining cuff of left atrium is transected while visualizing the orifice of right pulmonary veins from within the atrium. An appropriate residual atrial cuff should have a rim of atrial muscle around each of the pulmonary vein orifices (Figure 13.2).

The SVC is transected between ties. This is followed by division of the aorta proximal to the cross-clamp and the PA at the site of cannulation. The heart is then passed off the
field. Next, we use a Foley catheter to deliver about 250 cc of retrograde pulmonary flush via each of the pulmonary vein orifices.

The mediastinal contents are now removed en bloc. This avoids injury to the hilar structures and preserves maximal soft tissue for collateral flow to the airway. The superior mediastinal tissues are divided and the trachea encircled several cm above the carina. The endotracheal tube is backed into the proximal trachea. The trachea is divided between staple lines. The esophagus is also divided using a stapler (Figure 13.3).

The lungs are retracted inferiorly and superior mediastinal tissue divided down to the spine. Staying directly on the spine the posterior mediastinal tissue is divided to the level of the mid-thoracic spine. Now the dissection shifts inferiorly. The pericardium

Figure 13.1 Cross clamping during procurement. Cardioplegia cannula in place in the ascending aorta and a cannula in the main pulmonary artery (PA). Venting of blood is via the inferior vena cava and the left atrial appendage.

just superior to the diaphragm and the inferior pulmonary ligaments are divided. The supradiaphragmatic esophagus is divided with the linear stapler followed by division of the posterior mediastinal tissue including the aorta. Now the dissection is connected with the superior dissection and the lungs are removed en bloc.

If the lungs are to be used at separate institutions, they are separated on the back table. The donor esophagus and aorta are removed and the pericardium is excised. The lungs are separated by division of the posterior pericardium, left atrium between the pulmonary veins, division of the main PA at the bifurcation, and division of the left bronchus close to the carina. The lungs are placed in three layers of plastic bags, with cold preservation solution and transported on ice. The hila are prepared by dissecting the pulmonary arteries back to their first branches. The donor bronchus is divided one ring proximal to the upper lobe orifice while minimizing proximal peribronchial dissection to preserve collateral flow.

Figure 13.2  The heart is being explanted leaving a rim of atrium around each pulmonary vein orifice.
Non-heart beating donor

DeAntonio et al. have published their procurement technique with uncontrolled non-heart beating donors. After systemic heparinization, the donor is placed on arteriovenous extracorporeal membrane oxygenation via a femoral approach. A fogarty catheter is placed in the supradiaphragmatic aorta for better abdominal organ perfusion and bilateral chest tubes are placed for topical lung cooling with cold Perfadex. Bronchoscopy is performed and the chest is opened. Ventilation is now resumed with 100% FiO₂ and 5 cm of positive end-expiratory pressure (PEEP). The pleural spaces are drained and pericardium opened. The aorta is clamped and both venae cavae ligated. Antegrade lung perfusion is performed with 5–6 L of Perfadex followed by infusion of 300 cc of donor blood through the PA. A blood gas analysis is performed on the left atrial effluent. Retrograde perfusion and the lung procurement are now performed in routine fashion.

For the controlled non-heart beating donor, support is withdrawn by extubation in the intensive care unit (ICU) or the OR. Once cardiac activity ceases, the donor is declared dead, endotracheal intubation done, and a bronchoscopy performed. A median

Figure 13.3 Division of the trachea and esophagus prior to double-lung bloc extraction after cardiectomy.
sternotomy is performed and the lungs expeditiously evaluated. If the lungs are deemed suitable, the remaining operation proceeds as for a brain-dead donor. If the donor does not expire within 60 min of withdrawal of support, the procurement is abandoned. A thorough evaluation of institutional guidelines is mandatory prior to initiating a DCD lung transplantation program.

**Procurement problems**

Injuries often involve the right inferior pulmonary vein, occurring during the division of the left atrial cuff or division of the IVC, due to excessive dissection of the inferior pulmonary ligament or unnecessary dissection of the atrial cuff within the pericardium. Several novel techniques have been described for salvage in this situation. A bronchus suis (i.e., a tracheal upper lobe bronchus) is a common anomaly and may represent a segmental or a lobar bronchus. If the bronchus is determined to be a segmental bronchus, it may be simply overseen. If the entire upper lobe bronchus arises as an abnormal tracheal bronchus, the options are donor right upper lobectomy, left single-lung transplantation, or incorporating the bronchus intermedius and the aberrant upper lobe bronchus into a modified anastomosis with the recipient bronchus.

**Recipient implantation**

**Recipient anesthesia and intraoperative conduct**

An experienced anesthesia team well-versed with double lumen tube management, bronchoscopy, and transesophageal echocardiography (TEE) is invaluable to the conduct of the operation. An epidural catheter is placed unless systemic heparinization for cardiopulmonary bypass is anticipated. Patients with cystic fibrosis undergo therapeutic bronchoscopy and suctioning via a large single lumen endotracheal tube. Radial and femoral arterial lines, a PA catheter, TEE probe, and an infraumbilical heating blanket are routine. The patient is placed supine with arms tucked. We employ vasopressors as indicated and avoid excessive volume resuscitation.

We use epoprostenol and/or nitric oxide for acute refractory pulmonary hypertension in the perioperative period with inhaled nitric oxide also being used for poor oxygenation.

**Operative approach**

Bilateral anterolateral thoracotomy without sternal division is our preferred incision for bilateral lung transplant. The chest cavity is entered in the fourth interspace (Figure 13.4).

A transverse sternothoracotomy (clamshell incision) additionally involves division of the sternum (Figure 13.5). This incision provides excellent exposure and requires the division of both mammary arteries. A clamshell incision is used for providing added exposure when a concomitant cardiac procedure is performed or when cardiomegaly, or a relatively small chest cavity, make hilar exposure difficult. The sternum is reapproximated using two figure-of-eight #5 sternal wires.
Figure 13.4  Bilateral anterolateral thoracotomy with two retractors placed at right angles.  

Figure 13.5  The sternum has been divided for a clamshell incision providing excellent exposure to the thorax.  
Median sternotomy is used if the recipient is undergoing concomitant cardiac surgery or in women with large breasts which compromise the exposure via anterolateral thoracotomy.

A small antero-axillary thoracotomy has been found comparable to the more conventional incisions in terms of operating times and ability to go on central cardiopulmonary bypass (CPB).39,40

Prior to excision of the recipient lungs bilateral hilar dissection and adhesiolysis should be completed and donor lungs should be prepared. The lung with the poorer function, based upon a preoperative ventilation perfusion scan, is transplanted first as the other lung will better support single-lung ventilation.

The phrenic, vagus, and recurrent laryngeal nerves must be protected. The right PA is transected about 1 cm beyond the truncus anterior branch and the left PA beyond the second branch to the left upper lobe. This downsizes the recipient PA and may provide better donor-recipient size match and the first branch (ligated) of the recipient PA provides an anatomic landmark for orientation during the anastomosis. Next, the pulmonary veins are divided at secondary branch points and the pericardium opened widely. The peribronchial tissue is divided, and bronchial arteries controlled with cautery or ligatures. The bronchus is divided just proximal to the upper lobe origin and the lung removed. All posterior mediastinal and posterior chest wall bleeders are controlled as this is the only opportunity to access this area safely. We set up hilar exposure by gently retracting the PA and pulmonary veins anteriorly, ready for the bronchial anastomosis.

The donor lung is covered with a cold sponge and placed in a bed of ice slush into the thoracic cavity. The bronchial anastomosis is performed in an end-to-end fashion using two strands of 4-0 PDS stitch in running fashion. The anastomosis is started on the membranous part and carried around over the anterior cartilaginous part with the second suture (Figure 13.6). If there is a significant size mismatch, we modify the anastomosis by approximating the cartilaginous part with simple interrupted 3-0 vicryl sutures. The peribronchial tissue on the donor and recipient sides is used to cover the anterior aspect of the anastomosis to offer some protection to the overlying vascular anastomoses in case of bronchial anastomotic breakdown. End-to-end airway anastomosis has been found to be superior to the telescoped anastomosis technique.41

Next, a vascular clamp is placed on the recipient PA, the donor and recipient PAs trimmed, and an end-to-end anastomosis performed using a continuous 5-0 polypropylene stitch (Figure 13.7).

The vein stumps are then retracted laterally and a Satinsky-type clamp is placed centrally on the recipient’s left atrium. The recipient pulmonary venous stumps are amputated and the two openings connected to create the atrial cuff. The anastomosis is fashioned with continuous 4-0 polypropylene. Stitches are placed in a mattress technique, which achieves intima-to-intima apposition and excludes potentially thrombogenic atrial muscle (Figure 13.8.).

The last few sutures are left loose, the lung partially inflated, and the PA clamp is released momentarily. This maneuver flushes out air and perfusate from the lung. The left
atrial clamp is then opened to completely de-air the atrium. The atrial suture line is pulled up tight and tied down. All clamps are removed.

The pleural spaces are usually drained with two drains in each pleural space, one placed apically and one along the diaphragm. The ribs are reapproximated with heavy interrupted figure-of-eight monofilament non-absorbable suture.

A flexible bronchoscopy is performed after exchanging the double lumen tube for a single lumen tube to evaluate the airway anastomoses and remove blood and secretions.

We employ cardiopulmonary bypass selectively in our patients. It is indicated in children, small-statured patients in whom a double lumen tube cannot be placed, lobar transplants, concomitant intracardiac procedures, and most patients with pulmonary hypertension. CPB is also indicated for refractory hypoxemia, hypercarbia, pulmonary hypertension, or hemodynamic instability. Difficult exposure may necessitate CPB too. This is typically seen with a small pleural space in patients with IPF with the heart shifted to the left, thus making exposure of the left hilum difficult.
Figure 13.7  The PA anastomosis is performed using a running 5-0 polypropylene suture.  

Figure 13.8  A large Satinsky is placed centrally across the left atrium. Both vein stumps are amputated and the bridge between connected to create a left atriotomy suitable for anastomosis.  
Reproduced from Patterson GA: Bilateral lung transplant: Indications and technique. Semin Thorac Cardiovasc Surg 4:95–100, 1992 with permission from Elsevier
Recently, we have used the Urchin heart positioning device to elevate the heart (Medtronic, Inc, Minneapolis, MN) to improve exposure and avoid CPB.\textsuperscript{42}

Lungs that are larger than the recipient's thoracic cage are downsized by performing a lobectomy on the back table, or bilateral wedge resections (lingula and the right middle lobe) after implantation.

At the conclusion of the operation, if the patient is unstable or shows continuous oozing due to a coagulopathy, we prefer to close skin only and resuscitate the patient in the ICU with closure planned in 24–48 hours. This strategy does not increase wound complications.\textsuperscript{43}

**Postoperative management and selected complications**

**Routine care**

The patients are transported to the ICU and ventilated. Extubation is performed in accordance with standard parameters within 24–48 hours. After single-lung transplantation for emphysema, preventing hyperinflation of the native lung and compression of the freshly implanted lung are the main concerns.\textsuperscript{44} This is accomplished by avoiding the use of PEEP and using lower tidal volumes. In single-lung recipients with pulmonary vascular disease, we use a prolonged period (48 hours) of elective ventilation. The patient is positioned to keep the native lung dependent to maintain inflation and appropriate drainage of the transplanted lung. Tidal volumes are standard, but a higher PEEP of 7.5–10 cm H$_2$O is applied. Postoperatively, a quantitative lung perfusion scan to assess for adequate patency and graft flow is usually performed.

Vigorous chest physiotherapy, postural drainage, inhaled bronchodilators, and frequent clearance of pulmonary secretions are required in the postoperative care, with early involvement of the physiotherapy team ensuring ambulation as soon as possible.

**Immunosuppression**

Postoperative induction therapy is controversial. Potential benefits include lower rates of acute rejection, protection from nephrotoxicity due to the delayed introduction of a calcineurin inhibitor, and a decrease in the occurrence of BOS (bronchiolitis obliterans syndrome). Disadvantages are the higher risk of infectious complications and post-transplantation malignancies. About 40\% of patients undergoing lung transplantation receive induction immunosuppression.\textsuperscript{5} Agents used include polyclonal antilymphocyte or antithymocyte preparations, monoclonal OKT3, and IL-2 receptor antagonists. All of the agents used in induction are generally associated with a decrease in the number of episodes of acute rejection, however their true impact on the incidence of BOS or overall survival remains to be determined. IL-2 receptor antagonists block activated T lymphocytes and may be associated with a lower risk of infectious complications and possibly post-transplantation lymphoproliferative disease.\textsuperscript{45,46} Other studies however indicate that no single induction agent is superior to the other.\textsuperscript{47}
For maintenance therapy we rely on triple-agent therapy for consisting of corticosteroids, a calcineurin inhibitor, and a cell cycle inhibitor. About 75% of lung transplant recipients are receiving a calcineurin inhibitor and a purine synthesis inhibitor at 1 and 5 years after transplantation, respectively.\(^3\)

Cyclosporine and tacrolimus are calcineurin inhibitors which suppress the transcription of IL-2 and inhibit proliferation of T lymphocytes. Azathioprine inhibits de novo purine synthesis and suppresses proliferation of both T and B lymphocytes. Mycophenolate mofetil (MMF) is a prodrug of mycophenolic acid, which produces inhibition of de novo purine synthesis. Despite the lack of evidence for the superiority of MMF over azathioprine in lung transplantation, its use now exceeds that of azathioprine in lung transplant recipients.\(^48,49\) Recently, a randomized, placebo-controlled, double-blind, multicenter trial on efficacy of inhaled cyclosporine in lung transplant recipients under a conventional triple immunosuppressive regimen was published.\(^50\) Although the study had some limitations, and did not reach its primary efficacy endpoint (prevention of acute rejection), both survival and freedom from chronic rejection were significantly increased in the cyclosporin (CsA) arm, compared to placebo.\(^50\) The same group has presented data on 30 transplanted patients, where aerosolized CsA in addition to conventional immunosuppression significantly preserved FEV1, versus placebo and historical controls.\(^51\)

Sirolimus and its derivative everolimus, have been recently introduced into clinical lung transplantation. These agents block growth factor-driven cell cycle progression and proliferation of lymphocytes and other non-hematopoietic cells such as vascular smooth muscle cells. In an international, randomized multicenter study enrolling 213 BOS-free lung transplant recipients, efficacy was evaluated between azathioprine and everolimus. Although at 12 months the everolimus group showed a significantly smaller decline in FEV1 and had experienced less acute rejections, at 24 months only the incidence of acute rejection episodes still differed significantly between arms.\(^52\) The interested reader may refer to a recent review of immunosuppression in lung transplantation.\(^53\)

**Primary graft dysfunction**

Primary graft dysfunction (PGD) develops in up to 25% of lung transplant recipients.\(^54\) The ISHLT has issued a grading system for primary graft dysfunction based on the Pao2/Fio2 ratio and findings on chest radiographs\(^55\) (Table 13.1). Ischemia-reperfusion injury likely accounts for most cases of PGD. Levels of IL-8, a potent chemoattractant for neutrophils, increase during reperfusion of lung grafts, and correlate with the duration of the ischemic time, and negatively correlate with early lung function.\(^56\)

PGD is managed with aggressive cardiopulmonary support in the intensive care unit. Appropriate ventilatory strategies, inhaled nitric oxide,\(^57\) and aerosolized prostacyclin\(^58\) are employed. In most patients, PGD resolves over several days of intensive care support. Extracorporeal membrane oxygenation (ECMO) support is employed if conservative management appears to be unsuccessful. In a review of our experience with 983 lung transplant recipients, ECMO was used in 9.7% of the pediatric and 2.8% of adult
Recipients. Only 38% of patients who received ECMO survived to discharge from the hospital. The Duke University group advocates the use of venovenous ECMO due to much fewer complications encountered.

The use of controlled reperfusion in combination with leukocyte depletion has been proposed as a preventive strategy. Lick and colleagues have published their original technique for the same. We do not routinely employ this method, as PGD likely contributes to chronic rejection.

Infections

Details of infection prophylaxis are beyond the scope of the current chapter. In brief, we routinely employ broad-spectrum antibacterial chemotherapy for several days post-transplantation. For the first year after transplantation we routinely give acyclovir for herpes simplex prophylaxis. In patients at high risk for cytomegalovirus (CMV) infection we use 12 weeks of IV ganciclovir starting 7–14 days post-transplantation. For transplants we use CMV-negative or leukocyte-reduced blood products. Lifelong Pneumocystis carinii prophylaxis is employed.

Bacterial infections are common in the early post-transplant period and remain the primary cause of mortality in the early post-transplant period. Wound infections are generally due to conventional bacteria such as staphylococci. CMV disease is the most commonly noted postoperative infectious complication. It occurs in 13–75% of transplant patients depending on definitions of CMV disease and use of CMV prophylaxis. Most programs match seronegative donors with seronegative recipients. Prophylactic regimens include oral or IV ganciclovir, with or without CMV IV immunoglobulin. Valganciclovir, an oral prodrug of ganciclovir, has been used as a prophylactic agent. Although CMV infection is uncommon during prophylaxis, the rate of CMV disease increases after cessation of prophylactic therapy. Candidal infections are most commonly associated with airway anastomotic complications. The most frequent cause of significant fungal infection after transplantation is Aspergillus. Invasive infection is the most feared complication and carries a high mortality. More commonly, however,
Aspergillus growing in sputum or bronchoalveolar lavage (BAL) cultures represents colonization.

**Airway complications**

Anastomotic complications resulting from airway ischemia include infection, dehiscence, stenosis, and malacia. The reported incidence of these complications is 7–14% of patients.\(^{61-63}\) In a review of our experience, the rate of airway complications was during the initial period of the lung transplantation experience from 1988 through 1993, was 16%; this decreased to less than 10% during later time periods. Airway complications did not seem to have an adverse impact on overall survival.\(^{54}\)

From a technical standpoint, a shortened donor bronchial length (one ring proximal to the upper lobe takeoff) reduces the length of donor bronchus dependent on collateral flow. Peribronchial tissue on the donor bronchus is preserved during preparation of the lung.

Occasionally, patchy areas of superficial necrosis of donor bronchial epithelium are observed. These areas are of no concern and ultimately heal. Membranous wall defects typically heal without airway compromise, whereas cartilaginous defects usually result in some degree of late stricture. Massive dehiscence of the airway with uncontrolled leak or mediastinal contamination requires retransplantation. Lesser degrees of dehiscence can be managed expectantly. Necrotic tissue at the bronchial anastomosis is an ideal medium for the growth of fungi. Nunley and colleagues found that saprophytic fungal infections involving the bronchial anastomosis occurred in 25% of recipients. In 47% of those patients with fungal involvement of the anastomosis, airway complications occurred.\(^{64}\)

Chronic airway stenoses result from surgical stenosis, granulation tissue, infection, or bronchomalacia, with ischemia as the universal common denominator. Bronchoscopic balloon dilation and stent placement are the usual options.\(^{65,66}\) Treatment of the granulation tissue consists of a combination of laser or forceps debridement, dilatation, and stenting.\(^{66}\) Recurrent airway stenosis have been managed with topical application of mitomycin C\(^{67}\) and high-dose brachytherapy.\(^{68}\) If lesser approaches fail, sleeve resection and retransplantation are other options.

**Chronic rejection—bronchiolitis obliterans (BO)**

Because of the difficulties in documenting BO histologically, a clinical deterioration in lung function (termed bronchiolitis obliterans syndrome, or BOS) has been adopted as its surrogate and current diagnostic criteria have been outlined.\(^{69}\) By 5.6 years post-transplantation, 51% of patients will have developed BOS.\(^{15}\)

Many reports have shown an association between viral respiratory infections and the development of BOS.\(^{70,71}\) Also, it has been postulated that chronic aspiration of gastric contents damages the lung allograft and contributes to chronic allograft dysfunction and that a fundoplication performed early after lung transplantation may reduce the incidence of BOS.\(^{72}\)
Standard treatment protocols consist of augmenting immunosuppression in an attempt to stabilize the disease process. Regimens such as high-dose corticosteroids, cytolytic therapy, substitution of mycophenolate mofetil for azathioprine, and conversion of cyclosporine to tacrolimus have on occasion been successful in preserving pulmonary function at a stable level.\textsuperscript{23,24} Recently mTOR inhibitors have been used in several single-center programs to stabilize lung function after the diagnosis of BOS.\textsuperscript{75,76}

Other therapeutic strategies have included inhaled cyclosporine, inhaled high-dose corticosteroids, and photopheresis.\textsuperscript{53} Rapamycin, azithromycin, and clarithromycin,\textsuperscript{77} statins,\textsuperscript{78} and IL-2 receptor antagonists\textsuperscript{45} may hold promise in altering the outcomes from BOS. Retransplantation may be an option in carefully selected patients with BOS.\textsuperscript{79}

**Results**

Generally speaking, patients are off supplemental oxygen and have significantly improved exercise tolerance by 4–6 weeks after transplantation. Registry data on overall survival for recipients of lung transplants from 1994\textsuperscript{12} demonstrated unadjusted survival of 89% at 3 months, 79% at 1 year, 64% at 3 years, 52% at 5 years, and 29% at 10 years. Compared with data beginning in 1988, overall survival has consistently improved by era. The improvement in survival in the more current era is largely driven by improvements in 1-year survival. Among patients surviving at least 1 year, those with diagnoses of cystic fibrosis, primary pulmonary hypertension, sarcoidosis, and Alpha 1 antitrypsin deficiency had significantly better survival at 10 years after transplantation (48%, 45%, 44%, and 41%, respectively) than those with COPD (28%) and IPF (30%), most likely because COPD and IPF patients are older with more comorbidities.\textsuperscript{12}

The major identified causes of death in the first 30 days are graft failure and non-CMV infections. After the first year, BOS and non-CMV infections were the predominant causes of death. Death caused by malignancies rises consistently until the 10-year mark, accounting for 12% of all deaths between 5 and 10 years after transplant.\textsuperscript{12}

**Conclusions**

Lung transplantation is well established as a viable therapy for end-stage lung disease. Appropriate patient and donor selection, meticulous attention to technique, and continued improvement in the postoperative care of these patients will lead to optimal outcomes. Research to increase the donor pool and to prevent or manage BOS is the key to the future of lung transplantation.

**References**

REFERENCES


Index

Notes
Tables, figures and boxes are indicated by an italic t, f, or b following the page number.
vs. indicates a comparison or differential diagnosis

Abbreviations
AVR    aortic valve replacement
BITA   bilateral internal thoracic artery
CABG   coronary artery bypass graft
ITA    internal thoracic artery
LITA   left internal thoracic artery
MCS    mechanical circulatory support
MIDCAB minimally invasive direct coronary artery bypass
MIMVS  minimally invasive mitral valve surgery
ONCAB  on-pump coronary artery bypass grafting
OPCAB  off-pump coronary artery bypass grafting
PTCA   percutaneous transluminal coronary angioplasty
RA     radial artery
RGEA   right gastroepiploic artery
RITA   right internal thoracic artery
SVG    saphenous vein graft
TAVI   transcatheter aortic valve implantation
TECAB  totally endoscopic coronary artery bypass

ablation technology, atrial fibrillation, 177–81, 182
radiofrequency energy ablation, 179–80
see also cryoablation; high-intensity focused ultrasound (HIFU)
ABO compatibility, lung transplantation, 245
ACE inhibitors see angiotensin-converting-enzyme (ACE) inhibitors
acquired von Willebrand syndrome, 217
ACROBAT stabilizer (Maquet), 41
activated clotting time (ACT), OPCAB, 39
acute aortic regurgitation, 114
acute ascending aortic dissection, 113–14
acute DeBakey type IIIA/IIIB aortic dissections, 125–6
acute rejection, heart transplantation, 232
acute Stanford type B aortic dissections, 125–6
Adamson, P B, 158
Ad, N, 183
ADVANCE BTT trial, 205
adventitia
LITA, 1
RA, 10
SVG, 13
Aesop 3000 voice-activated camera manipulator, 145
AH-TECAB (arrested heart totally endoscopic coronary artery bypass), 59, 66
airway complications, post-lung transplantation, 257
alemntuzumab, 231
Alfieri, O, 141
allogenic stem cell injections, LVADs and, 203
American Correction, MIMVS, 149
American Heart Association (AHA) guidelines, AVR tissue vs. mechanical valves, 97
anastomoses, proximal, 45, 46f, 47
anesthesia
lung transplantation, 249
MIMVS, 149–50, 149f
OPCAB, 38–9
transcatheter aortic valve implantation, 101
Angelini, G D, 68
angiotensin-converting-enzyme (ACE) inhibitors
cardiac allograft vasculopathy, 233
heart transplantation, 225
annular calcium, mitral valve open repair, 142
anterior prolapse, mitral valve open repair, 139–41, 140f, 141f
anterolateral thoracotomy/coronary artery bypass (LT-CAB), 57
anticoagulants
MCS, 215
OPCAB, 39
antiplatelet agents, MCS, 215
antithrombotic barrier, endothelium, 2
aorta
acute regurgitation, 114
ascending see ascending aorta
descending thoracic see descending thoracic aorta repair/replacement
dissections see aortic dissections
insufficiency, MCS complications, 216–17
porcelain aorta, 115–16
aorta (Cont.)
  proximal aorta/aortic root replacement, 113–16
  thoracic aorta, 111
  thoracic aorta surgery see thoracic aortic surgery
  thoracoabdominal see thoracoabdominal aortic
  aneurysms (TAAA) open repair
  thoracoabdominal aorta see thoracoabdominal
  aorta repair/replacement
  thoracoabdominal aortic aneurysms, 117, 122f
  ventriculo-aortic junction, 73, 74f
  see also intra-aortic balloon pump (IABP)
aortic arch repair/replacement, 116, 119–21
  endovascular repair, 121
  hybrid arch repair, 121
  open aortic arch repair, 120–1
aortic dissections
  acute DeBakey type IIIA/IIIB aortic
  dissections, 125–6
  acute Stanford type B aortic dissections, 125–6
  aortic arch repair/replacement, 116
  CT, 112
  descending thoracic aorta repair/replacement, 125–6
aortic insufficiency classification, 75, 76f, 77
  MCS, 214
  repair-oriented, 75f
aortic root
  indications for replacement, 119
  thoracic aortic surgery, 118–19
aortic stenosis, MCS, 214
aortic valve
  anatomy and function, 73–5, 74f
  commissural plication, 119
  cusps, 73
  repair see aortic valve repair
  replacement see aortic valve replacement (AVR);
  aortic valve-sparing root replacement–
  reimplantation technique
  see also bicuspid aortic valve (BAV)
aortic valve repair, 73–96
  aortic root and annulus intervention, 78–9
  bicuspid aortic valve techniques, 85, 87, 87f, 88f,
  89f, 90f, 91, 92f
  exposure and assessment, 77–8, 78f
  free margin resuspension, 85, 86f
  indications for, 119
  intraoperative echocardiography, 91
  outcomes, 91, 93–4
  resuspension, 119
  subcommisural annuloplasty, 79, 79f
  sub-valvular region, 74–5, 74f
  valve-related complications, 94
  valve-sparing root replacement-reimplantation
  technique see aortic valve-sparing root
  replacement–reimplantation technique
aortic valve replacement (AVR), 97–110
  elderly patients, 100
  low-risk patient outcome, 97
  minimally invasive access, 99, 103–4, 103f
  patient-prosthesis mismatch, 98
  prosthetic aortic valve replacement, 214
  stentless valves, 98–9
  surgical, 102
  technical steps, 102–4
  tissue vs. mechanical, 97–8
  see also transcatheter aortic valve
  implantation (TAVI)
aortic valve-sparing root replacement–
  reimplantation technique, 79–84
  aortic root preparation, 80, 80f
  leaflet assessment/repair, 83–4
  prosthesis preparation/fixation, 82, 83f
  prosthesis sizing, 80–1, 81f
  proximal suture line, 81–2, 82f
  valve reimplantation, 83
aortoiliac atherosclerosis, 60
apical access, TAVI, 104–5, 105f
arrested heart totally endoscopic coronary artery
  bypass (AH-TECAB), 59, 66
arterial blood gas measurements, thoracic aortic
  surgery, 113
artificial chordae
  anterior prolapse in mitral valve open
  repair, 139–41, 140f
  posterior prolapse in mitral valve open
  repair, 138–9
ascending aorta
  aneurysm, 115
  thoracic aortic surgery, 118–19
ascending aortic dissection, 113–15
  acute, 113–14
  chronic, 114–15
Aspergillus infections
  heart transplantation infection, 233
  pneumonia in post-lung transplantation, 256–7
aspirin
clopidogrel and, 68
OPCAB, 39
atrial fibrillation surgery, 175–96
  ablation technology, 177–81, 182
  see also cryoablation; high-intensity focused
  ultrasound (HIFU)
Cox-Maze procedure see Cox-Maze procedure
critical mass hypothesis, 189–90
  electrocardiographic imaging, 190
  future work, 189–91
  left atrial lesion sets, 183–4, 187–8
  minimally invasive techniques, 190–1
  mitral valve open repair, 142–3
  prevalence, 175
  pulmonary vein isolation, 184–5, 188–9
  surgical results, 182–5
atrioventricular (AV) leaflets, 73
autologous stem cell injections, LVADs
  and, 203
AVR see aortic valve replacement (AVR)
azathioprine
  post-heart transplantation, 231
  post-lung transplantation, 255
azithromycin, 258
bacterial infections, post-lung
  transplantation, 256–7
  bail-out suggestions, TAVI, 107–8
Barlow’s disease, 141–2
Barnard, C, 163, 224
baseline renal function, thoracic aortic surgery, 113
basiliximab, 231
BAV see bicuspid aortic valve (BAV)
Bax, J J, 160–1
beating- heart totally endoscopic coronary artery bypass (BH-TECAB), 59
anastomotic creation, 66
Benchmark Registry and Society of Thoracic Surgeons National Database IABP procedures, 168
β adrenoceptor agonists, 2
β adrenoceptor agonists, ITA, effects on, 2
beta- blockers, post- heart transplantation, 225, 234
BH- TECAB see beating- heart totally endoscopic coronary artery bypass (BH-TECAB)
bicuspid aortic valve (BAV), 115
repair outcomes, 93–4
bilateral internal thoracic artery (BITA), 6, 7, 15–20, 16f, 24
bi- ventricular assist devices (BIVAD), 163
bi- ventricular support, bridge to transplant MCS, 206–7
blood urea nitrogen (BUN), 204
bone marrow cells, intramyocardial injection, 166
Borst, H, 120
BOS (bronchiolitis obliterans syndrome), 254, 257–8
brain- dead donors, lung transplantation, 244–7, 246f, 247f, 248f
brainstem death, heart transplantation donor, 226
Bretschneider solution, heart preservation, 227
BTP (bridge to candidacy) mechanical circulatory support, 197
definition, 209
bridge to recovery (BTR) mechanical circulatory support, 197, 199–203
long-term recovery, 201–3
short-term recovery, 199–201
bridge to transplant (BTT) mechanical circulatory support, 197, 203–7
biventricular support, 206–7
continuous flow devices, 204–6
bronchiolitis obliterans (BO), 257–8
bronchiolitis obliterans syndrome (BOS), 254, 257–8
BCT (bridge to candidacy) mechanical circulatory support, 209
BTD see bridge to decision (BTD) mechanical circulatory support
BTR see bridge to recovery (BTR) mechanical circulatory support
BTT see bridge to transplant (BTT) mechanical circulatory support
BUN (blood urea nitrogen), 204
CABG see coronary artery bypass graft (CABG)
CAD see coronary artery disease (CAD)
CAG (cardiac allograft vasculopathy), 233
calcineurin inhibitors nephrotoxicity, 234
post- lung transplantation, 255
calcium channel blockers cardiac allograft vasculopathy, 233
post- heart transplantation hypertension, 234
cancer, post- heart transplantation, 234
candidiasis, post- lung transplantation, 256
carbon dioxide insufflation, TECAB, 61
cardiac allograft vasculopathy (CAG), 233
cardiac output, 165
cardiac surgery
low cardiac output syndrome, 167
perioperative mortality, 166
survival maximization, 166–7
transplantation see heart transplantation cardiogenic shock, 200
cardiopulogia, 83
cardiopulmonary bypass (CPB)
heart transplantation, 228
see also centrifugal blood pump support
cardiopulmonary perfusion, MIMVS, 150–1, 151f
cardiopulmonary support, primary graft dysfunction, 255
Carpentier, A, 145
Carpentier classification of mitral valve insufficiency, 75
Carrel, A, 223
catheterization, right- heart, 232
cyclosporine, post- lung transplantation, 255
Celsior solution, heart preservation, 227
centrifugal blood pump support, 169–70, 205
CentriMag (Thoratec), 201, 206
CentriMag ventricular assist system Pivotal Trial, 201
CF devices see continuous flow (CF) devices
CF HeartMate II left ventricular assist device, 202
CHADS score, atrial fibrillation surgical ablation, 181
chest radiography, heart transplantation donor, 226
Chitwood, W R Jr, 145, 147
cordal replacements with polytetrafluoroethylene neochords, 149
chronic airway stenosis, 257
chronic ascending aortic dissection, 114–15
chronic DeBakey type IIIA aortic dissections, 126
chronic DeBakey type IIIIB aortic dissections, 126
chronic obstructive pulmonary disease (COPD), 159
chronic rejection, post-lung transplantation, 257–8
chronic Stanford type B aortic dissections, 126
chronic systolic heart failure, 200
Chu, D, 34, 36
circulatory shock, 168–9
clamp- and- sew technique, 122–3, 123f, 124f clarithromycin, 258
clopidogrel
aspirin and, 68
MCS, 215
OPCAB, 39
CMV see cytomegalovirus (CMV) infections
Cohn, L H, 145, 146
commissural prolapse, mitral valve open repair, 141
computed tomography (CT)
aortic dissections, 112
contrast-induced nephropathy, 112
DynaCT, 105–6
MIMVS, 148
robotically assisted revascularization, 59
thoracic aortic surgery, 112
congestive heart failure prevalence, 157
CONSENSUS trial, 157
continuous flow (CF) devices, 197
bridge to transplant MCS, 204–6
contrast-induced nephropathy, CT adverse effects, 112
controlled reperfusion, lung transplantation, 256
Cooley, D A, 120
COPD (chronic obstructive pulmonary disease), 159
Copeland, J G, 207
coronary angiography, 233
BITA, 6, 15–20
cardiac transplantation vs., 159–61
decision tree propositions, 22f, 23f, 24
graft configuration, 15–23
left coronary system revascularization see left coronary system revascularization
LITA, 1–4, 3f, 5f
see also left internal thoracic artery (LITA)
minimally invasive coronary bypass, 57
myocardial functional response, 160–1
off-pump vs. on-pump see off-pump (OPCAB) vs. on-pump (ONCAB) coronary artery bypass grafting
OPCAB, 42–5
RA, 8–12, 11f, 12f
RGCA, 7–8, 9f
right coronary system revascularization, 20–1, 21f, 24
RITA, 4, 6–7, 7f
SVG, 12–15
coronary artery bypass graft conduits, 1–15
LITA see left internal thoracic artery (LITA)
coronary artery disease (CAD)
MCS, 214
prevalence, 157
coronary stenosis, LITA CAGB, 2, 4
CORONARY trial, 34
corticosteroids
acute rejection heart transplantation, 232
bronchiolitis obliterans syndrome, 258
post-heart transplantation, 232
post-lung transplantation, 255
Cosgrove, D M 3rd, 145
Cox, J, 175
Cox-Maze procedure, 175–7, 176f
adoption of, 176–7
Cox-Maze III, 176, 177f
Cox-Maze IV, 176, 178f, 185–7, 186f, 187f
results, 182–3, 182f
CPB see cardiopulmonary bypass (CPB)
Crawford classification, thoracoabdominal aortic aneurysms open repair, 126–7
Cremer, J, 8
critical mass hypothesis, atrial fibrillation, 189–90
cryoablation
atrial fibrillation, 178–9
results of, 182
crystalloid cardioplegic solutions, heart preservation, 227
CT see computed tomography (CT)
cytophosphamide, 232
cytopsorine
nephrotoxicity, 234
post-heart transplantation, 231
post-lung transplantation, 255
cytolytic therapy, bronchiolitis obliterans syndrome, 258
cytomegalovirus (CMV) infections
heart transplantation infection, 233
post-lung transplantation, 256
dacizumab, 231
Dake, M D, 111
Dallas Lesion Set, 190–1
DAPT (dual antiplatelet therapy), 68, 69, 70
David, T E, 93
da Vinci Si (Intuitive Surgical, California), 58
da Vinci Surgical System (Intuitive Surgical systems) in MIMVS, 145–55
DAVP (desmopressin acetate), 210–11
DCD (donation after circulatory death) donors, cardiac transplantation, 236
deAntonio, D G, 248
DeBakey type I ascending aortic dissection, 113–14
DeBakey type II ascending aortic dissection, 113–14
DeBakey type III aortic dissection, 117–18
deep hypothermic circulatory arrest (DHCA), 120
descending thoracic aorta aneurysm open surgical repair, 124
Demikhov, V, 224
DeRose, J J Jr, 169
descending thoracic aorta repair/replacement, 117–18, 121–6
aneurysm open surgical repair, 122–4
aneurysms, 117, 122f
aortic dissections, 125–6
endovascular repair, 124–5
type B/DeBakey type iii aortic dissection, 117–18
desmopressin acetate (DAVP), 210–11
destination therapy (DT) mechanical circulatory support, 164, 197, 207–9
DHCA see deep hypothermic circulatory arrest (DHCA)
diabetes, 225
diffusing capacity of the lungs for carbon monoxide (DLCO), 59
dipyridamole, 215
direct aortic root cannulation, TECAB, 60
diuretics, 225, 234
DLCO (diffusing capacity of the lungs for carbon monoxide), 59
dobutamine, 167
donation after circulatory death (DCD) donors, cardiac transplantation, 236
dopamine, 167
double-lung transplantation, single-vs., 242
driveline infections, MCS complications, 217
dry unipolar radiofrequency devices, 179
DT (destination therapy) mechanical circulatory support, 164, 197, 207–9
dual antiplatelet therapy (DAPT), 68, 69, 70
DuraHeart (Terumo Heart Inc.), 205
DynaCT, 105–6
EACTS (European Association for Cardio-Thoracic Surgery), 101
echocardiography
atrial fibrillation surgery, 190
heart transplantation donor, 226
intraoperative, aortic valve repair, 91
thoracic aortic surgery, 113
transesophageal see transesophageal echocardiography (TEE)
two-dimensional, thoracic aortic surgery, 112–13
ECMO see extracorporeal membrane oxygenation (ECMO)
Edgerton, J R, 184–5
drive-to-edge repair, anterior prolapse in mitral valve open repair, 141
EDHF (endothelium-derived hyperpolarizing factor), 2, 10
elderly patients, AVR, 100
electrocardiogram (EKG), heart transplantation donor, 226
Elefteriades, J A, 117
elephant trunk repair
open aortic arch repair, 120–1
thoracoabdominal aortic aneurysms open repair, 128
emergent conversion, OPCAB vs. ONCAB CABG, 35
endo-ACAB (endoscopic atraumatic coronary artery bypass), 56
endoaortic balloon, 60
endoscopic atraumatic coronary artery bypass (endo-ACAB), 56
endoscopic suturing, TECAB, 60
endothelial function
RA, 10
SVG, 14
endothelin receptor antagonists, 243
endothelium-derived hyperpolarizing factor (EDHF), 2, 10
endothelium function, LITA, 2
endovascular repair
aortic arch, 121
descending thoracic aorta repair/replacement, 124–5
end-stage cardiac disease, heart transplantation, 225
ENDURANCE trial, 209
epinephrine, 167
Euro-Collins solution, heart preservation, 227
European Association for Cardio-Thoracic Surgery (EACTS), 101
European Heart Survey, transcatheter aortic valve implantation, 100
everolimus
post-heart transplantation, 231–2
post-lung transplantation, 255
exercise capacity, left ventricular ejection fraction, 159
exercise rehabilitation program, lung transplantation recipient selection, 241
exposure, OPCAB, 39–41
extracorporeal membrane oxygenation (ECMO) bridge to recovery MCS, 201
post-heart transplantation, 230
primary graft dysfunction (PGD), 255–6
extracorporeal perfusion, lung transplantation donor selection, 244
femoro-femoral cardiopulmonary bypass, 60
FEV1 (forced expiratory volume in 1s), lung transplantation, 242–3
FFR (fractional flow reserve), in situ LITA to the LAD territory and free RITA implanted in Y or T fashion in LITA, 18
FK see tacrolimus (FK506)
folding plasty
MIMVS, 149
posterior prolapse in mitral valve open repair, 138, 139f
forced expiratory volume in 1s (FEV1), lung transplantation, 242–3
fractional flow reserve (FFR), in situ LITA to the LAD territory and free RITA implanted in Y or T fashion in LITA, 18
Frazier, O H, 203
free margin resuspension, aortic valve repair, 85, 86f
fungal infections, post-heart transplantation, 233
fusiform aneurysms, aortic arch repair/replacement, 116
Gaita, F, 184
Gammie, J S, 145
ganciclovir, 233
ganglionated plexus (GP) ablation, 184–5
gastro-epiploic artery (GEA), LITA histology vs., 1
GEA (gastro-epiploic artery), LITA histology vs., 1
gender, LITA CABG patency, 4
Gillinov, A M, 184
Glineur, D, 4, 6–7, 8, 18, 19, 21, 21f, 24
Golding, L A, 169
Gould, K L, 158
GP (ganglionated plexus) ablation, 184–5
graft patency, OPCAB vs. ONCAB CABG, 36–7
Guthrie, C C, 223
Haas, F, 160
Hadinata, I E, 20–1
Hannan, E L, 34
Hardy, J, 224
heart contractility improvement, 165–6
heart failure
  ascending aortic dissection, 114
  end-stage patients, 157–8
  Stage D (New York Heart Association (NYHA) Class IV), 157
heart failure surgery, 157–73
  ischemic cardiomyopathy, 158–9
  pathology-based, 158
  see also cardiac surgery; coronary artery bypass graft (CABG); heart transplantation; left ventricular assist devices (LVADs); mitral valve repair
HeartMate I
  left ventricular assist devices, 165
HeartMate II, 204
  Clinical Investigations publications, 204–5
  control device, 209
  surgical implantation, 211–12
HeartMate 3, 206
HeartMate IP (Implantable Pusher Plate), 203
HeartMate VE, 203–4, 207, 208f
HeartMate XVE, 204
Heartstring III\(^{TM}\), 47
heart transplantation, 157–8, 163, 223–40
  acute rejection, 232
  allograft vasculopathy, 233
  animal to human, 224
  clinical outcomes, 234–6
  coronary bypass surgery vs., 159–61
  future work, 236–7
  heterotopic, 229
  historical aspects, 223–5
  immunosuppression, 230–2
  implantation, 228–9
  infection, 233
  late complications, 234
  organ procurement and preservation, 226–7
  postoperative management, 229–30
  recipient management, 225–6
  recipient operation, 228
  recipient selection, 225
HeartWare HVAD (HeartWare Intl.), 205, 209
hemodynamic status, heart transplantation donor, 226
hemorrhage, MCS complications, 216
heparin
  acute rejection heart transplantation, 232
  induced thrombocytopenia, 210–11
OPCAB, 39
heterotopic heart transplantation, 229
HIFU (high-intensity focused ultrasound), 180
high-intensity focused ultrasound (HIFU), 180
histocompatibility antigen matching, 243–4
histology, LITA, 1
human leukocyte antigen (HLA)
  heart transplantation, 225
  matching, 243–4
humoral immune responses, acute rejection heart transplantation, 232
hybrid aortic arch repair, 121
hybrid coronary revascularization, 68–70
  current state, 68–69
  definition, 68
  prior percutaneous intervention, 69–70
  prior surgical intervention, 69
  robotically assisted MIDCAB and, 58
  simultaneous procedures, 70
  technical considerations, 69
  timing considerations, 70
hyperlipidemia, post-heart transplantation, 234
hyperplasia, neo-intimal, 12–13, 13–14\(^b\)
hypertension
  cardiomyopathy, 157
  post-heart transplantation, 234
  pulmonary, OPCAB, 38, 39
IABP see intra-aortic balloon pump (IABP)
IABP-SHOCK II trial, 199–200
IEA (inferior epigastric artery), 1
IL-2 receptor blockers see interleukin-2 (IL-2) receptor blockers
IMA see internal mammary artery (IMA)
  imaging
    magnetic resonance angiography, thoracic aortic surgery, 112
    magnetic resonance imaging, ischemic cardiomyopathy, 159
    thoracic aortic surgery, 111–13
    see also computed tomography (CT); radiography; ultrasound
IMH (intramural hematoma), 114
immunosuppression
  post-heart transplantation, 230–2
  post-lung transplantation, 254–5
Impella 2.5 (Abiomed), 200
  implantation, heart transplantation, 228–9
  incision and port placement, MIMVS, 151–2, 152f
  induction, post-heart transplantation, 230–1
  infections
    heart transplantation, 233
    MCS, 206
    post-lung transplantation, 256–7
    proximal aorta/aortic root replacement, 115
  inferior epigastric artery (IEA), 1
inotropes
  low cardiac output syndrome management, 167
  post-heart transplantation, 229–30
INSTEAD XL trial, 126
Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), 197–9, 198f
  biventricular support, 206
  bridge to recovery MCS, 199, 201
INTERMACS Cardiac Recovery Score (I-CARS), 202
interleukin-2 (IL-2) receptor blockers
  bronchiolitis obliterans syndrome, 258
  post-heart transplantation, 231
  post-lung transplantation, 254
INTERMACS see Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)
internal mammary artery (IMA)
  MIDCAB, 53
  RA endothelial function vs., 10
  RGEA vs., 8
see also left internal mammary artery (LIMA); right internal mammary artery (RIMA)
International Registry of Acute Aortic Dissection (IRAD), 114
International Society for Heart and Lung Transplantation (ISHLT), 234
intima
  LITA, 1
  RA, 9
  SVG, 13
intra-aortic balloon pump (IABP), 166–7
  bridge to recovery MCS, 199
effects of, 167–8
intramural hematoma (IMH), 114
intramyocardial injection, bone marrow cells, 166
intraoperative conduct, lung transplantation, 249
intraoperative echocardiography, aortic valve repair, 91
intrathoracic revascularization, robotically assisted, 58–9
intravascular ultrasound (IVUS), cardiac allograft vasculopathy, 233
IRAD (International Registry of Acute Aortic Dissection), 114
ischemic cardiomyopathy, 158–9
  functional improvement, 166
ischemic heart failure without angina, 160
ISHLT (International Society for Heart and Lung Transplantation), 234
Jarvik 2000, 204
Kantrowitz, A, 224
Khan, N E, 36
Kim, K B, 37
Kondo, Y, 224
Krebs solution, heart preservation, 227
LAD see left anterior descending artery (LAD)
LAD anastomoses see left anterior descending artery (LAD) anastomoses
Lamy, A, 36
LAS (lung allocation score), 241, 242–3
  leaflet resection with annuloplasty (LRA), 146–7
  learning curve, OPCAB, 38
left anterior descending artery (LAD)
  LIMA MIDCAB and PTCA, 69
  TAVI, 105
left anterior descending artery (LAD) anastomoses
  MIDCAB, 53
  OPCAB, 43–5
left atrial lesion sets, atrial fibrillation surgery, 183–4, 187–8
left coronary system revascularization, 15–20
  BITA, 15–20, 16f
  in situ LITA to the LAD territory and free RITA implanted in aorta, 15, 17f, 20
  in situ LITA to the LAD territory and free RITA implanted in Y or T fashion in LITA, 15, 17f, 18–20, 19f
  in situ LITA to the LAD territory and in-situ RITA to circumflex territory through transverse sinus, 15–17, 17f
  in situ RITA to the LAD territory and in-situ LITA to circumflex territory, 15, 17–18, 17f
left internal thoracic artery (LITA), 1–4
  CABG, 1–4, 31, 5t, 24
  endothelium function, 2
  histology, 1
  RITA vs., 4
see also left coronary system revascularization
left internal mammary artery (LIMA)
  anterolateral thoracotomy/coronary artery bypass, 57–8
  LAD MIDCAB and PTCA, 69
  MIDCAB, 53
  OPCAB, 43–5
  RA CABG vs., 12, 12f
left ventricular assist devices (LVADs), 163, 164, 197
  stem cell injections and, 203
left ventricular ejection fraction (LVEF)
  heart failure surgery, 158
  improvements in, 165
left ventricular end systolic volume index (LVESVI), 158
left ventricular remodeling, ischemic cardiomyopathy, 162
Levitronix Centrimag short-term ventricular assist device, 169–70
LIMA see left internal mammary artery (LIMA)
LITA see left internal thoracic artery (LITA)
Li, Z, 34
long-term circulatory support, 164–5
long-term mortality, OPCAB vs. ONCAB CABG, 36
low cardiac output syndrome, 167–8
Lower, R, 224
low-risk patient outcome, AVR, 97
LRA (leaflet resection with annuloplasty), 146–7
LT-CAB (anterolateral thoracotomy/coronary artery bypass), 57
lung allocation score (LAS), 241, 242–3
lung transplantation, 241–62
  brain-dead donors, 244–7, 246f, 247f, 248f
  complications, 255–8
  donor procurement, 244–9
  donor selection, 243–4, 243b
  non-heart-beating donors, 244, 248–9
  postoperative management, 254–5
  procurement problems, 249
  recipient implantation, 249–54, 250f, 252f, 253f
  recipient selection, 241–2, 242b
  results, 258
  single- vs. double-transplantation, 242
  specific indications, 242–3
split-lung technique, 244
lung volume reduction surgery (LVRS), 242
Lüscher, T F, 2
LVADs see left ventricular assist devices (LVADs)
LVEF see left ventricular ejection fraction (LVEF)
LVESVI (left ventricular end systolic volume index), 158
LVRS (lung volume reduction surgery), 242
MA-AVR (minimally invasive access aortic valve replacement), 99, 103–4, 103f
MACCE (major adverse cardiac and cerebrovascular events), robotically assisted revascularization, 59
machine perfusion, heart preservation, 227
magnetic resonance angiography (MRA), thoracic aortic surgery, 112
magnetic resonance imaging (MRI), ischemic cardiomyopathy, 159
maintenance therapy, post-heart transplantation, 231–2
major adverse cardiac and cerebrovascular events (MACCE), robotically assisted revascularization, 59
Mann, F C, 223
Marfan syndrome, 117
McClelland, J H, 184
MCS see mechanical circulatory support (MCS)
mechanical circulatory support (MCS), 197–222 adverse effects, 206 complications, 215–19, 216f considerations, 214–15 historical aspects, 197, 198f indications for, 197–9 patient selection, 209–10 preoperative considerations, 210–11 surgical implantation, 211–14 see also bridge to decision (BTD) mechanical circulatory support; bridge to recovery (BTR) mechanical circulatory support; bridge to transplant (BTT) mechanical circulatory support; left ventricular assist devices (LVADs)
media
LITA, 1
RA, 10
SVG, 13
median sternotomy, 111 mitral valve open repair, 136
OPCAB, 39–40 Medtronic freestyle valve, 98 Medtronic Octopus Tissue Stabilizer, 41 Micromed, 204 MICS-CABG (minimally invasive coronary artery bypass grafting), 58 MIDCAB see minimally invasive coronary bypass (MIDCAB)
mid-term mortality, OPCAB vs. ONCAB CABG, 36 Mihaljevic, T, 147 milrinone, 167 MIMVS see minimally invasive mitral valve surgery (MIMVS)
minimal lumen diameter (MLD) values, RGEA CABG, 8
minimally invasive approach aortic valve replacement, 99, 103–4, 103f atrial fibrillation surgery, 190–1 coronary artery bypass grafting, 58 see also minimally invasive coronary bypass (MIDCAB)
mitrval valve open repair, 136
mitral valve surgery see minimally invasive mitral valve surgery (MIMVS)
minimally invasive coronary artery bypass grafting (MICS-CABG), 58
minimally invasive coronary bypass (MIDCAB), 53–72 bilateral, 57
IMA, 53
LAD, 53
LIMA, 53
LIMA to LAD and PTCA, 69 multivessel minimally invasive procedures, 57–8 operation conduct, 54–6, 54f, 55f, 56f preoperative considerations, 53–4 robotically-assisted, 56, 58 thoracoscopic, 56–7
mitral valve repair
heart failure in, 161–2
ischemic cardiomyopathy, 162
minimally-invasive see minimally invasive mitral valve surgery (MIMVS)
open repair see mitral valve open repair
mitral valve replacement (MVR)
MCS, 215
open repair vs., 135–6
MMF see mycophenolate mofetil (MMF)
Modi, P, 146
Mohr, F W, 140, 145
MOMENTUM 3 trial, 206
monoclonal antibodies, post-heart transplantation, 231
mortality
long-term, OPCAB vs. ONCAB CABG, 36
mid-term, OPCAB vs. ONCAB CABG, 36
off-pump vs. on-pump coronary artery bypass grafting, 33–7, 35f
perioperative, cardiac surgery, 166
MRA (magnetic resonance angiography), thoracic aortic surgery, 112
MRI (magnetic resonance imaging), ischemic cardiomyopathy, 159
nTOR inhibitors, 258
Multicenter Study of MagLev Technology, 206
multivessel minimally invasive procedures, MIDCAB, 57–8
multivessel small thoracotomy (MVST), 58
multivessel totally endoscopic coronary artery bypass, 68
Murphy, D A, 147
MVO₂ (myocardial energy, and oxygen consumption), 165
MVR see mitral valve replacement (MVR)
MVST (multivessel small thoracotomy), 58
mycophenolate mofetil (MMF)
bronchiolitis obliterans syndrome, 258
post-heart transplantation, 231
post-lung transplantation, 255
myocardial energy, and oxygen consumption (MVO₂), 165
myocardial functional response, CABG, 160–1
myocardial infarction, ascending aortic dissection, 114
myocardial protection, MIMVS, 150–1
near-infrared spectroscopy (NIRS), 118
neointimal hyperplasia, SVG failure, 12–13, 13–14b
nephrotoxicity, calcineurin inhibitors, 234
neurologic outcomes
MCS, 206
OPCAB vs. ONCAB CABG, 36–7
NIRS (near-infrared spectroscopy), 118
nitric oxide (NO), 2
post-heart transplantation, 230
RA endothelial function, 10
nitroglycerin, 230
NO see nitric oxide (NO)
non-heart-beating donors, lung transplantation, 244, 248–9
off-pump (OPCAB) coronary artery bypass grafting, 38–47, 40f, 42f, 43f, 44f, 45f, 46f
anesthesia, 38–9
anticoagulation, 39
coronary grafting, 42–5
exposure, 39–41
learning curve, 38
minimally invasive coronary artery bypass grafting vs., 58
patient variables, 38
positioning and stabilization, 41–2
proximal anastomoses, 45, 46f, 47
robotically assisted MIDCAB vs., 58
off-pump (OPCAB) vs. on-pump (ONCAB) coronary artery bypass grafting, 33–51
emergent conversion, 35
graft patency, 37–8
mid- and long-term mortality, 36
neurologic outcomes, 36–7
operative mortality, 33–7, 35f
outcomes, 33–8
revascularization completeness, 37
OKT3, 254
ONCAB (on-pump coronary artery bypass grafting) see off-pump (OPCAB) vs. on-pump (ONCAB) coronary artery bypass grafting
on-pump (ONCAB) coronary artery bypass grafting see off-pump (OPCAB) vs. on-pump (ONCAB) coronary artery bypass grafting
OPCAB see off-pump (OPCAB) coronary artery bypass grafting
open aortic arch repair, 120–1
open distal anastomoses, 118
operation conduct, MIDCAB, 54–6, 54f, 55f, 56f
operative approach, lung transplantation, 249, 250f, 251–2, 252f, 253f, 254
operative mortality, off-pump vs. on-pump coronary artery bypass grafting, 33–7, 35f
optical angulation of the C-arm, TAVI, 105–6, 106f
oxygenator, CentriMag ventricular assist system
Pivotal Trial, 201
Pae, W E Jr, 168
Parodi, J C, 111
partial sternotomy, mitral valve open repair, 136
PARTNER trial, 102
Pass-Port™ Proximal Anastomosis System, 47
Patel, N C, 35
patency
LITA CABG, 2, 3t, 4, 5t
RA CABG, 10–12, 11t
RGEA CABG, 8, 9t
RITA CABG, 6–7, 7t
SVG, 14–15
patient positioning, OPCAB, 41–2
patient position, MIMVS, 149–50, 150f
patient-prosthesis mismatch (PPM), AVR, 98
patient variables
OPCAB, 38
SVG patency, 14
PAU (penetrating atherosclerotic ulcer), 114–15
percutaneous coronary intervention (PCI)
penetrating atherosclerotic ulcer (PAU), 114–15
percutaneous coronary intervention (PCI)
bridge to recovery MCS, 199
MIDCAB, 57
percutaneous transluminal coronary angioplasty (PTCA), 68
percutaneous ventricular assist device (PVAD), 206
perioperative mortality, cardiac surgery, 166
perioperative therapy, post-heart transplantation, 231–2
peripheral vasculopathy, ischemic cardiomyopathy, 159
phosphodiesterase inhibitors, 243
photopheresis, 258
plasmapheresis, 232
Pneumocystis carinii infection, 233
polyclonal antibodies, post-heart transplantation, 230–1
polyclonal antilymphocyte antibodies, 254
polyclonal antithymocyte antibodies, 254
porcelain aorta, 115–16
postcardiotomy cardiogenic shock, 168–9
posterior leaflet mitral valve repair, MIMVS, 147–8
posterior prolapse, mitral valve open repair, 137–9, 138f, 139f
postoperative induction therapy, post-lung transplantation, 254
post-transplant proliferative disease (PTLD), 233
pregnancy, proximal aorta/aortic root replacement, 116
preoperative planning
MIDCAB, 53–4
MIMVS, 148–9
PREVENtion of Heart Mate II Pump Thrombosis Through Clinical Management (PREVENT) study, 213–14
Priestley, J T, 223
primary graft dysfunction (PGD)
lung transplantation, 255–6, 256f
post-heart transplantation, 230
post-heart transplantation mortality, 234–5
procurement problems, lung transplantation, 249
prostacyclins, 2
lung transplantation, 243
post-heart transplantation, 230
prostaglandin E1, 230
prosthetic aortic valve replacement, MCS, 214
protamine, 170
Protect I/II trial, 200
proximal anastomoses, OPCAB, 45, 46f, 47
proximal aorta/aortic root replacement, 113–16
PTCA (percutaneous transluminal coronary angioplasty), 68
PTLD (post-transplant proliferative disease), 233
pulmonary hypertension, OPCAB, 38, 39
pulmonary vascular resistance (PVR), heart transplantation, 225
pulmonary vein isolation (PVI), atrial fibrillation surgery, 184–5, 188–9, 190–1
pump thrombosis
HeartMate 2 device, 213
MCS, 206
PURSUIT trial, 166
Puskas, J D, 34
PVAD (percutaneous ventricular assist device), 206
PVI (pulmonary vein isolation), atrial fibrillation surgery, 184–5, 188–9, 190–1
PVR (pulmonary vascular resistance), heart transplantation, 225
quality of life (QoL), AVR in elderly patients, 100
radial artery (RA)
anatomy, 8–9
CABG, 9–12, 11f, 12f, 24
histology, 9
LITA histology vs., 1
SV vs., 11
Radial Artery Potency and Clinical Outcomes (RAPCO), 20–1
radiofrequency energy ablation, atrial fibrillation, 179–80
radiography
heart transplantation donor, 226
thoracic aortic surgery, 111–12
Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study, 157, 164–5, 207–9, 208f
rapamycin, 258
RAPCO (Radial Artery Potency and Clinical Outcomes), 20–1
RGEA see right gastroepiploic artery (RGEA)
RECOVER I trial, 200
regional cerebral oxygen saturation (rSO2), 118
regional myocardial function, OPCAB, 39
rejection, post-lung transplantation, 257–8
REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure study), 157, 164–5, 207–9, 208f
remission from Stage D Heart Failure Study (RESTAGE-HF), 202–3
renal problems
ischemic cardiomyopathy, 159
post-heart transplantation, 234
reperfusion, lung transplantation, 256
RESTAGE-HF (remission from Stage D Heart Failure Study), 202–3
retrograde cerebral perfusion, 120
revascularization completeness, OPCAB vs. ONCAB
CABG, 36
right coronary system revascularization, 20–1, 21f, 24
right gastroepiploic artery (RGEA)
CABG, 7–8
right coronary system revascularization, 21, 21f, 24
right-heart catheterization, acute rejection heart transplantation, 232
right internal mammary artery (RIMA)
anterolateral thoracotomy/coronary artery bypass, 57–8
_in situ_ LITA to the LAD territory and free RITA implanted in Y or T fashion in LITA, 16
right internal thoracic artery (RITA)
anatomy, 4, 6
CABG, 4, 6–7, 7_t
endothelium function, 4, 6
histology, 4, 6
LITA vs., 4
right coronary system revascularization, 20, 21, 21_f, 24

see also left coronary system revascularization
right mini-thoracotomy, mitral valve open repair, 136
right ventricle dysfunction, OPCAB, 38
failure, MCS complications, 216
right ventricular assist devices (RVAD), 163
RIMA see right internal mammary artery (RIMA)
risk factors
LITA CABG patency, 4
post-heart transplantation mortality, 234
RITA see right internal thoracic artery (RITA)
robotically-assisted minimally invasive coronary bypass, 56
robotically assisted revascularization, 58–68
cannulation considerations, 60–1
intrathoracic revascularization, 58–9
major adverse cardiac and cerebrovascular events (MACCE), 59
MIDCAB, 58
preoperative evaluation, 59
TECAB see totally endoscopic coronary artery bypass (TECAB)
totally endoscopic CABG, 59
totally endoscopic coronary artery bypass (TECAB), 59
robotically assisted right chest approaches, mitral valve open repair, 136
ROOBY trial, 33–4
Rotaflow (Maquet), 201
rotational thromboelastometry (ROTEM), 210–11
ROTEM (rotational thromboelastometry), 210–11
routine care, post-lung transplantation, 254
Royse, A G, 18
sSO_2_ (regional cerebral oxygen saturation), 118
RVAD (right ventricular assist devices), 163

saccular aneurysms, aortic arch repair/ replacement, 116
SAM (systolic anterior motion), 137
saphenous vein graft (SVG), 12–15
anatomy, 13
histology, 13–14
patency, 14–15
RA CABG vs., 11
right coronary system revascularization, 20, 21, 21_f
SAVR (surgical aortic valve replacement), 102
Schafer, H J, 93
Scherlag, B J, 185
Shroyer, A L, 36
Shumway, N, 224
single-lung transplantation, double- vs., 242
single photon emission tomography (SPECT), ischemic cardiomyopathy, 159
single-vessel small thoracotomy direct vision bypass grafting (SVST) see minimally invasive coronary bypass (MIDCAB)
sinotubular junction (STJ), 73, 74_f
sinuses of Valsalva, 73
sirolimus, 231–2, 255
skeletonization, RA CABG, 11
Society of Thoracic Surgeons (STS) National Database
AVR low-risk patient outcome, 97
AVR tissue vs. mechanical valves, 97
Cox-Maze procedure, 176–7
minimally invasive mitral valve repair, 145
operative mortality in OPCAB vs. ONCAB CABG, 34–5
thoracoscopic MIDCAB, 56
SPECT (single photon emission tomography), ischemic cardiomyopathy, 159
spirometry, thoracic aortic surgery, 113
split-lung lung transplantation, 244
stabilization, OPCAB, 41–2
Stanford A ascending aortic dissection, 113–14
Starfish/Sea urchin Heart Positioner (Medtronic), 41
statins
bronchiolitis obliterans syndrome, 258
cardiac allograft vasculopathy, 233
stentless valves, AVR, 98–9
sternotomy
median see median sternotomy
mitral valve open repair, 136
STICH (Surgical Treatment of Ischemic Heart Failure), 162
STJ (sinotubular junction), 73, 74_f
stroke
ascending aortic dissection, 114
atrial fibrillation surgical ablation, 181
OPCAB vs. ONCAB CABG, 36–7
St Thomas Hospital solution, heart preservation, 227
subcommissural annuloplasty, aortic valve repair, 79, 79_f
substance P, 4, 6, 6_f
surgical aortic valve replacement (SAVR), 102
Surgical Treatment of Ischemic Heart Failure (STICH), 162
SVG see saphenous vein graft (SVG)
SVST (single-vessel small thoracotomy direct vision bypass grafting) see minimally invasive coronary bypass (MIDCAB)
systolic anterior motion (SAM), 137
systolic heart failure, chronic, 200
tacrolimus (FK506)
bronchiolitis obliterans syndrome, 258
post-heart transplantation, 231
post-lung transplantation, 255
TAH (total artificial hearts), 206–7
tamponade, pericardial, ascending aortic dissection, 114
Tandem heart Percutaneous Ventricular Assist Device (pVAD: Cardiac Assist Inc.), 200
TAVI see transcatheter aortic valve implantation (TAVI)
TECAB see totally endoscopic coronary artery bypass (TECAB)
TEE see transesophageal echocardiography (TEE)
temporary mechanical circulatory support, 163–4
ThermoCardioSystems HeartMate XVE left ventricular assist device, 169
thoracic aorta, 111
thoracic aortic surgery, 111–33
aortic arch repair/replacement, 116
aortic root pathology, 118–19
ascending aortic pathology, 118–19
descending/thoracoabdominal aorta repair/replacement, 117–18
diagnostic modalities, 111–13
preoperative assessment, 113
proximal aorta/aortic root replacement, 113–16
see also ascending aortic dissection
thoracoabdominal aorta repair/replacement, 117–18, 126–9
type B/DeBakey type iii aortic dissection, 117–18
thoracoabdominal aortic aneurysms (TAAA) open repair, 117, 122f, 126–9, 127f, 128f
Crawford classification, 126–7
elephant trunk repair, 128
hybrid and endovascular repair, 128–9
thoracoscopic minimally invasive coronary bypass, 56–7
thoracotomy, mitral valve open repair, 136
thorascopic approach, pulmonary vein isolation, 188
thrombosis, SVG failure, 12
tobacco smoking
LITA CABG patency, 4
lung transplantation donor selection, 243
Toronto Lung Transplant Group, 244
total artificial hearts (TAH), 206–7
totally endoscopic coronary artery bypass (TECAB) anastomotic creation, 66
arrested heart see arrested heart totally endoscopic coronary artery bypass (AH-TECAB)
cardiopulmonary bypass, 60
cardiopulmonary bypass, 60
multivessel, 68
post-anastomosis procedure, 67
postoperative considerations, 67–68
procedural details, 61–2, 62f, 63f, 64f
robotically assisted, 59
target vessel exposure, 62, 64–5, 65f, 66f, 67f
toxoplasmosis, 233
transapical access, transcatheter aortic valve implantation, 101–2
transcatheter aortic valve implantation (TAVI), 100–2
apical access, 104–5, 105f
bail-out suggestions, 107–8
complications, 107–8
current outcomes, 102
imaging, 105–6
optical angulation of the C-arm, 105–6, 106f
patients, 101
setup, 104
technical steps, 104–8
transfemoral vs. transapical access, 101–2
valve positioning/implantation, 106–7, 107f
transesophageal echocardiography (TEE)
MIMVS, 148–9
mitral valve open repair, 136
OPCAB, 38–9
pre-pulmonary vein isolation (PVI), 188
TECAB, 61
transfemoral access, transcatheter aortic valve implantation, 101–2
transplant half-time, 235
transsthoracic clamping, TECAB, 60
triangular and posterior leaflet "haircut" resections, MIMVS, 149
triangular resection, posterior prolapse in mitral valve open repair, 137–8, 138f
tricuspid regurgitation, MCS, 215
trileaflet aortic valve repair, 94
triple-agent therapy, post-lung transplantation, 255
two-dimensional (2D) echocardiography, thoracic aortic surgery, 112–13
type 0 bicuspid aortic valve techniques, 87
type 1 bicuspid aortic valve techniques, 85, 87, 88f, 89f, 90f, 92f
type A (DeBakey Type I) aortic dissection, 119
type B aortic dissection, 117–18
Ueda, Y, 120
ultrasound
high-intensity focused ultrasound, 180
intravascular ultrasound, cardiac allograft vasculopathy, 233
United Network for Organ Sharing (UNOS) Thoracic Organ Committee, 241, 242–3
University of Wisconsin solution, heart preservation, 227
Urchin heart positioning device (Medtronic), 253f
VAD (ventricular assist device), 163, 225, 230
vagal denervation, atrial fibrillation surgery, 185
VAJ (ventriculo-aortic junction), 73, 74f
valganciclovir, 233
valve positioning/implantation, TAVI, 106–7, 107f
valve-sparing aortic replacement, outcomes, 93
valvular disease, MCS, 214
valvular regurgitation, OPCAB, 38–9
vasculopathy, peripheral, 159
Vassiliades, T A Jr, 56
ventricular assist devices (VADs), 163, 225, 230
ventricular reconstruction, heart failure in, 161–2
ventriculo-aortic junction (VAJ), 73, 74f
Veterans Affairs medical centers, 36
Volodos, N L, 111
Von Uppell, U O, 140
von Willebrand factor (vWF), 205
von Willebrand syndrome, acquired, 217

warfarin
atrial fibrillation surgical ablation, 181
MCS, 215
Washkansky, L, 224

XPOSE positioner (Maquet), 41

Y-graft configuration
LITA vs. RITA, 4
right coronary system revascularization, 20
Yoshida, F, 158