Invited paper

Choice of conduits for coronary artery bypass grafting: craft or science?

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Summary

Long-term patency of a bypass graft is an important determinant in reducing morbidity and increasing survival after coronary bypass surgery. The purpose of this review is to analyse factors contributing to improved outcomes of commonly used conduits. Progress has been limited by the lack of uniform definitions of graft failure and development of appropriate statistical models. Evolving techniques for assessing patency at more frequent intervals has provided insight into the time and sites of early disease. The explosion of scientific knowledge of graft physiology has added to improving harvest, storage and early protection procedures thereby reducing early morbidity. Similarly, the understanding and management of risk factors have contributed to graft durability and possibly survival. Conduits have different characteristics and applications, which are patient dependent. Competitive flow remains a problem especially with arterial conduits; functional studies as opposed to anatomy of the target artery may improve understanding of the contribution of the collateral circulation. Selected patency data provide comparison between grafts. The role of the second internal thoracic artery graft is the subject of the Arterial Revascularisation Trial. Off-pump bypass procedures and patient characteristics affect conduit selection. Stroke is a major complication, which can be minimised by avoiding the aorta especially during off-pump surgery. There are few randomised controlled trials on the late outcomes comparing different bypass grafts and between bypass grafting and current percutaneous intervention methods. Accurate reporting of outcomes of graft patency will improve the scientific content and emphasise the importance of surgery in the management of coronary disease.

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Keywords: Coronary artery disease; Coronary artery bypass grafts; Graft patency

1. Introduction

Coronary artery surgery has faced an unprecedented challenge in recent times from percutaneous therapies, but many centres report a trend now for greater referral for surgery for multivessel disease compared with recent years. This is likely to be at least in part explained by a growing acceptance of the long-term durability of revascularisation by CABG, which contrasts with the higher requirements for reintervention after percutaneous therapies in randomised studies (such as SOS and ARTS) comparing techniques [1,2]. Graft patency is important therefore both to the patient, in terms of clinical outcome, and to the surgeon, regarding professional satisfaction and the fate of our specialty. A thorough understanding of the factors predisposing to graft failure is thus essential in protecting the interests of both parties in a CABG operation. The purpose of this review is to explain why reported results vary so widely, by assessing the factors which determine patency and the evidence on which these results are based. The report concentrates on papers that contain level A and B evidence and class IIA recommendations [3].

The fate of a patient having a coronary bypass operation can be predicted by a number of explanatory variables. The main categories relate to the patient, the target artery, or are conduit related. Of these, the appropriate selection, acceptable quality and application of the bypass graft are major predictors of survival and avoidance of major morbidities. Each of these is considered in turn.

Any discussion of graft patency needs to begin by recognition of inconsistencies in definition, classification and statistical manipulation of patency data. Far from mere semantics, this is an essential caveat, which has limited our understanding of this field and thus the development of guidelines for revascularisation.
2. Assessment

2.1. Definitions of graft patency

Commonly used anatomic definitions of graft failure are: total occlusion, greater than 75% or 50% stenosis, string-sign and Fitzgibbon A, B, and O class (A = patent or stenosis less than 50%, B = stenosis greater than 50%, O = total occlusion) [4]. A frequently used definition of a combined end point for a failed graft merges these: total occlusion, stenosis greater than 75% or string-sign. Stenoses in the body of a graft or at either anastomotic site should be considered a failure. Proximal aortic or distal disease in a target artery, which could cause graft dysfunction, should be recorded but not considered graft failure (Fig. 1a).

Physiological parameters are also used, for example TIMI flow 0 = no perfusion, 1 = minimal entry of dye, 2 = partial and 3 = normal perfusion [5].

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Fig. 1. (a) Diagram showing the potential sites for graft stenoses or occlusion. Disease in the body of a bypass conduit provides the best information about the biological properties of the graft. Proximal or distal disease in aorta or target arteries may cause graft failure; similarly poor anastomotic techniques may cause failure. Neither of these latter forms of conduit failure is related necessarily to the graft properties. (b) Crossover in situ RITA grafted to LAD, in situ LITA sutured to circumflex marginal branches, using sequential anastomoses to avoid handling the thoracic aorta (RITA: right internal thoracic artery; LAD: left anterior descending artery LITA: left internal thoracic artery; RA: radial artery). (c) The thoracic aorta is avoided by using composite bilateral ITA grafts. The in situ LITA is grafted to the LAD and diagonal branch with a sequential technique and RA Y graft used to graft the circumflex marginal branch. The RITA with RA extension supplies the posterior descending branch of the RCA (ITA: internal thoracic artery; LITA: left internal thoracic artery; LAD: left anterior descending artery; RITA: right internal thoracic artery; RA: radial artery; RCA: right coronary artery). (d) Alternative strategies to avoid a diseased ascending thoracic aorta using arterial grafts: in situ LITA sequential grafts to the diagonal and LAD, in situ RITA to anterior circumflex marginal, via transverse sinus and GEA to posterolateral branch of RCA (LITA: left internal thoracic artery; LAD: left anterior descending artery; RITA: right internal thoracic artery; GEA: gastroepiploic artery; RCA: right coronary artery).
2.2. Graft angiography

Selective coronary angiography remains the diagnostic standard. Recently, sub-millimetre computer tomographic angiography provides images of coronary grafts that compare favourably with those from selective angiograms with a sensitivity and specificity of 95% [6]. Images of graft stenoses, anastomoses and small post-anastomotic vessels are less satisfactory and often overlooked [7]. A recent comparison of multidetector computed tomographic angiography (CTA) with coronary angiography confirms the reliability of CTA in assessing the patency of coronary artery bypass grafts. In a total of 147 bypass grafts (100 venous and 47 internal thoracic arteries), 28 were occluded and 103 were patent. Eighty-three percent of distal anastomoses were adequately evaluated, but 17% were not well visualised due to clips and/or calcification artefacts. Overall, sensitivity for detecting occluded grafts was 93% with a specificity of 100%; positive predictive value was 100% with a negative predicted value of 98%. The sensitivity for detecting grafts with a stenosis >50% was 100%. The authors concluded that CTA is a valuable tool for assessment of coronary artery bypass graft patency and that dysfunctional grafts can be detected with high diagnostic accuracy [8]. CTA is therefore a useful diagnostic tool to assess patency but not severity of disease. Physiological measurement, for example TIMI flow, is a useful adjunct to describe graft adequacy, but is subjective and not reproducible. Quantitative coronary angiography (QCA) has proven an accurate method of quantifying native vessel stenoses. QCA has been applied less often to measure coronary bypass grafts: stenoses of lesions in the graft trunk are readily measured but narrowings within anastomotic sites are difficult to estimate.

2.3. Analyses of graft patency

Three methods are commonly employed to estimate risks of graft failure but each measure is different, and if not specified, any comparison between publications is difficult or impossible [9].

2.4. Kaplan—Meier estimate

The standard Kaplan—Meier (K—M) method assumes ‘right censoring’ rather than interval censoring. It is suitable for dealing with time to event data in which, in some patients, the outcome has not yet occurred. If it is used to analyse graft patency data, there is an inherent difficulty in needing to make an assumption about the timing of graft failure among patients whose angiography shows that this has occurred. Clearly, there will be biases in assuming that it has ‘just’ happened, or even in assuming that it occurred half way between the known times of patency and non-patency. If it is assumed that graft failure corresponds to the time of angiography, there will be a right shift of the patency curve giving the impression that patency is better than it really is. To assume it occurred at any fixed point in time, however reasonably chosen, is to inject an appearance of accuracy of measurement that is intrinsically lacking in reality.

2.4.1. Interval censoring analysis

There are methods that respect the interval-censored nature of graft patency data [10–13]. These have not been adopted widely, and are not well developed for the inclusion of explanatory variables in modelling.

2.4.2. Symptom-directed angiography

Observational angiography contains a high proportion of patients in whom the study was initiated by evidence of ischaemia. The failure rate in this group is approximately double that found in trial patients who have planned angiography [14].

3. Conduits

3.1. Graft pathology and selection

Internal thoracic arteries are elastic arteries with a muscular sphincter at either end [15]. They are resistant to atherosclerosis [16]. In contrast, radial arteries (RAs) are prone to intimal hyperplasia, atheroma and calcification (Fig. 2). The gastroepiploic artery (GEA) has a thick smooth muscle media that is prone to spasm. Grafts may fail for many reasons, including biologic, graft choice, unsatisfactory preparation, inappropriate operative strategy or poor technique.

3.2. Graft preparation

Many of the events that lead to graft failure occur early in the operation. Careful harvesting, vasodilatation and storage prior to implantation are necessary to prevent graft ischaemia and to optimise late results [17,15]. There are a number of vasoconstrictor pathways that can be blocked or attenuated to minimise potentially lethal graft spasm [18]. Many vasodilator mechanisms are endothelium dependent and care should be taken to protect and preserve endothelial function.

Histopathology of RA (n = 150)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.7%</td>
</tr>
<tr>
<td>Intimal hyperplasia</td>
<td>94%</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>5.3%</td>
</tr>
<tr>
<td>Medial Calcification</td>
<td>13.3%</td>
</tr>
</tbody>
</table>

Fig. 2. Histologic sections of consecutive 150 from which RAs were harvested for coronary bypass grafting. Only 0.7% were normal, 94.3% had reactive intimal hyperplasia and 5.3% had atherosclerotic changes. In addition to the intimal disease, 13% had medial calcification (RA: radial artery). Source: Ruengsakulrach et al. [109].
function during harvest and storage. The more important vasodilator/vasoconstrictor mechanisms are: nitric oxide-guanylate cyclase (NO-cGMP), renin-angiotensin, alpha adrenergic sympathomimetic, serotonin, endothelin, and thromboxane (Table 1).

3.3. Antiplatelet management for patients after coronary bypass surgery

Aspirin at a dose between 150 and 325 mg daily should be given to all patients without contraindications to improve the long-term patency of vein grafts. No evidence exists to support the use of aspirin to improve the patency of arterial grafts. Aspirin use should commence no later than 24 h after coronary bypass grafting (grade A: recommendation). Clopidogrel 75 mg daily is an acceptable alternative to the use of aspirin (grade B: recommendation) [19].

3.4. Venous conduits

3.4.1. Long saphenous vein

K—M estimates of patency at 10 and 20 years are about 60% and 20% respectively (Table 2). In contrast, interval analyses reveal higher patencies of between 50% and 60% at 10 and 20 years (Fig. 3) [20]. There is a suggestion that the late results of saphenous vein (SV) grafting have improved. Saphenous vein grafts attached to the largest non-LAD artery treated with vasodilators at the time of implantation and statin therapy demonstrated a 5-year patency of over 80% [21]. This has been attributed to more careful conduit selection, improved harvesting, and surgical techniques together with risk-factor management, for example by the use of HMG co-A reductase inhibitors.

3.4.2. Short saphenous vein

The short saphenous has occasionally been used as the graft of last resort; however there are few reports of their patency [22]. Amongst 26 patients, 65% of short saphenous grafts were found patent at 6 years after surgery, compared with 10% for arm veins and 93% for ITAs [23].

3.5. Arterial conduits

Surgeons and cardiologists have been aware of the limitations of saphenous vein grafts for some time. Extensive arterial revascularisation has developed over the last 10 years following the general consensus that two internal thoracic artery grafts were superior to the use of a single internal thoracic artery graft, although this has never been proven. Innovative strategies have developed to improve the number of distal anastomoses using sequential and composite internal thoracic grafts [24—30].

Despite widening the applications of internal thoracic arteries, coronary reconstructions may still be limited by premature failure of supplementary vein grafts. The radial artery introduced by Carpentier in 1971 [31] initially fell into disrepute because of high failure rates [32], but was revisited by Acar after the findings that many of these original grafts were widely patent at 6 years [33]. Radial artery usage continues to increase and has provided an additional arterial conduit which has advantages over other arterial grafts such as the gastroepiploic or inferior epigastric arteries. The radial artery was initially used as a free graft in a fashion similar to that of the saphenous vein graft. More recently it has been used as a T or Y graft from the left internal thoracic artery (LITA) or an extension graft from the distal right internal thoracic artery (RITA). These applications have been enhanced further by the additional use of sequential techniques. Off-pump surgery has provided another impetus for the use of complete arterial grafting. Despite wider applications of arterial grafting no biologic comparison exists between the radial artery and the free right internal thoracic artery, or the saphenous vein graft.

Table 1
Major regulatory mechanisms that control flows in coronary bypass conduits.

<table>
<thead>
<tr>
<th>Vasodilators</th>
<th>Vasoconstrictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitric oxide*</td>
<td>Adrenaline</td>
</tr>
<tr>
<td>Endothelin-1 acting on ET&lt;sub&gt;α&lt;/sub&gt;</td>
<td>Endothelin-1 acting on ET&lt;sub&gt;β&lt;/sub&gt;</td>
</tr>
<tr>
<td>Angiotensin II acting on AT&lt;sub&gt;1&lt;/sub&gt;R</td>
<td>Angiotensin II acting on AT&lt;sub&gt;2&lt;/sub&gt;R</td>
</tr>
<tr>
<td>Prostaglandin (PGH&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>Prostaglandin (PGI&lt;sub&gt;2&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Thromboxane (TXA&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>Endothelium derived hyperpolarising factor (EDHF)*</td>
</tr>
</tbody>
</table>

* Endothelium dependent vasodilatory mechanisms.

Table 2
Saphenous vein graft patency: symptom-directed observational data.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n assessed</th>
<th>Patency (%)</th>
<th>Follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hayward and Buxton</td>
<td>2007</td>
<td>244</td>
<td>82</td>
<td>5</td>
</tr>
<tr>
<td>Sabik et al.</td>
<td>2005</td>
<td>4045</td>
<td>57</td>
<td>10</td>
</tr>
<tr>
<td>Zacharias et al.</td>
<td>2004</td>
<td>588</td>
<td>63</td>
<td>6</td>
</tr>
<tr>
<td>Goldman et al.</td>
<td>2004</td>
<td>85</td>
<td>61</td>
<td>10</td>
</tr>
<tr>
<td>Desai et al.</td>
<td>2004</td>
<td>440</td>
<td>86</td>
<td>1</td>
</tr>
<tr>
<td>Shah et al.</td>
<td>2003</td>
<td>3715</td>
<td>61</td>
<td>8</td>
</tr>
</tbody>
</table>

* Programmed angiography (RAPCO definition: patent: < 80% stenosis of the graft trunk including proximal, and distal anastomoses).
3.6. Left internal thoracic artery

K–M estimates of patency suggest that about 85–92% of LITA grafts are patent at 15 years [34,35]. Shah et al. found interval patency to be 97% at a mean of 12 years (Table 3) [36]. There are few properly scaled trials of the benefits of LITA versus SV grafting. Overwhelming clinical and radiological evidence over 3–4 decades has resulted in nearly universal acceptance of the LITA. Skeletonisation of the pedicle may provide more length and flexibility, but there is little sound evidence that skeletonisation improves outcome. Concern has been expressed about the potential loss of patency of sequential anastomoses or when composite T or Y grafts are constructed. Although these techniques are popular they are supported by little scientific evidence [37]. Anatomic assessment of outcomes following Y and sequential techniques has been unreliable because of the number of variables. A breakthrough has been the addition of a functional outcome measure using quantitative angiography and TIMI flow to define any benefits from the use of composite grafts [38].

3.7. Right internal thoracic artery

Right internal thoracic artery grafts overall have a greater but not significantly different failure rate compared with the LITA. However, when grafted to the left anterior descending (LAD) artery, the patencies are similar [36]. Even so, the RITA has been used relatively infrequently [39]. In-situ RITA grafts to the distal right coronary artery (RCA), with a stenoses < 70%, fail more frequently than when grafted to the left system, and some surgeons elect to use free ITAs or SVs (Table 3). Competitive flow from grafting target arteries with lowgrade stenoses reduces patency [40,42]. Most surgeons prefer to attach the RITA to left-sided targets where the benefits have been well documented [34,40]. When grafted to the largest non-LAD artery, the free RITA patency is not significantly different from that of the RA [41,42].

Many questions remain unresolved. Should the RITA be used in situ or take origin from the aorta or the LITA? Is the RITA better skeletonised or pedicled? Should in-situ grafts to the left side be passed anterior to the aorta or through the transverse sinus? Is repeat sternotomy more difficult in the presence of a cross over RITA? Documentation of outcomes from different RITA grafting strategies has been poor, with outcomes of different techniques inappropriately pooled together in most series.

3.8. Bilateral internal thoracic artery grafting

The benefits from using a second ITA graft are not clear despite the large volume of surgical literature. The most

Table 3

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n assessed</th>
<th>Patency (%)</th>
<th>Follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ITA graft patencya</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yie et al. [59]</td>
<td>2008</td>
<td>129</td>
<td>99</td>
<td>2.8</td>
</tr>
<tr>
<td>Hayward and Buxton [97]</td>
<td>2007</td>
<td>204</td>
<td>96</td>
<td>5.1</td>
</tr>
<tr>
<td>Gansera et al. [99]</td>
<td>2007</td>
<td>618</td>
<td>93</td>
<td>3.8</td>
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<tr>
<td>Bonacchi et al. [100]</td>
<td>2005</td>
<td>155</td>
<td>97</td>
<td>2</td>
</tr>
<tr>
<td>Sabik et al. [34]</td>
<td>2005</td>
<td>249</td>
<td>92</td>
<td>15</td>
</tr>
<tr>
<td>Goldman et al. [35]</td>
<td>2004</td>
<td>137</td>
<td>85</td>
<td>10</td>
</tr>
<tr>
<td>Shah et al. [36]c</td>
<td>2004</td>
<td>268</td>
<td>97</td>
<td>12</td>
</tr>
<tr>
<td>Cameron et al. [101]</td>
<td>2004</td>
<td>51</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>Possati et al. [102]</td>
<td>2003</td>
<td>82</td>
<td>96</td>
<td>5</td>
</tr>
<tr>
<td>Right ITA patencya</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-situ grafts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shah et al. [36]</td>
<td>2004</td>
<td>317</td>
<td>86</td>
<td>6.5</td>
</tr>
<tr>
<td>LAD graft</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bonacchi et al. [100]</td>
<td>2005</td>
<td>155</td>
<td>94</td>
<td>1.4</td>
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<tr>
<td>Rashkow et al. [103]</td>
<td>2003</td>
<td>58</td>
<td>81</td>
<td>5.9</td>
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<td>Aorto-coronary grafts</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hayward and Buxton [97]</td>
<td>2007</td>
<td>52</td>
<td>88</td>
<td>5.1</td>
</tr>
<tr>
<td>Shah et al. [36]d</td>
<td>2004</td>
<td>307</td>
<td>91</td>
<td>6.5</td>
</tr>
<tr>
<td>LAD graft</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Composite grafts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calafiore et al. [104]</td>
<td>2000</td>
<td>63</td>
<td>99</td>
<td>1.5</td>
</tr>
</tbody>
</table>

ITA: internal thoracic artery.

a Ischaemia-directed observational data.
b Programmed angiography (*RAPCO definition: patent: < 80% stenosis of the graft trunk including proximal anastomosis, and distal anastomosis).
c Interval analyses.
d RAPCO definition: patent: < 80% stenosis of the graft trunk including proximal anastomosis, and distal anastomosis.

Fig. 4. (a) Comparison of matched pairs of patients receiving BITA and SITA grafts. The numbers of patients surviving at selected follow-up intervals are listed (p < 0.001). Each symbol represents a death, and vertical bars depict the 68% confidence limits (equivalent to one standard error) of Kaplan—Meier estimates. Solid lines, enclosed within 68% confidence limits, are parametric estimates (BITA = bilateral internal thoracic artery; SITA = single internal thoracic artery). Source: Lytle et al. [40]. (b) Hazard function curves demonstrate the increased risk of death associated with SITA grafting with increasing follow-up interval. Dashed lines are 68% confidence bands (BITA: bilateral internal thoracic artery; SITA: single internal thoracic artery). Source: Lytle et al. [40].
instructive observational publication is by Lytle et al. [40].
After risk adjustment, they concluded that there was a survival benefit and a lower reintervention rate in favour of bilateral over single ITA grafting in a wide range of patients that continued into the third decade after surgery (Fig. 4a and b). A similar survival benefit from use of bilateral ITA was described in Taggart’s meta-analysis of multiple smaller studies of this field, but Taggart conceded that only a full RCT could satisfactorily confirm any perceived benefit [43].

Arterial Revascularisation Trial (ART) is a prospective randomised trial with the objective of testing the hypothesis that two ITA grafts are superior to a single ITA graft [2]. The aim is to determine whether the use of both ITAs in coronary artery bypass grafting (CABG) improves the survival rate and reduces the requirement for further interventions. ART is an international multicentre trial with a parallel, open-label design. Patients with multivessel coronary artery disease (CAD) were eligible for enrolment, but the trial excluded those with single grafts, re-operation for CAD, evolving myocardial infarction (MI), and those requiring concomitant valve surgery or other cardiac procedures.

Patients were randomised to use of one or two ITAs supplemented by vein or other arterial conduits as per surgeon’s choice. For patients having bilateral ITAs, it was recommended that both conduits be grafted to left-sided arteries. The sample size is 3000 with a 1:1 randomisation. The primary outcome measure is survival. Secondary outcomes are cause-specific mortality, 30-day mortality, reintervention by PCI or further surgery, quality of life, and cost-effectiveness. Recruitment was started in 2004 and follow-up is up to 10 years. Recruitment was completed in December 2007 resulting in a total of 3102 enrolled patients. The final results are expected in 5 to 10 years.

3.9. Radial artery

There are over 300 reports of RA use in CABG. Nearly all were observational studies and only two were RCTs [44].

Graft patency data were limited and the results varied widely [45] (Table 4). Many believe RA results are superior to those of SVGs [44,46]. The routine use of calcium channel blockade in order to reduce vasospasm is widespread, and has been reviewed. All studies were underpowered; no study provided evidence of its benefit [47]. Complete arterial grafting has become feasible with the combinations of ITAs and RAs in most patients even those with extensive multivessel disease using Y and sequential anastomoses. However, concern has been raised about the patency of some sequential techniques using RA conduits [48].

Preliminary results from two randomised trials did not confirm conclusions from many of these observational studies. The radial artery patency study (RAPS) compared the patency of the RA with the SVG when grafted to the largest non-LAD artery, that is, the circumflex or RCA system. By using a clever design, the trial graft was sutured to the circumflex system and the control graft was anastomosed to the alternative coronary target, such as the RCA, or vice versa. This method results in two graft angiograms for each patient who acts as his/her own control. The disadvantage is that it is not possible to identify any clinical outcome differences because of the same graft set in each patient. The authors used the end-point definition of total graft occlusion. The failure rates were RA 8.2% versus SVG 13.6% (p = 0.009). They concluded that the RA was superior to the SVG. However if the seven RA conduits which had the ‘string-sign’ were considered failures, instead of patent (see definitions), the results were almost identical [49].

In a recent review of the impact of target vessel properties on graft patency, the Radial Artery Patency Study investigators confirmed that small target vessel size adversely affected outcome and grafting to a target vessel with more severe proximal stenosis improved patency. Five year angiographic data is being compiled [50].

The radial artery patency and clinical outcomes (RAPCO) trial compares the RA with the free RITA as the conduit of second choice in patients under 70 years and SVGs in older patients [51]. The rates of survival, relief of angina, freedom from MI, cardiac failure, and the frequency of re-operation are also assessed. At 5 years, the trial mid-point, there are no clinical or angiographic differences between RA and free RITA or the SVG graft [41,52]. Improved SV performance during the trial may have accounted for these unexpected results. The follow-up is 10 years; most of the graft failures are expected in the latter 5 years of the study. The trial is expected to be completed by 2012.

3.10. Gastroepiploic artery

Two large studies of about 1000 cases have indicated 5-year patencies of 62% and 86% [53,54] (Table 5). A current review indicated right GEA performance was similar to that of the SV.

Table 4
Radial artery conduits for coronary artery bypass grafting: current perspective.*

<table>
<thead>
<tr>
<th>Authors</th>
<th>RA conduits used</th>
<th>RA conduits reassessed</th>
<th>Original grafts reassessed (%)</th>
<th>Angiographic patency (Fitzgibbon grade A %)</th>
<th>Follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acar et al. [105]</td>
<td>910</td>
<td>64</td>
<td>7</td>
<td>83</td>
<td>5.6 ± 1.1</td>
</tr>
<tr>
<td>Iaco et al. [106]</td>
<td>164</td>
<td>91*</td>
<td>47</td>
<td>95</td>
<td>4.0 ± 2.3</td>
</tr>
<tr>
<td>Tatoulis et al. [107]</td>
<td>8420</td>
<td>280 (369*)</td>
<td>3</td>
<td>90</td>
<td>1.2 ± 0.9</td>
</tr>
<tr>
<td>Possati et al. [102]</td>
<td>91</td>
<td>84</td>
<td>92</td>
<td>88</td>
<td>8.8 ± 0.8</td>
</tr>
<tr>
<td>Khot et al. [108]</td>
<td>–</td>
<td>319</td>
<td>–</td>
<td>51</td>
<td>1.5 ± 1.4</td>
</tr>
<tr>
<td>Yie et al. [59]</td>
<td>488</td>
<td>174</td>
<td>–</td>
<td>92</td>
<td>2.8</td>
</tr>
<tr>
<td>Zacharias et al. [98]</td>
<td>242</td>
<td>157</td>
<td>–</td>
<td>71</td>
<td>1.8 ± 1.5</td>
</tr>
<tr>
<td>Hayward and Buxton [97]*</td>
<td>363</td>
<td>99</td>
<td>–</td>
<td>90</td>
<td>5.0 ± 0.5</td>
</tr>
</tbody>
</table>

* Modified and updated from Mussa et al. [46].
* Numbers represent anastomoses reassessed.
* Programmed angiography (RAPCO definition: patent: <80% stenosis of the graft trunk including proximal anastomosis, distal anastomosis).
In a recent follow-up of 1352 patients with multivessel disease who had CABG using (in addition to ITAs, RAs and SVGs) a gastroepiploic graft to the LAD (5%), circumflex (20%) or RCA (75%), the early mortality was 1.3% and the 5-, 10- and 15-year survivals rates were 92%, 84%, and 71%, respectively. The cumulative patency rates were 92% at 1 year, 86% at 5 years and 67% at 10 years. Patency rates in skeletonised grafts were 93% at 1 year and 86% at 4 years [54]. In a recent review the authors concluded that the 3-year GEA patency was inferior to the ITA, but not significantly different to the RA or SVG [55]. In a small RCT comparing the SV and GEA to reconstruct the RCA, the venous patency at 6 months (85%) exceeded that of the GEA (62%). The authors used minimal lumen diameter of the proximal RCA assessed by quantitative coronary angiography rather than percent stenosis as a surrogate for competitive flow. They concluded that a minimal lumen diameter <1 mm is recommended to assure GEA patency [56].

### 3.11. Target artery

Competitive flow and low-flow profoundly affect graft patency. Low-grade graft stenoses in the target artery proximally are a major cause of competitive flow. SVGs and in-situ ITAs are more tolerant than the RAs and GEAs. This is likely to be related to the thick layer of smooth muscle or poor endothelial function in these muscular conduits. The RAPS investigators recommend avoiding grafting target arteries with a stenosis less than 90% with RA grafts [49]. Other surgeons graft vessels with a stenosis greater than 75% [57—59]. Unlike SVGs, arterial grafts autoregulate in response to demand: when the requirements are low, arterial grafts constrict. The interaction between the severity of proximal native coronary stenosis and target vessel diameter is complex. Secondly, the short-term gains of SVGs should be weighed against the late durability of arterial conduits [60].

The diameter and the quality of the target artery are critical factors in determining graft patency. Saphenous vein grafts, when attached to large target vessels produce comparable patency rates to the ITA [35]. A randomised controlled trial reported similar findings when the free ITA or SVG were grafted to the largest non-LAD coronary graft [21].

Severity of proximal native vessel stenosis is only one factor that influences competitive flow. Native vessel stenosis alone does not take into consideration the role of the collateral circulation supplying the distal circulation. Functional rather than anatomic severity is a more important predictor in determining graft outcome. A totally occluded target artery with a well-developed collateral circulation may result in greater resistance to graft flow than a lesser stenosis in the target artery with a poor collateral supply to the distal circulation. A fractional flow reserve-guided study revealed a 9% failure with functionally significant versus a 21% for non-significant lesions [61].

The progression of native coronary artery stenoses has been reported to result in recovery in function of some in-situ ITAs; recovery of flow in free arterial grafts is less well documented. A deficiency in assessing the impact of widespread disease is the difficulty in quantifying target arteries with diffuse arterial disease.

### 3.12. Off-pump coronary artery bypass grafting

In a systematic literature search of 132 publications comparing graft patency in off-pump coronary artery bypass (OPCAB) with conventional surgery, Lim et al. found only five trials that were sufficiently robust to make a meaningful comparison. The relative risk of graft patency using OPCAB versus conventional surgery was 0.95 (95% CI 0.93—0.80, p = 0.001). In this meta-analysis the authors concluded that there was a small but significantly lower patency and higher revascularisation rates in the OPCAB compared with the conventional group. Whilst the results of different studies are not always consistent [62], it has been suggested that potential disadvantages of OPCAB are lower graft patency rates and more incomplete revascularisation, with the potential for long-term morbidity and mortality. The role of graft choices in OPCAB surgery is not clearly defined.

Graft choices for OPCAB surgery have not been critically studied and indeed there are no RCT comparing vein grafts to arterial grafts, or various arterial grafts with one another in OPCAB surgery.

The most important choice in OPCAB surgery is selecting the right graft for the right target artery to achieve maximum graft patency and improved clinical results. Another recent meta-analysis of prospective randomised trials comparing graft patency in OPCAB versus ONCAB (on-pump coronary artery bypass) by Takagi et al. [63] suggests that patency rates of LITA to LAD remain comparable, but ongoing questions have been raised about overall vein graft patency in OPCAB cases. In considering these studies, it is important to recognise that the five studies that comprise this meta-analysis contain only 1098 total patients. It has been suggested that these facts may create some uncertainty in the conclusion reached by Takagi that OPCAB risks effective revascularisation [63,64]. In general, patency of the LITA graft has not been shown to be different with either OPCAB or ONCAB in randomised [63,65—70] and non-randomised studies [71]. When not grafted to a diseased LAD territory, an alternative is to graft the LITA to the circumflex territory and the crossover in situ RITA is used to graft the LAD. Patency of the LITA to the circumflex territory is comparable between OPCAB and ONCAB [66]. In addition the patency of the in situ RITA to the LAD is similar to the patency of LITA to the LAD (100% vs 98% at 3 months in Al-Ruzzeh et al. [66] and 98% vs 98% at 1 year in Kim et al. [71]), and is unaffected by use of off-pump or on-pump techniques (RITA to LAD: OPCAB 100% vs ONCAB 100%).

Data relating to clinical and angiographic performance of RAs in OPCAB is less well known as the SV graft has been used more frequently in most studies. Among the randomised trials, data on RA patency was given in only two studies. One study did not find a difference in overall graft patency when

### Table 5

Gastroepiploic artery patency: observational studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Patients</th>
<th>n assessed</th>
<th>% patent</th>
<th>Follow-up (years)</th>
</tr>
</thead>
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<tr>
<td>Takahashi et al.</td>
<td>2004</td>
<td>1020</td>
<td>86</td>
<td>5</td>
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<td>Suma et al.</td>
<td>2007</td>
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<td>124</td>
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</tr>
<tr>
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<td></td>
<td></td>
<td>1002</td>
<td>87</td>
<td>0.16</td>
</tr>
<tr>
<td>Glineur et al.</td>
<td>2008</td>
<td>90</td>
<td>62</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>
comparing OPCAB 50/56 (89%) with ONCAB 55/60 (92%) [66], whereas the study by Khan et al. shows significant decrease in patency at 3 months, of the RA in OPCAB 26/34 (76%) compared to ONCAB 22/22 (100%) (absolute difference of 24% (9.3% to 37.8%) [69].

Alternative factors, such as a desire to perform a no-touch technique on the aorta, may influence graft choices in OPCAB. Experienced cardiac surgeons can recognize patients in whom an off-pump grafting technique may be safer. Therefore a no touch technique would favour the use of bilateral in-situ ITAs or construction of Y grafts off the LITA. Again surgeon preference for construction of Y grafts off the LITA with either a free RITA, RAs or vein grafts will dictate conduit choice. Graft choices do not need to be limited by minimal access approaches. Endoscopic techniques are available for ITA, SV and RA harvesting providing the surgeon and patient with minimal incisions, which is sometimes the goal of OPCAB surgery, particularly those with hemisternotomies, lateral thorracotomies or robotic approaches.

The utilisation of OPCAB resulted in the development of technologies to facilitate the creation of aorto-coronary graft anastomoses to enable the construction of proximal aortic anastomoses without the use of a side biting clamp, thus reducing the aortic manipulation and microemboli [72]. The majority of devices were designed for vein grafts. Fewer devices were designed for distal coronary anastomoses using either vein graft or ITA. These devices favoured the use of vein grafts in the past, but many have produced poor results and been withdrawn from the market [73—75]. Other devices such as the Heartstring Proximal Seal System (Guidant, Cupertino, CA) allow the construction of an angled hand-sewn proximal aortic anastomoses, with either venous or arterial grafts [76].

4. Patient factors

4.1. Diabetes mellitus

The patient with diabetes mellitus presents surgeons with a variety of dilemmas. The coronary arteries are more diffusely diseased than in those without diabetes, and there is a tendency for more 2- and 3-vessel disease [77]. Then there is the performance of specific bypass conduits. There is little known about the RA from randomised trials; however it has been suggested that RA is more likely to be calcified in diabetic patients [78]. Choudhary et al. found that RA grafts from patients with diabetes mellitus have impaired endothelial function and are more prone to vasospasm [79]. SVs, however, are known to be more calcified and to have changes in all layers of the wall than non-diabetics [80]. The ITA has much less risk of intimal damage than the SV, and retains biological integrity [81,80]. Therefore the ideal grafting strategy for diabetic patients would seem to be bilateral ITA grafts [37]. Initially endorsed in the seminal paper from the Cleveland Clinic [82] the caveat was an increased risk of sternal infection.

The risk of sternal infection ranges up to 4.7% following BITA harvest (compared with 0.2—2% for SITA harvest) and the risk in diabetics can exceed 10%. These figures improve with skeletonisation of the ITA, which reduces chest wall trauma and may protect collateral blood supply from the intercostal arteries [83]. However, many surgeons avoid RITA grafting in the obese (body mass index > 35), severe diabetic patients, those with advanced pulmonary disease, and the elderly [83]. Other complications are also increased in the diabetic population, such as CVA, mortality, MI and recurrent angina [77]. Sabik et al. recently showed an increased need for reinterventions in diabetic patients [84], however BITA strategy decreased the rate of reintervention.

The use of BITA would seem appropriate in many patients with diabetes, if the surgeon is comfortable with the technique of skeletonisation. Alternatively, a single ITA supplemented by RA grafts if the target vessel stenosis exceeds 70%. There is little scientific data to suggest a preference between the RA and SV as the supplementary graft of choice. However, harvesting from the arm reduces the risk of complications in diabetic patients with peripheral vascular disease.

4.2. Atherosclerosis and calcification of the ascending aorta

Extreme disease of the ascending thoracic aorta in patients who require CABG creates a problem for the surgeon. Manipulation of the aorta is associated with a high risk of embolism. Cannulation, clamping of the aorta, and proximal grafting are difficult and in some circumstances, impossible. Complete grafting and avoiding the aorta can be achieved by using combinations of LITA, RITA, and a GEA as in-situ grafts, supplemented by RAs and SVGs as Y grafts. Sequential anastomoses further increase the number of distal targets (Fig. 1b—d). The use of a Heartstring or similar device for construction of proximal anastomoses without aortic clamping may permit a more traditional graft configuration. A proximal anastomosis with the innominate artery provides another solution. Off-pump techniques, in combination with composite ITA conduits, allow the aorta to be avoided completely, thereby minimising the risk of embolism [85].

4.3. Elderly patients

Cardiac surgeons are operating on older patients with more comorbidities. In spite of this, there has been an improvement in the outcomes for these patients over the past 20 years [86,87]. The role of myocardial revascularisation in the elderly patient should encompass the following objectives: prolong life, relieve distress, restore function, and prevent long-term disability and dependency [88].

In terms of the conduit best suited to this population, there has been a reluctance to use arterial grafts because of the presumed limited life expectancy of these patients in spite of the known benefits of single ITA grafting [89] and bilateral ITA grafting, even in the elderly [40] (Fig. 5a and b). Indeed, these authors showed a higher incidence of repeat angina when patients received SV grafts. Another randomised trial comparing RA and SV has shown no difference in clinical and angiographic outcomes between the two conduits at 5 years [51]. The conduits themselves are subject to changes as a result of advancing age of the patient. The RA is likely to undergo medial calcification, although this is not always clinically relevant [90]. SV grafts similarly will calcify over
time, although the use of appropriate adjuvant medication such as cholesterol lowering agents will attenuate these changes [91]. The ITA rarely undergoes these tendencies.

Extensive arterial revascularisation, using ITAs supplemented by RAs, is readily performed in the elderly with little increase in morbidity or mortality. In this group of patients, many of whom have peripheral vascular disease, the SV is often sclerotic. RAs offer a satisfactory alternative in many elderly patients. Arterial conduits combine well with ITAs as composite grafts for aortic no-touch procedures using off-pump techniques in the elderly [92,93].

### 4.4. Renal failure

Patients with impaired renal function and those on renal support are prone to early complications such as further loss of kidney function, sternal and other infection, and progressive deterioration of graft function [94–96]. The choice of grafts needs to be considered with potential complications in mind. A single ITA is desirable but the risks of a second ITA may not be justified. The requirement of a RA for a fistula likewise limits the use of both RAs. Therefore SVGs are employed despite the rapid progression of disease.

### 5. Conclusion

The durability of LITA and RITA grafts has been confirmed to 20 years and beyond. Careful harvesting storage, and implantation, together with improvements in surgical grafting techniques, has broadened the use of both ITA bypass grafts. Single or bilateral ITA conduits form the basis for nearly all surgical reconstructions for coronary artery disease. The benefits of bilateral over single ITAs remain unproven. In conjunction with SVGs, RAs, GEA, and other arterial conduits, extensive arterial grafting for obstructive coronary artery disease is now feasible in most patients. RCTs comparing RA patency with SVGs show no convincing benefits, however these trials are well short of the 10-year follow-up.

### 6. Recommendations

The choice of the most appropriate conduit(s) for a coronary bypass operation depends on a number of considerations. Many recommendations are based on low levels of evidence. More rigorous scientific standards are required, with improved guidelines, for the reporting of coronary bypass graft results. EACTS could play a leading role in developing firmer guidelines. Minimal requirements should include: use of one of the commonly accepted definitions of graft failure; whether the data is collected from ischaemia or programme driven angiographic studies; details of graft selection, preparation and storage of various conduits, grafting configurations, and patient details, quantification of native vessel stenosis. Postoperative management is now recognised as an important determinant of outcome. Secondary prevention of coronary disease should include avoidance of smoking, the use of aspirin, statins and other cholesterol lowering agents, and control of hypertension and diabetes, as well as general health care measures.

Observational studies of graft patency and patient outcomes suffer from selection bias. Nonetheless large population studies provide important longitudinal information and subset information not readily available from RCTs. Large suitably powered RCTs give the most reliable information about cause and effect, but the conclusions can only be applied to the specific graft types and patient groups, defined by the trial entry criteria. The most appropriate statistical methods for analysing patency are debatable; each method has its merits, the problem is that they all produce different results. Longitudinal studies are essential. Patient survival estimates are reliable when linked to a national database. Different levels of data, for example patient variables that are common to all grafts, need to be treated separately from graft variables. System failures which result from assuming that grafts occlude at the time of angiography can lead to large inaccuracies, for example a graft which fails at operation may be recorded as a failure at 20 years post surgery. The development of interval censoring models based on the few documented early failure rates may reduce these inaccuracies.

This review suggests that the increased use of single or bilateral internal thoracic artery grafts, supplemented by an additional arterial conduit, used as separate or composite grafts, is the standard treatment for patients with multi-
vessel disease. Randomised clinical trials are in progress and conclusive evidence will not be available until completion [2,50,51]. The results of OPCAB series are not consistent [62]. The optimal graft choice in OPCAB surgery is not clearly defined as yet, and is derived primarily from extrapolation of data from on-pump series. The use of in situ ITAs and RA, Y or sequential grafts, thereby avoiding aortic manipulation and minimising stroke risk, is the preferred technique.

Cardiac surgeons are capable of delivering outstanding late results from CABG surgery. When we are facing a barrage of short-term data on coronary artery revascularisation from cardiologists it is important that our data are presented in a scientific and credible form.

References


results from a Department of Veterans Affairs Cooperative Study. J Am Coll Cardiol 2004;44:2149—56.


Classification of recommendations

Class I  Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II  Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

   IIa  Weight of evidence is in favor of usefulness/efficacy.

   IIb  Usefulness/efficacy is less well established by evidence/opinion.

Class III  Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

Level of evidence

A. Data are derived from multiple randomised clinical trials or meta-analyses.

B. Data derived from a single randomised trial, or non-randomised studies.

C. Only consensus opinion of experts, case studies, or standard of care.

Eagle et al. [3].