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Conduit Selection for Improved Outcomes in Coronary Artery Bypass Surgery

Zane B. Atkins^{1,2,*}, Kristine V. Owen³ and Walter G. Wolfe^{1,2}

¹*Department of Surgery, Veterans Affairs Medical Center Durham, NC*

²*Department of Surgery, Duke University Hospital Durham, NC*

³*Department of Medicine, Charles George Veterans Affairs Medical Center Asheville, NC*

USA

1. Introduction

Coronary artery bypass grafting (CABG) is one of the most studied operations in medical history, but many of the data forming the basis for clinical decisions in patients with coronary artery disease (CAD) were derived in the 1970s and 1980s, when the procedure and medical therapy were in their relative infancy. Advances in medical therapy (beta adrenergic blockers, thienopyridines, statins, and others), percutaneous coronary interventions (PCI), and surgical techniques have changed the decision making for patients with CAD. In addition, patient populations referred for surgery have changed since the original studies documenting advantages of CABG over other forms of therapy.

Since percutaneous transluminal coronary angioplasty (PTCA) was introduced, significant advances have been made in the percutaneous treatment of CAD. When drug-eluting stents (DES) were introduced in the early 2000s, many predicted the demise of CABG surgery. Enthusiasm for percutaneous treatment of CAD has most recently led to promoting PCI for unprotected left main coronary artery (LMCA) disease, an anatomical state typically reserved for CABG [1-3]. Percutaneous options have indelibly changed the face of CABG surgery and raise questions concerning the “gold standard” of care in coronary revascularization. For instance, recent reports document that patients referred for redo coronary artery surgery have declined, presumably due to the increased enthusiasm, possibly among surgeons themselves, for PCI in this setting [4]. Despite this, few studies have actually compared PCI with CABG. Two notable studies are recently available, both demonstrating advantages for CABG over PCI for left main CAD and/or three-vessel CAD [5, 6].

Concurrently, details pertaining to short-term outcomes of CABG have been questioned. For example, historical saphenous vein graft (SVG) patencies were reported as approximately 50% at 10 years [7]. However, several studies published in the mid-2000s indicate that early-term patencies of aorto-coronary SVG conduits are not as good as the historical figures that are still often quoted [8-10]. While the long-term patency and performance of the left internal mammary artery (LIMA) has not been questioned, the recent poor performance of

* Corresponding Author

SVG, coupled with increasing enthusiasm and demand for DES has led to the emergence of “hybrid” coronary revascularization, typically consisting of LIMA-to-LAD and PCI of other coronary lesions. [11].

Coronary artery surgery itself has undergone several iterative changes recently. In the 1990s, great enthusiasm existed for the “mid-CAB” (minimally-invasive direct coronary artery bypass) procedure, an approach integral to “hybrid” revascularizations and primarily involving a small left anterior thoracotomy to harvest the LIMA and expose the left anterior descending [LAD] coronary artery. However, outside of the context of hybrid procedures, mid-CAB has had little widespread applicability, particularly since most patients referred for coronary surgery have multivessel disease. Introduction of mid-CAB procedures help usher in the era of off-pump CABG, which was heralded as an approach to reduce the risks associated with on-pump CABG, particularly myocardial dysfunction and cerebrovascular complications [12]. Finally, technology has introduced minimally invasive platforms for performing multi-vessel CABG, most recently the introduction of “totally endoscopic” and robotic CABG surgery [13]. However, it should be noted that these “improved techniques” continue to utilize the same conduit selection and comparative trials with objective evidence are lacking. Since minimally invasive strategies for CABG do not routinely incorporate changes to the operation known to improve short- and long-term results, there appears little reason to suspect that graft patency rates will be improved by less invasive procedures. Rather, one could argue that these alterations in approach to CABG are primarily based on industry involvement, public demands for less invasive procedures, and as marketing strategies by hospital systems.

Are there alternatives to CABG, which could improve long-term outcomes for graft patency and the composite of major adverse coronary events (MACE) particularly when compared with PCI? The answer is a resounding “yes,” and it is found in arterial conduits for coronary bypass. CABG with multiple arterial grafts have been shown to have improved graft patency, reduced need for reoperation or reintervention, and prolonged survival compared with patients undergoing CABG with one IMA and SVG [14-17]. For instance, Sabik et al reviewed a 27-year experience at the Cleveland Clinic with regard to need for reintervention after primary CABG and found that the extent of arterial grafting correlated with freedom from subsequent reintervention [18]. Specifically, patients who received two IMA grafts at initial surgery had approximately 10% risk for reintervention at 10 years; those with one IMA had 20% risk; and those with no IMA had approximately 30% risk for reintervention at 10 years [18].

However, the surgical community has not fully utilized these assets despite numerous, compelling data [19-23]. Jones succinctly summarized the decision point facing conventional, open surgery in the face of rapidly advancing technologies, particularly PCI, and the impact on referral trends for surgical intervention: “improve the long-term outcome, lessen resources used, or both.” [24]. Therefore, one important philosophic principle regarding use of multiple arterial conduits is that the focus is on the *long-term* results, not the short-term.

The purpose of this chapter is to review the data available for CABG with multiple arterial grafts including bilateral IMA use, radial artery, and other conduits. Finally, we will demonstrate the advantages of multiple arterial grafting and make the argument that this strategy yields superior long-term results compared to any strategy for coronary revascularization based on PCI or CABG with traditional conduit selection.

2. Percutaneous coronary interventions

PCI was introduced in 1977 and has undergone consistent improvements in technologies and approaches, offering a less invasive treatment modality for CAD [25]. With the introduction of DES in 2003, the percentage of CAD patients treated with PCI have increased consistently [26, 27]. However, recent studies evaluating long-term outcomes for DES have revealed increased morbidity and mortality secondary to late stent thrombosis [28-30]. While DES therapy has reduced need for target lesion reintervention [31, 32], there is a strict therapeutic requirement for dual anti-platelet therapy (DAPT). Current DAPT recommendations are for at least one year after DES therapy, but the ideal length of treatment still not yet known [33].

3. Comparing coronary bypass surgery and PCI

Shortly after the emergence of PCI as a reliable and durable therapy for CAD, comparisons between angioplasty and CABG were designed in order to determine the relative advantages of each modality. The BARI (Bypass Angioplasty Revascularization Investigation) trial compared balloon angioplasty with CABG in patients with multivessel CAD and severe angina or inducible coronary ischemia. After 5 and 10 years follow-up, no difference in long-term survival was demonstrated [34, 35]. Similar results were noted in other randomized trials of PTCA versus CABG [36, 37]. It was commonly noted in these trials that reintervention for recurrent angina symptoms was significantly more common for patients treated with an initial strategy of PTCA [BARI, RITA, GABI]. However, on subgroup analysis, survival advantage for CABG was demonstrated among diabetic patients in the BARI trial [35]. Finally, a meta-analysis of 13 randomized controlled trials comparing CABG with PTCA showed improved survival for CABG at 5-8 years in those with multivessel CAD and in diabetic patients [38].

Even as studies comparing PTCA with CABG were enrolling, bare-metal stents (BMS) were introduced, and trials to compare the new technology with CABG emerged. The randomized Stent or Surgery (SoS) trial compared multivessel CAD treatment by CABG or by PCI with BMS [39]. At a median follow-up of 2 years, these data showed reduced rates of coronary reintervention and significantly fewer deaths after CABG. Similar trials comparing CABG and PCI with BMS did not demonstrate a survival advantage for either therapy [40], although diabetic patients appeared to have improved survival after CABG in the Arterial Revascularization Therapies Study (ARTS 1) [41].

The US Food and Drug Administration approved DES therapy in 2003, stimulating another round of comparisons between CABG and PCI with the newer technology. Hannan et al reviewed risk-adjusted data from the NY State Dept of Health comparing patients who underwent CABG or PCI with DES for multivessel CAD over a 15-month period shortly after DES approval [5]. At a mean follow-up of 19 months, CABG patients experienced reduced hazard ratio for death, reduced mortality, reduced death/myocardial infarction composite, and less need for repeat revascularization [5]. However, the data were not acquired in the context of a randomized trial. Finally, the SYNTAX trial, a prospective randomized trial conducted across Europe and the US, compared PCI with DES and CABG in patients with 3-vessel CAD, left main CAD, or both [6]. The primary outcomes were major adverse cardiovascular or cerebrovascular events, and follow-up was provided for 12 months after intervention. The SYNTAX data demonstrated increased rates of MACE in the

PCI group, primarily related to the increased need for repeat intervention. Death and post-procedure MI were not significantly different between the two groups, but there was an increased stroke rate in the CABG group compared with PCI, which is somewhat offset by the fact that surgical patients were not managed with aggressive antiplatelet therapy as compared to the PCI group, and many of the cerebrovascular events occurred outside of the perioperative period. More recently, three-year follow up SYNTAX data were reported confirming advantages of CABG over PCI with regard to MACE. Unlike 12-month data, however, composite safety endpoints were no longer different between the two groups, including a similar stroke rate [42]. The SYNTAX authors concluded that CABG remains the preferred therapy for 3-vessel or left main CAD but recommend longer follow up, as is planned for an additional two years [6].

Despite the favorable data for CABG emanating from carefully designed and conducted randomized trials, rates of CABG referral have decreased consistently since the introduction of PCI with stent technologies [43]. Preference for PCI appears driven by disparate interpretation of PCI-versus-CABG studies, by strong patient preference for less invasive procedures with presumed lower periprocedural risk, and by the promise for faster recovery. As a result, the percentage of patients referred for CABG with previous PCI has increased steadily [44] with higher acuity relative to patients without previous intervention [45]. Additionally, technical details of CABG in current surgical practices are considered more challenging compared with previous eras due to more diffuse CAD, subjectively smaller distal coronary targets, particularly among diabetic patients, and the high incidence of prior PCI [46]. Consequently, contemporary results for CABG following PCI are characterized by worse perioperative outcomes when compared with CABG patients without previous intervention. For example, higher rates of postoperative mortality, MACE, and other perioperative complications following CABG in both diabetic and nondiabetic patients have been observed [47-50]. More importantly, increased mid-term mortality in diabetic patients with prior PCI has been observed after CABG [50], and Rao et al demonstrated increased long-term mortality in patients with prior PCI who subsequently underwent CABG [51].

4. Saphenous vein graft conduits

Reversed saphenous vein grafts (RSVG) have been utilized for CABG since the procedure's inception [52] and remain an important graft conduit option in the present era and in numerous clinical scenarios [53, 54]. Historically, patency rates of RSVG aorto-coronary artery grafts have been observed to be approximately 50-60% at 10 years [7, 55]. However, as previously noted, recent RSVG patency data are less encouraging [8-10]. For example, the PREVENT-IV study evaluated 3,000 patients undergoing CABG with 1-year routine angiographic follow-up. At this early time point, 30% of RSVG conduits were occluded and over 45% had "failed," as defined by $\geq 75\%$ stenosis [10]. Importantly, study patients with vein graft failure had significantly increased rates of perioperative complications including MI, death or MI, or MACE relative to the cohort without vein graft complications [10]. Similar results have been noted elsewhere [56-59]. Additionally, surprisingly poor early-to-mid-term RSVG patency rates have been reported elsewhere. The Portland Endoscopic SVG Harvest Trial demonstrated 69% [8], patency by angiography at 6-months, while the PRAGUE 4 trial showed one-year RSVG patency of 52.5% [9]. The potential impact of poor vein graft performance cannot be overstated as RSVG failure is significant contributor to

redo coronary surgery [60]. In addition, early vein graft failure is associated with increased perioperative myocardial infarction [10, 61], which consequently affects survival after CABG [58, 59].

Several potential explanations exist for the recently chronicled poor performance of RSVG as aorto-coronary conduits including early technical errors, endothelial injury, and early thrombosis, which may be related to insufficient biologic reaction to aspirin or inadequate antiplatelet effect of aspirin [62-64]. One important contributor to poor RSVG conduit performance, receiving significant recent attention, may be the practice of harvesting the conduit endoscopically (EVH). This technique was introduced and popularized in the 1990s and has been widely adopted due to increased incisional comfort and patient satisfaction, and decreased wound complications compared to open vein harvesting [65, 66] such that at least 70% of CABG patients undergo EVH based on recent Society of Thoracic Surgeons Database reporting [67]. However, EVH has been associated with increased endothelial injury, which may have significant negative consequences including graft patency and possibly long-term survival [68, 69]. Desai et al recently demonstrated using optical coherence tomography that EVH operators had a steep learning curve with regard to subtle RSVG injuries and that vein grafts with four or more intimal or medial dissections showed significantly worse early patency rates than those with fewer intimal injuries (67% vs. 96%) [70].

In contrast, when RSVGs are harvested using a “no touch” technique, better patency results have been noted. The “no touch” method avoids vein stripping, taking surrounding tissue, and avoids over-distending the vein conduit as it is being prepared for coronary anastomosis [71]. This has also been shown recently to preserve the venous vasa vasorum [72]. Perhaps this helps to explain differences in contemporary SVG patency rates versus those reported historically, which were always done by an open surgical technique. Other predictors of improved vein patency include grafting to the LAD coronary artery versus other target sites, smaller venous conduit size, and larger diameter target coronary artery. In contrast, young age and low EF reduced long-term patency [60]. The type of distal anastomosis (sequential, y- or t-grafts, or other composite grafts) did not affect long-term patency [60]. Based on these data, some suggest SVG from the calf/lower leg since size and possible thickness of the vein is better [60]. Additionally, EVH is more difficult to perform on the lower leg; therefore, programs committed to EVH likely neglect this potentially advantageous conduit.

Current surgical patient cohorts have also been implicated in reduced vein graft patencies. For example, it is generally accepted that contemporary patients referred for surgery are older and more medically complex [73]. For example, many patients referred for CABG are diabetic, a condition that is notorious for more complicated and diffuse CAD [46, 74]. In addition, it has been proposed that venous grafts in elderly may be of inferior quality relative to younger patients [75].

5. General advantages of arterial grafting

Several advantages to arterial grafting have been demonstrated relative to CABG without arterial grafts. Most notably, the LIMA-LAD graft has been shown to be an independent predictor of survival after CABG when compared with patients not receiving LIMA-LAD [76]. In addition, using more than one IMA graft reduces the need for subsequent reintervention and prolongs survival relative to patients receiving only one arterial grafts

[15, 17]. Similarly, Guru et al evaluated the potential benefit of multiple arterial grafting in over 53,000 patients undergoing primary CABG between 1991 and 2001. After propensity matching, patients receiving ≥ 2 arterial grafts had decreased rates of cardiac readmission and reduced incidence of the composite of cardiac readmission, death, and repeat revascularization relative to those with ≤ 1 arterial grafts [23]. Furthermore, patients receiving ≥ 2 arterial grafts had improved survival compared with patients receiving only one arterial graft [23]. Similar findings were reported by Nasso, et al, who found no differences at 2 years between groups receiving RA, in-situ RIMA, or free RIMA as the 2nd arterial graft, although each of these groups was superior to patients receiving only one arterial graft (LIMA-LAD) with respect to cardiac event-free survival [77]. Zacharias et al also demonstrated advantages of RA grafting as a 2nd arterial conduit on long-term survival when compared to RSVG conduits [14].

In addition, multiple arterial grafts and their arrangements in all coronary distributions have been proven superior to venous grafts with regard to long term patency regardless of the anatomic details of the native coronary and distal anastomosis [55]. These results are particularly applicable in the context of recurrent angina [16, 55, 78]. Finally, perhaps one of the best recent demonstrations of the advantages of arterial grafting over RSVG conduits was provided by Gaudino et al, who studied 60 CAD patients who had previously undergone PCI and developed in-stent restenosis. After undergoing CABG, patients receiving IMA and RA grafts had patency rates of 90% while those undergoing RSVG had patency rates of 50% at a mean follow-up of 52 months [79].

5.1 Total arterial revascularization

Since SVG conduits inevitably fail, particularly late [62], there has been increased enthusiasm for total arterial revascularization for CABG. Total arterial revascularization may obviate the concerns of vein graft failure and has been shown to have good short-term results [80]. However, little evidence is available to suggest that outcomes are improved with “all-arterial” grafting [81]. Zacharias et al have recently demonstrated that patients with multi-vessel CAD undergoing all-arterial grafting had improved 12-year survival compared with matched patients who underwent standard CABG with LIMA-LAD and RSVG to other distal targets [82]. Furthermore, complete coronary revascularization and use of all-arterial grafting strategy was associated with improved 12-year survival [82, Figure].

It has been estimated that all-arterial grafting is possible in 90% of patients using various conduits and their configurations [55], and even patients with advanced age have been shown to benefit from all-arterial revascularization strategies in terms of freedom from recurrent coronary events and improved graft patency [83].

6. Bilateral internal mammary artery conduits

In the 1980s, the LIMA-to-LAD graft was shown to be an independent predictor of improved short- and long-term results when used as a conduit for CABG compared to RSVG-only grafting [76]. Unequivocal advantages of the LIMA-LAD graft include prolonged survival relative to use of RSVG to LAD, reduced rates of recurrent angina, reduced postoperative MI and other ischemic events, and decreased need for coronary reintervention [76, 84]. The superiority of the LIMA in comparison to other CABG conduits

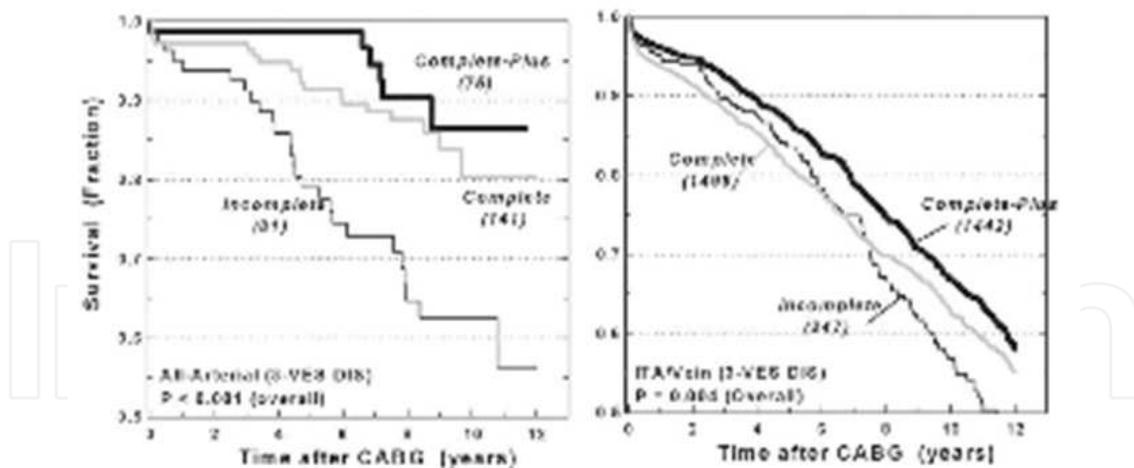


Fig. 1. Effects of completeness of revascularization on 12-year old Kaplan-Meier survival in triple-vessel disease (3-Ves Dis) patients. (Left) All-arterial patients. (Right) Internal thoracic artery/saphenous vein (ITA/Vein) patients. Incomplete - completeness of revascularization index (CRI) less than 1, or 2 grafts; complete CRI equal to 1, or 3 grafts; complete plus - CRI greater than 1, or 4 or more grafts. All p values by log-rank (Mantel-Cox) test. (CABG - coronary artery bypass graft surgery.)

may be related to its unique freedom from arteriosclerosis and due to the rich run-off bed provided by the LAD coronary and its branches [85]. Since there is no basis for suggesting or concluding that the biological and mechanical properties of the right IMA are different from the LIMA, successes with the LIMA have prompted investigation of the potential benefits of bilateral IMA (BIMA) grafting.

The original description of BIMA for CABG is credited to Kay in 1969 [86]. Since then, multiple centers including our own have investigated the impact of BIMA grafting on long-term results of CABG. Advantages of BIMA have been somewhat difficult to prove definitively without randomized controlled trials in this area, which have not been conducted secondary to cost concerns and administrative requirements associated with studies inherently requiring significant longitudinal follow-up [87]. Instead, investigation and documentation of BIMA benefits have relied on evaluating institutionally maintained observational databases to show differences between the "treatment group" and the "control group" by way of propensity matching [87]. Analysis of these data show improved long-term results for patients receiving BIMA grafting as compared with single IMA grafting. However, survival curves do not separate until several years postoperatively, which has been a consistent finding [15, 88, 89; Figure]. The demonstrated clinical advantages of BIMA grafting strategies include prolonged survival and reduced need for coronary reintervention on the basis of recurrent myocardial ischemia, including freedom from the need for coronary reintervention [15, 88, 90] which hold true for women as well as for men, where it has been demonstrated that use of BIMA had 3-fold improved cardiac-related survival compared with patients who did not receive an IMA graft [91].

Reported rates of BIMA use in CABG range from 4.0% to nearly 50% depending upon several factors including the contributing authors' practice preferences and the particular patient cohort treated [19-22, 92]. However, it has been estimated that up to 80% would be candidates for BIMA grafting [93]. Subjective and potential obstacles to BIMA use include increased surgical times, increased technical challenges, especially related to the positioning

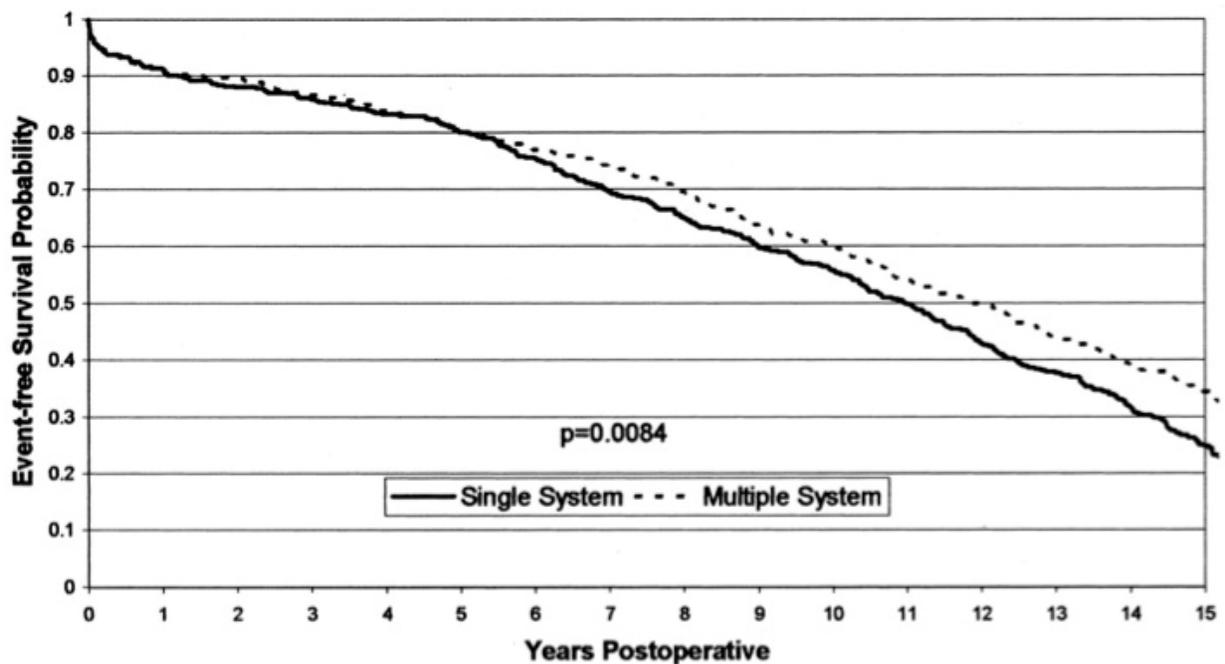


Fig. 2.

of the non-LIMA-to-LAD graft, and increased rates of sternal wound complications relative to patients with one or less IMAs harvested [94]. After 10 years of experience with BIMA CABG, Gansera et al noted increased OR and aortic cross clamp times among BIMA patients compared with single IMA CABG patients. In addition, patients receiving BIMA grafting had higher rates of bleeding requiring postoperative mediastinal reexploration (2.9% vs. 0.6%) along with increased rates of wound complications [95]. However, they also noted that nearly one full additional distal graft was completed when both IMAs were used and, most importantly, BIMA grafting was associated with improved 30-day survival, particularly among diabetic patients, compared with only one IMA graft. [95]. In this same study, a grafting strategy not incorporating 2 IMA conduits was an independent predictor of *perioperative* mortality, directly disputing biases that BIMA grafting is associated with increased *perioperative* complications [95]. Similarly, Kurlansky et al reviewed their collective experience with more than 4,500 consecutive CABG procedures (2,369 single IMA; 2,215 BIMA) and demonstrated that hospital mortality was significantly reduced among patients undergoing BIMA grafting compared with controls [92].

Nevertheless, selection of patients for BIMA grafting should be performed cautiously, particularly when performing surgery through a standard median sternotomy incision. This is primarily related to the well-demonstrated risk for sternal wound infection after BIMA grafting in patients with diabetes, obesity, and other comorbidities [96-100]. However, BIMA grafting can be performed safely without significant increased risk for sternal wound infection as has been frequently demonstrated [24, 98, 100, 101]. For example, Jones et al reviewed their experience with 500 consecutive patients undergoing BIMA CABG over an 11-year period, excluding only those with proximal coronary stenoses <70% and emergency cases with HD instability. Nevertheless, the reported rates of *perioperative* complications were low: operative mortality was 1.8%; deep sternal wound infections were 1%; and 1.8% had take back for bleeding. Incredibly, only 2 patients out of the 500 required reoperation for myocardial ischemia in the follow-up period. [24]. Interestingly, however, Jones et al

point out that if strict criteria for selecting patients for BIMA grafting had been used, nearly 70% of patients in their series would have been excluded [24].

As noted previously, RSVG conduits for CABG have not been compared directly to DES, but comparisons of BIMA grafting with a strategy primarily employing DES for coronary revascularization do exist [102, 103]. After matching for multiple comorbidities, significantly improved angina, reduced need for reintervention, and improved reintervention-free survival at one year have been observed among patients undergoing BIMA CABG relative to PCI [102]. In a similar study, Locker et al examined BIMA CABG versus PCI in diabetic patients and demonstrated more complete coronary revascularization, improved angina, reduced need for reintervention, and increased cardiovascular event-free survival (80% vs. 30%, $p < 0.001$) in patients undergoing BIMA CABG [103]. More importantly, 6-year survival among patients with left main CAD or 3-vessel CAD was significantly better with BIMA revascularization, providing rare evidence for superiority of multiple arterial grafting strategy relative to PCI [103].

One controversial and often-debated point concerning BIMA CABG relates to the native coronary artery planned as a target for the second (right) IMA. Initial opinion considered best results of BIMA CABG to occur when the RIMA was grafted to the “next most” important coronary bed angiographically, assuming that LIMA to LAD was nearly always performed [104]. Schmidt et al found that multiple left-sided grafts lead to improved survival relative to a cohort of patients in which the RIMA was placed to the right coronary artery distribution along with LIMA-LAD grafting [104]. However, it should be noted that graft patency was quite good in both groups (91.7% vs. 89.6%), as was survival, and freedom from heart failure, angina and need for reintervention [104]. They argued that maximum long-term benefit from BIMA grafting is realized when the 2nd IMA is placed to the coronary distribution subtending the most amount of viable myocardium, which was most commonly the circumflex artery distribution.

The requirement for the 2nd IMA targeted to the left coronary system has been refuted by other data. Analysis of Cleveland Clinic data shows that benefits of BIMA CABG are similar regardless of the recipient coronary artery for the 2nd IMA graft [89]. Sabik et al found that risk-adjusted and unadjusted outcomes did not differ between a strategy for the 2nd IMA going to the right coronary or the circumflex coronary artery territory, but several important caveats are applicable, particularly with regard to the right coronary artery if the RIMA is to be used as an in situ graft to this coronary distribution. For instance, the distal RCA should be free of disease, and the proximal RCA stenosis should be $\geq 70\%$ in diameter to avoid competitive native coronary flow, which may be detrimental to IMA patency. Finally, distal viable myocardium should be ensured [105]. More recently, Kurlansky et al reviewed their experience in over 2,200 consecutive patients who underwent BIMA grafting. In 2/3 of patients, the 2nd IMA was placed to the left coronary system, while in 1/3 of patients, the 2nd IMA was placed to the right coronary system. Incredibly, 98% of patients had complete coronary revascularization performed with in-situ arterial configurations, that is, avoiding free IMA utilization. At a mean follow-up of nearly 13 years, long-term survival was no different between groups [106, Figure].

Gansera et al recently described their strategy for with BIMA versus single IMA in which the RIMA was usually directed anteriorly and to the left as pedicled conduit for the LAD, while the LIMA was typically directed for revascularization of the lateral wall (circumflex artery distribution) [95]. Importantly, RIMA crossover grafts to the LAD coronary system appear to have patency rates that are not different from LIMA-LAD configurations [107]. In

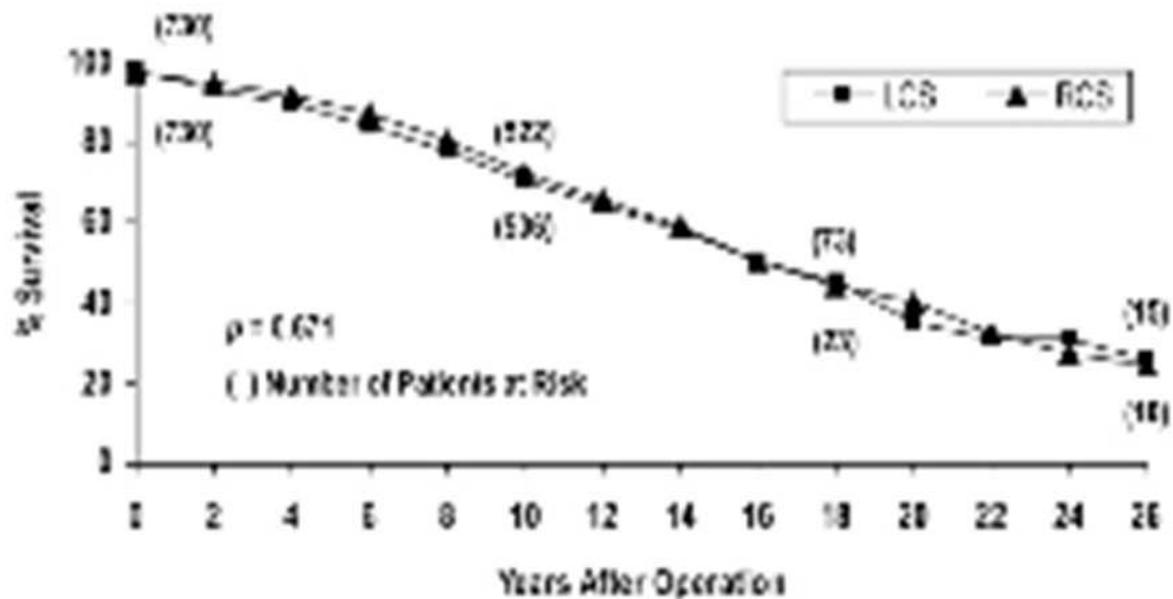


Fig. 3. Actuarial survival of optimally matched patients who underwent coronary artery bypass grafting to the left coronary system (LCS [boxes]) and the right coronary system (RCS [triangles]). Number of patients at risk is in parentheses; results are mean \pm standard error of the mean.

fact, Chow et al reported that RIMA patency was similar to LIMA patency regardless of the coronary distribution to which the artery was grafted [108]. However, a “crossover” configuration for the RIMA places the RIMA-LAD graft at significant risk for injury during subsequent redo sternotomy (as potentially required for aortic valve replacement or other procedures). Consequently, when performing this procedure, we often apply a protective barrier to the mediastinum prior to sternal closure (Repel-CV, SyntheMed, Inc., Iselin, NJ, USA) and often reapproximate the thymic remnant to protect the RIMA-LAD graft [108].

Therefore, the specific BIMA configuration doesn't seem to affect MACE, graft patency, or morbidity/mortality outcomes [110]. Glineur et al evaluated BIMA grafting with both IMA grafts targeted to the left coronary system in either an in-situ or Y-graft configuration, noting equivalent patencies and other mid-term results. In addition, the T-graft configuration has been shown to be safe and effective in grafting multiple distal coronary targets [111].

Most results with BIMA grafting are improved by harvesting the conduit as a “skeletonized” graft rather than as a pedicled graft, in which the accompanying mammary veins and surrounding chest wall muscle and fascia were mobilized along with the artery. Skeletonized IMA harvesting preserves sternal perfusion relative to pedicled IMA harvesting [112, 113]. As a result, skeletonized IMA harvesting is associated with reduced sternal wound complications and longer IMA graft length, allowing more distal coronary targets to be bypassed [Figure, 92, 98, 100]. Skeletonized IMAs also have increased blood flow through the conduit [114], possible as the result of decreased spasm, since skeletonized IMA is typically accomplished without the need for electrocautery on the chest wall [100, 106, 115].

7. Radial artery

Professor Alain Carpentier is credited with introducing the radial artery (RA) as an alternative conduit for CABG [116], but initial results with the RA were unfavorable, leading Carpentier

and others to abandon its use. Subsequently, several RA grafts were empirically observed to be patent at follow-up coronary angiography, leading to the concept's reintroduction in the late 1980s [117]. Since then, the RA has since been widely used and aggressively investigated as a conduit option for CABG due to ease of use, availability in at least 90% of patients, good length allowing reach to any distal target for anastomosis, and it is amenable to concurrent harvesting methods (the IMA, SVG, and RA can be harvested simultaneously) [118]. Depending upon the details of RA grafting, including the target coronary bed and the proximal degree of coronary artery stenosis, long-term RA graft patency approaches 90% and can approximate that of pedicled IMA graft patencies [55, 119, 120].

Since most coronary grafting strategies employing RA grafts do so to evaluate alternatives to SVG conduits, numerous trials comparing RA with SVG for patency and long-term outcomes have been conducted recently [14, 78, 121-123]. In general, these data demonstrate equivalent or improved patency for the RA compared with SVG. One recent randomized controlled trial in the US Veterans Affairs system evaluated RA and SVG as coronary bypass grafts to the "best remaining recipient vessel," with the primary end point of one-year angiographic patency [123]. These data demonstrated equivalent graft patencies for RA compared with SVG, but one-year patency for both groups approached 90% [123]. This is in line with many previous reports on early RA patency, and far exceeds other recent estimations of early graft SVG patency for [8-10]. In contrast, the Radial Artery Versus Saphenous Vein Patency (RSVP) trial compared 5-year graft patency for RA versus SVG when placed to circumflex coronary artery branches that were at least 70% stenotic [121]. These data demonstrated a significantly improved patency for RA grafts (98.3%) relative to SVG grafts (86.4%) [122].

Perhaps the most recognized comparison of RA and SVG is provided by the Radial Artery Patency Study (RAPS), which randomized 561 patients at 13 centers (Canada, New Zealand) to receive a RA graft to the right coronary system or the circumflex coronary system [78]. Saphenous vein grafts were placed to the coronary system not receiving the RA graft, and all patients underwent LIMA-LAD grafting. One-year angiographic follow-up was performed in 440 patients and demonstrated significantly improved patency for RA grafts compared with SVG (91.8% vs. 86.4%, $p = 0.009$). However, angiographic "string sign" was significantly increased in RA grafts compared with SVG (7% vs. 0.9%, $p = 0.001$) [78]. It is unclear as to the long-term significance of this finding; as Carpentier originally noted, others have since reported that patency of the RA graft with a "string sign" may actually improve as the native disease worsens [124]. When patient characteristics and target vessel characteristics were considered in the interpretation of the RAPS data, RA grafts were protective of graft patency by multivariable analysis, while smaller distal targets, less proximal coronary artery stenosis, and diabetes were associated with reduced patency rates for SVG or RA grafts [125]. Graft occlusion was significantly more common among diabetics with SVG (19%) compared with RA grafts in diabetics (12%). In fact, RA grafting conferred even greater protection effect from graft occlusion was among diabetic patients than in the study cohort as a whole [125].

Despite the positive comparisons of RA with SVG patency rates, it has been more difficult to ascribe improved clinical outcomes with RA versus SVG [126]. However, some data suggest that better long-term survival is seen in those receiving RA conduits as compared with SVG (Figure). Zacharias et al evaluated the influence of RA and SVG as a 2nd graft (all patients receiving LIMA-LAD) with regard to survival in 2 groups of 925 matched patients each [14]. 6-year survival was improved in RA patients [14, Figure].

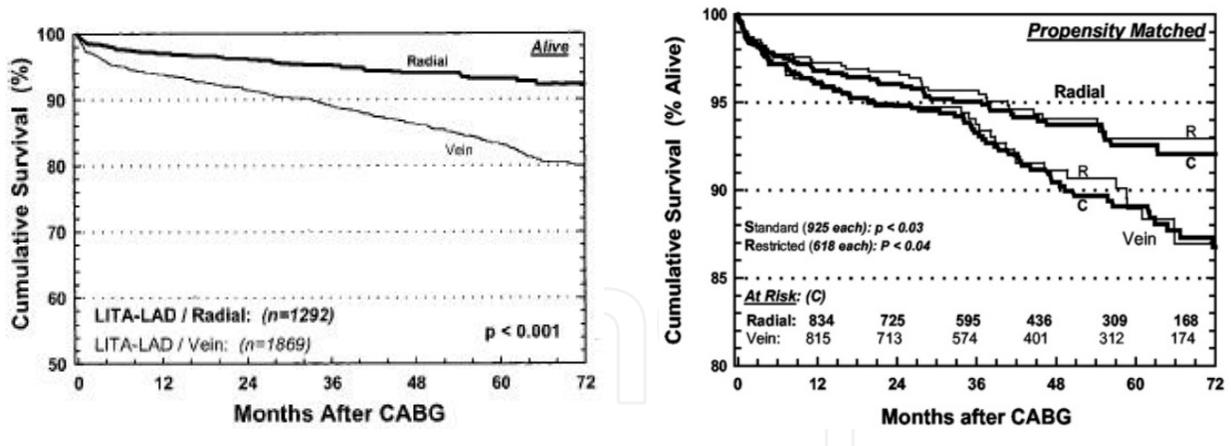


Fig. 4.

Similar data have been reported by Tranbaugh et al, who compared over 800 patients undergoing CABG utilizing LIMA, RA, and SVG with matched patients undergoing CABG with LIMA and SVG only [127]. They showed significantly improved survival in the RA group in addition to improved patency of RA as compared to SVG (81% vs. 47%) in symptomatic patients who subsequently underwent diagnostic angiography after CABG (mean time to repeat catheterization 4.3 years) [127]. Importantly, RA use emerged as independent predictor of survival at 14 years when the data were assessed by multivariable analysis [127, Figure].

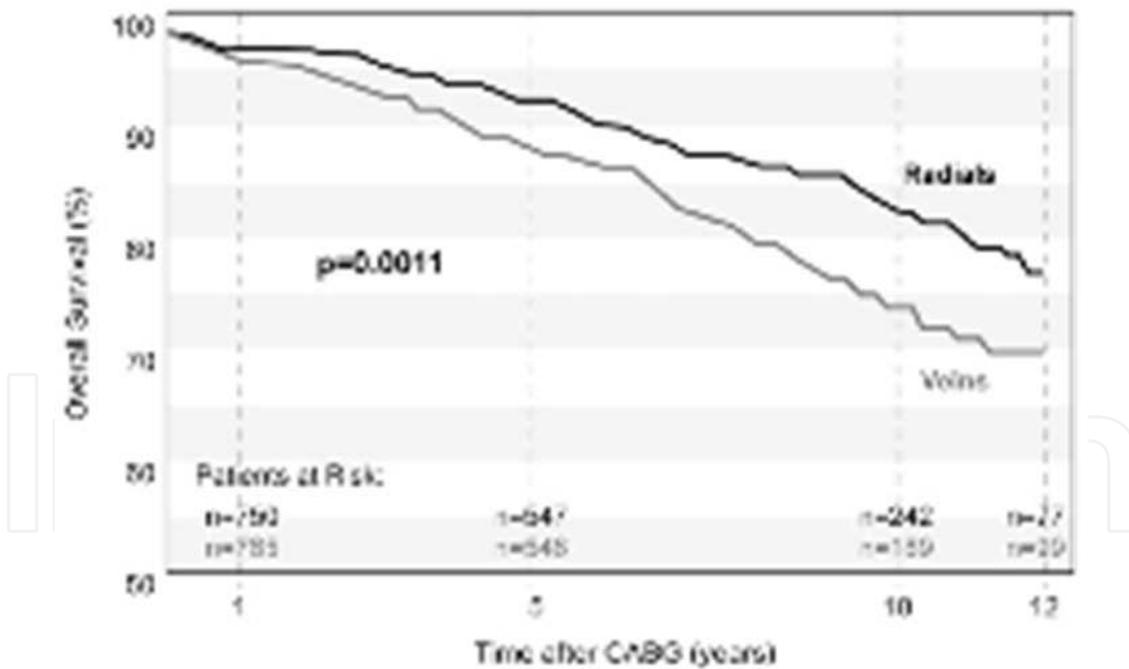


Fig. 5. Comparison of Kaplan-Meier survival for propensity-matched patients (p = 0.0011, log rank test), CABG - coronary artery bypass graft surgery.

Conduct of these well-designed trials incorporating angiographic follow-up of RA grafts has provided a wealth of insight into features important to successful RA grafting. For example, as noted, early graft failures in the form of “string sign” have been noted in randomized trials [78], and several explanations for this are possible. For example, RA grafts appear

notoriously susceptible to competitive flow within the native coronary circulation, as may occur when native coronary stenosis is not severe ($\leq 70\%$) [128, 129]. Based on this frequent observation, use of the RA is not recommended as a conduit for CABG unless the native coronary artery stenosis is high grade ($\geq 70\%$). This strategy has been associated with improved patency and reduced "string sign" in the RAPS study [78]. Radial artery graft patency is also dependent upon coronary target location, as has been noted for the RIMA graft [89]. For instance, Maniar et al found that grafts to the right coronary artery were more likely to be occluded compared with those placed to the LAD or to the circumflex coronary artery [129], which has been corroborated by others [130].

Certain inherent, unique characteristics of the RA may also contribute to "string sign" formation [131]. Limb arteries such as the RA are known to be more prone to spasm than somatic (IMA) or splanchnic arteries [132]. One key difference between the IMA and the RA is that the RA is significantly more muscular, leading to increased tendency for spasm requiring prolonged vasodilation [133]. Vasodilation of the harvested RA should begin intraoperatively by exposing the conduit to papaverine or verapamil/nitroglycerin. Verapamil/nitroglycerin may be more effective than papaverine in regards to degree of vasodilation and preservation of endothelial function, which can be a problem with papaverine (especially if injected intraluminally) and with the alpha-blocking agent phenoxybenzamine [118]. Postoperatively, most authors have recommended vasodilation with calcium channel blocking agents or long-acting nitrates for at least one month after surgery.

It is debated as to whether the proximal RA graft anastomosis should be performed to the ascending aorta or as a composite graft to other conduits. In a study of over 1,500 radial artery grafts, Maniar et al found no difference between these two types of grafting strategies [129]. Collins et al, reporting the results of the Radial Artery Versus Saphenous Vein Patency (RSVP) trial, demonstrated superior patency of RA grafts compared with SVG, and all proximal anastomoses were performed to the aorta directly [122]. Jung et al recently demonstrated using postoperative CT angiography that RA patency was better when the proximal anastomosis was made to the aorta and did not use the IMA as RA inflow [134]. However, Desai et al found that at one year, 21% of RA grafts going directly to the aorta had "some degree" of angiographic stenosis, which was significantly less than SVG proximal anastomoses [78].

Testing for appropriateness of RA harvesting to gauge the likelihood of hand ischemia after RA harvesting is recommended. The Modified Allen's Test (MAT) is abnormal in wide ranges ($<1\%$ to 27%), often attributed to observer variability [135]. When MAT was compared with Doppler ultrasonography of the thumb artery, MAT was noted to have a sensitivity of 100% and specificity of 97% for thumb ischemia [136]. Various adjuncts to the MAT have been proposed, including pulse oximetry, plethysmography, and Doppler ultrasonography of the hand [136-138]. However, none of these modalities have been proven to add significantly to the diagnostic accuracy of a properly performed MAT, which appears to accurately and safely select patients for RA harvesting.

Harvesting of the RA has been performed traditionally by the open, "no-touch" technique [127]. However, more recently, the trend appears to have shifted toward endoscopic RA harvesting with demonstrated functional and cosmetic advantages [139] and no increase in vasoreactivity or damaged endothelium [140]. However, harvesting the RA as a pedicle with harmonic scalpel appears to be less injurious than using electrocautery for tissue dissection [140]. Patency rates are similar regardless of method of harvesting [142].

8. Summary

Coronary artery bypass grafting remains one of the most frequently performed major operations worldwide. Even in the burgeoning era of percutaneous approaches to coronary heart disease, the indications for CABG continue to be based on relief of angina, prevention of myocardial damage from ischemic complications, and prolonged expected survival in select patients. In order to provide the best results for CABG patients, the surgeon's chief focus should be on improved long-term outcomes. Based on the information available, the best long-term outcomes of CABG are achieved when incorporating a strategy of grafting with arterial conduits.

9. References

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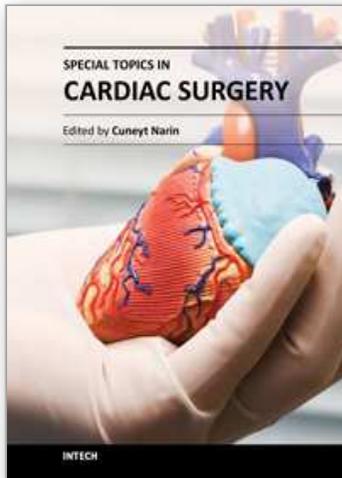
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This book considers mainly the current perioperative care, as well as progresses in new cardiac surgery technologies. Perioperative strategies and new technologies in the field of cardiac surgery will continue to contribute to improvements in postoperative outcomes and enable the cardiac surgical society to optimize surgical procedures. This book should prove to be a useful reference for trainees, senior surgeons and nurses in cardiac surgery, as well as anesthesiologists, perfusionists, and all the related health care workers who are involved in taking care of patients with heart disease which require surgical therapy. I hope these internationally cumulative and diligent efforts will provide patients undergoing cardiac surgery with meticulous perioperative care methods.

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Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
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