

Conduits for Coronary Bypass: Strategies

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Strategic planning is integral to any operation but complexity varies immensely and therefore the effort necessary to create the optimal plan. The previous three reports have discussed individual conduits and herein is an attempt to present approaches to common situations which the author favors. Although much has been learned over 45 years about use and subsequent behavior of venous and arterial grafts we continue to learn and, as a result, evolve new strategies or modify those now popular. Thus the reader must recognize that in spite of trying to be balanced and inclusive all surgeons have personal opinions and also prejudices which influence the approach taken and which may not be the optimal one for others or for the patient.

Key words: 1. Coronary artery bypass
2. Arterial conduits
3. Venous conduits

INTRODUCTION

Increasingly there is positive interaction among cardiologists and surgeons to provide optimal comprehensive care utilizing published guidelines created collectively by experts from both specialties and incorporating randomized clinical trials as well as observational data particularly from large databases. Providers consider available information impacting each situation and present recommendations to the patient including available treatment options from cardiology and surgery.

PCI, CAB OR, MEDICAL THERAPY

Coronary artery bypass (CAB), percutaneous coronary intervention (PCI), or intervention free medical therapy (MT) are available for treatment of coronary artery disease (CAD).

It must be said that all surgical patients require best medical management as without it an operation is even less palliative; just as PCI without ongoing MT would be unthinkable.

The best study yet (SYNTAX) comparing PCI (drug eluting stents) with CAB (more arterial grafts) in left main or three vessel disease (3VD) has reported five-year results showing equality for both therapies in lower risk patients with less extensive coronary disease but better outcomes for patients with more risk factors and more extensive coronary disease (SYNTAX score > 31) [1]. Compelling is the fact that 71% (n=3,075) of patients screened were included, either in the randomized (n=1,800) group or in the PCI or CAB registries (n=1,275) when not suitable for randomization. This fact resembles real world practice, answering a criticism of most prior studies where 5% of patients screened were recruited resulting in highly selected study groups. The 5-year results of SYNTAX for the randomized group found lower rates of

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repeat revascularization (13.7% for CAB versus 25.9% for PCI, $p < 0.0001$), a cardiac mortality benefit (5.3% for CAB versus 9% for PCI, $p < 0.003$) a reduction in major cardiac and cerebrovascular events (MACCE) (26.9% for CAB and 37.3% for PCI, $p < 0.0001$) and fewer myocardial infarctions (MI) (3.8% for CAB and 9.7% for PCI, $p < 0.0001$) [1]. The rates of all-cause mortality and stroke were not significantly different between the two groups [1].

SYNTAX incorporated three predefined subgroups with complex CAD: those with left main disease (LMD); 3VD with or without LMD; and those with medically treated diabetes. The 5-year MACCE rates for LMD were not significantly different between treatment groups (31.0% for CAB versus 36.9% for PCI, $p = 0.12$). In contrast patients with 3VD but without LMD had much greater rates of MACCE after PCI (24.2% CAB versus 37.5% PCI, $p > 0.001$). Diabetics also received similar benefits from CAB with regard to MACCE (29% for CAB versus 46.5% for PCI, $p < 0.001$) which was consistent with the FREEDOM trial (18.7% for CAB versus 26.6% for PCI, $p = 0.005$) [2].

Further support for CAB is a propensity matched five-year observational study from 2003 through 2005 using New York State's Cardiac Surgery Reporting System of 8,121 pairs of matched CAB and PCI patients which found a reduced risk of death for CAB over drug-eluting stents in all categories of coronary disease which included the left anterior descending artery (LAD) but not without LAD disease [3]. Survival at five years was 80.4% for CAB and 73.6% for stenting ($p < 0.001$). Survival benefit for CAB was found in all age groups and was smallest but significant at age 80 and above. A lower risk of death with CAB compared to drug-eluting stents was also found in a number of patient subgroups based on gender, ejection fraction, prior MI, cerebrovascular disease, peripheral vascular disease, congestive heart failure and diabetes [3]. (Professor Ki-Bong Kim provided an Invited Commentary published with this report.)

Another observational study selected 103,549 patients having PCI and 86,244 having CAB using claims records of the Centers for Medicare and Medicaid Services from 2003 through 2007 [4]. Propensity scoring and logistic regression were used to adjust for between group differences in baseline characteristics of patients and hospitals of more than two mil-

lion patients. Adjusted mortality was the same in the two groups at one year but at four years mortality was lower with CAB than with drug-eluting stents (16.4% versus 20.8%, risk ratio 0.79). Risk of death with CAB compared to PCI was reduced in subgroups defined by gender, age, presence or absence of diabetes, body-mass index, presence or absence of chronic lung disease, ejection fraction, and glomerular filtration rate [4].

The optimal intervention for diabetics with multi-vessel CAD has been debated for more than 15 years and a pooled analysis of 10 randomized trials involving 1,223 patients with diabetes confirmed a survival advantage of CAB over stenting but drug-eluting stents were not used and more recent trials in which they were used enrolled relatively few patients with diabetes [5]. It remained for the FREEDOM trial which enrolled 1,900 diabetic patients at 140 international centers to demonstrate the benefit of CAB over PCI with a composite primary outcome of death, nonfatal MI and nonfatal stroke at 5 years (18.7% versus 26.6%, $p = 0.005$) [2]. Stroke was more prevalent in the bypass group (5.2% versus 2.4%, $p = 0.03$) [2]. Five year results of SYNTAX also demonstrate better outcomes in diabetics with CAB over PCI [6]. Rates of MACCE were significantly higher for PCI versus CAB (46.5% and 29.0%, $p < 0.001$) and also for repeat revascularization (35.3% and 14.6%, $p < 0.001$). There were no differences in all-cause death, stroke, or MI [6].

In MASS II, a 10-year comparison of PCI, CAB, and MT which is underpowered but demonstrates equivalence in survival with each treatment modality, CAB and PCI were associated with a lower incidence of primary events than MT [7]. In stable patients this study supports an initial strategy of MT with careful follow-up to determine a later need for intervention [7]. In the COURAGE randomized trial of 2,287 patients comparing PCI with intensive MT and follow-up of 2.5 to 7.0 years (median, 4.6) there were no differences in measured outcomes [8]. During follow-up 21% of PCI patients had additional PCI and 32.6% of those in the MT group required PCI. In the PCI group 77 patients required CAB as did 81 patients in the MT group [9]. These two reports support use of vigorous MT for all patients as emphasized in FREEDOM [2]. In some low risk and also high risk patients continued MT without intervention until symptoms become

unmanageable or life threatening may be appropriate.

BENEFIT VERSUS RISK

Death at 30 days is a standard measure for quantitating intervention related risk and is <1% in some reports but up to 5% in others with 1% to 3% a usual range for randomized trials of CAB and PCI. Survival data to 10 and 20 years has been reported in observational reports of CAB which does not exist for PCI primarily because PCI is in continuous evolution which presents a moving target without durable endpoints. In contrast to the dynamic changes in PCI, primarily related to the evolution of stents, is the relatively stable status of CAB where the transition to more frequent use of arterial conduits has been painfully slow and remains incomplete except for a few enthusiasts. Although off-pump CAB has been utilized for over 20 years its frequency has declined somewhat from a peak 10 years ago.

In SYNTAX 5-year survival was similar for PCI (86.1%) and CAB (88.6%) but as presented above Kaplan-Meier estimates of MI, MACCE and the need for repeat revascularization were greater following PCI [1]. Additionally the composite endpoint of death, stroke and MI achieved significance in favor of CAB for the first time at five years [10]. The beneficial effects of CAB become more evident as the interval from intervention increases [10]. The higher stroke rate at one year after initial CAB has gradually evened over five years. There is evidence that the initial significantly elevated stroke rate can be equalized by a change in surgical technique. Off-pump CAB has variably reduced the stroke incidence but the potential benefit of not clamping the aorta has commonly been negated by partial or side clamping of the aorta in off-pump procedures which is pivotal in reducing the stroke rate [11]. Aortic clamping can be avoided with *in situ* arterial grafts or anastomosis of aorta based grafts using non-clamping techniques [11].

The SYNTAX trial has greatly influenced the treatment of patients with multi-vessel CAD by promoting the heart-team approach with cooperative decision making among team members with use of risk stratification based on the SYNTAX score [10]. Further improvement in the latter is anticipated as the SYNTAX score is integrated with important

clinical variables [10].

Quality of life is important but data are lacking. In COURAGE, comparing MT and PCI, there was incremental benefit from PCI for 6 to 24 months with greater benefit in patients with more severe angina [9]. By 36 months there was no significant difference in health status between groups. Because angina was the primary driver of quality and the fact that bypass surgery is more effective than PCI in relieving angina it can be speculated that quality with CAB would be better after 6 to 12 months and recovery from operative trauma.

CONDUIT CHOICE

Although associated with the poorest patency saphenous vein (SV) is favored by availability, ease of harvest and grafting, and unlimited flow capacity but ultimately it becomes a fibrous tube lacking vasomotion as a result of medial muscle necrosis and having limited endothelial biologic activity. Intimal hyperplasia occurs early, can progress up to a year, and many believe is a precursor to atherosclerosis which can be detected microscopically by several years [12]. Whether atraumatic harvest will improve patency, as suggested by one report, remains to be confirmed by others [13]. Nevertheless the SV remains widely used and will remain prevalent and dominant until more surgeons become convinced that multiple arterial conduits should become the standard which has been and remains the left internal thoracic artery (LITA) plus SV. Most now believe that longevity is significantly improved by one arterial graft, usually the LITA, placed to the LAD [14-16]. Because in many hearts the LAD is more important than the other two arteries it has been difficult to demonstrate additional survival advantage with a second arterial conduit and although some data (nonrandomized) support this it remains to be seen whether the currently on-going randomized trial (ART) of one versus two ITA grafts will demonstrate survival benefit [17]. If survival is improved then there will need to be a quest to see if a third artery bypass will have an additive survival benefit. The argument can be made that there are data showing that complete revascularization provides survival benefit over incomplete, at least to age 60, then this observation can be

transposed to support all arterial, or at least three arterials, with one placed to each of the three territories which is how most authors define 'complete revascularization' [18]. On the other hand the availability of multiple arterial conduits and their undeniable better patency without evidence of developing occlusive atherosclerosis dictates greater use than the 4% prevalence of multiple arterial conduits in the US and the 8% in Europe which rose to 19% in SYNTAX. In a separate report from one SYNTAX site 400 consecutive patients from 2004 to 2008 had all arterial grafting and were compared to the surgical arm of SYNTAX with significantly improved freedom from repeat revascularization, MACCE and symptomatic graft occlusion [19]. Another potential benefit of arterial grafts is a reduction in the rate of progression of coronary disease distal to the graft [20].

There are many reasons (excuses) for failure to utilize more arterial grafts. They include longer harvest time, which is true for the right internal thoracic artery (RITA) and gastroepiploic artery (GEA) but not the radial artery (RA) which can be harvested concomitantly with the LITA. It is true that arterial conduits are more delicate/fragile than SV but no more so than the coronary artery itself and that is what coronary surgery is about. Bilateral ITA (BITA) with skeletonization is not associated with increased risk of sternal infection except for the diabetic, particularly when obese, and skeletonization is rapidly becoming the standard if it is not already [21,22]. Observational data support BITA over LITA [15,16,23,24]. Multi or all arterial revascularization results in longer operative times but 30 day mortality is not increased in selected patients [19,25-27]. The choice becomes a longer operation with better long-term outcomes or the opposite. Some surgeons opt for the former but most select the option they prefer (are comfortable with) or think will provide the best outcome in their hands which may not reflect expert opinion based on fact and experience.

Thus, BITA grafting is the first choice for multi-arterial grafting. If the second ITA (RITA) is not appropriate (diabetes, obesity, chronic obstructive pulmonary disease, limited longevity or sternal considerations such as prior high dose radiation or osteoporosis) the RA becomes a consideration. Because of competitive coronary flow causing RA graft closure most surgeons desire a left coronary steno-

sis of 70% or more and 90% in the right coronary.

Glineur et al. [28] has championed quantitative coronary angiography instead of imprecise 'eyeball' measurement of stenosis severity and reported that a residual lumen diameter of > 1.1 mm in the right coronary allows competitive flow to reduce patency of RA and GEA grafts and also RITA. However, this measurement is not usually available while fractional flow reserve is a reproducible, physiologic, non-subjective measurement which is increasingly obtained at the time of catheterization in Europe and North America. A value of 0.80 (calculated as distal pressure over proximal pressure) is considered hemodynamically significant (flow restrictive) although some would choose a greater degree of stenosis, 0.75 [29,30].

Recognition of and then acceptance of the concept that coronary flow persists through a stenosis after it is bypassed with an arterial graft has required several decades. Flow is a function of pressure and resistance which is provided by a stenosis or a smaller, longer vessel (arterial conduit versus VG). The vein is much larger and lacks vasomotion (due to harvest related ischemic injury and conversion to a fibrous tube) whereas the artery is vasoactive and responds to endothelial signaling (primarily nitric oxide [NO] which is responsive to maintaining shear stress in a narrow range) to dilate (relax smooth muscle tone) or contract if this signal is reduced. Thus if coronary flow is not restricted flow through an arterial conduit will decrease because its length is longer than that of the coronary (more resistance) and the secondary decrease in shear stress will reduce NO elaboration with further decrease in graft caliber which in its extreme form becomes a 'string sign.' Interestingly isolated instances of string sign reversal were documented in the ITA when the stenosis progressed, flow through the graft increased and NO was produced causing vasodilation [31]. Remodeling of arterial conduits is a normal physiologic response to endothelial sensed shear stress which has been described in all types of arterial conduits but is influenced by the thickness of the media [32]. Thus the ITA media has many fewer smooth muscle cells than the other conduits while the RA has the most which appears to achieve obliteration of the lumen without reversibility (in my experience) although others have described reversible string signs in the RA. The GEA is likely equivalent

to RA with regard to patency and both are equally sensitive to competitive flow. The reported experience with GEA is relatively small but increasing [33]. Suzuki et al. [33] has reported the best patency (201/255, 90.2%) at eight years after operation at which 87% of grafted posterior descending arteries had more than 90% proximal stenosis. My preference is to use the GEA as a free graft to provide better and more reliable inflow, avoid routing issues, increase target options and avoid potential injury with laparotomy [34]. Traditional *in situ* use is clearly acceptable with excellent outcomes when the stenosis is severe and which saves an anastomosis [33]. Either the RA or GEA is appropriate if a third arterial conduit (after the two ITA's) is desired and each conduit has some similar as well as different limitations [35].

Many options exist for employment of multiple arteries. Most straight forward is three *in situ* grafts avoiding proximal anastomosis. I rarely use this approach now but have used it to avoid cannulation (off-pump) and/or clamping of the aorta; the latter requires peripheral cannulation for on-pump with coronary anastomosis on a beating heart or with hypothermic circulatory arrest (without aortic clamping) or totally off-pump which many would favor today. Three *in situ* grafts may not always reach selected targets because of inadequate length which has become less frequent with skeletonization. I would not cross the midline anteriorly with *in situ* RITA, although Buxton utilizes a high crossing to the left side behind the thymic tissue which protects the RITA from injury at reoperation [36]. I have no experience with routing of RITA posterior to the superior vena cava and innominate vein and also behind the aortic arch if needed for additional length which provides the ultimate protection from injury at re-ernotomy and/or cannulation of the aorta [37]. Alternatively the RITA can be routed through the transverse sinus or used as a composite Y-graft, usually from LITA. Y-grafting is extremely useful and it has a long track record with patency comparable to aortic anastomosis or *in situ* use since it was popularized by Calafiore [38]. Initially the RA, RITA or inferior epigastric artery was based on the *in situ* LITA but any *in situ* arterial graft can support a Y-graft. Some prefer aortic anastomosis which has patency equal to the Y-graft although a few have reported limited inflow with the Y-graft [39]. I do not like direct aortic anastomosis of arterial conduits

(although I have done many) because of the thickness of the aortic wall, particularly if the conduit is smaller, and would use a vein hood if there is one or, if not, a patch of pericardium or vein as an intermediary unless the conduit is large and the wall not thickened.

Historically many have favored the RITA for the left side but two reports indicate it does not matter [40,41]. RITA patency to the right side is reduced by competitive coronary flow (which also decreases patency for the RA and GEA) and is an argument for placing it to the left system in which the coronaries are of smaller diameter than the right coronary where the culprit lesion usually is. With a moderate right coronary stenosis the best choice may be SV while leaving it un-grafted is a not unreasonable option [42].

THE T-GRAFT

In some situations it may be desirable to utilize only two arterial conduits to achieve all arterial revascularization; most commonly when there are contraindications to RITA harvest and vein is unavailable or undesirable. The T-graft was introduced by Tector et al. [43] using BITA's with the free graft supplying the right and circumflex territories. The RA or GEA can also serve as the free graft to the circumflex and right coronary branches [19,26]. The latter two are longer than RITA which provides the greater length often required and gives the option of providing a short segment of free graft for secondary Y-grafts when anatomy is not optimal for sequential grafting. Although inflow potential is an obvious concern to some there are data supporting hemodynamic adequacy of this configuration which entails vasodilation and remodeling of conduits to provide greater flow as needed [26,44-47].

RADIAL CATHETERIZATION

Recent popularity of trans-radial cardiac catheterization raises the issue of endothelial injury and the ability of the endothelium to fully recover about which there are few data. I would not use such a RA within 3 to 6 months of the event and will await future studies of endothelial recovery after catheter interventions. In my experience it is the right RA

which is usually accessed but since I prefer the left for RA harvest as this facilitates simultaneous harvest of LITA and RA it is a non-issue. I have no concern about harvest from the dominant arm. The T-graft is more complex and demanding and requires attention to all details but has not been associated with greater morbidity or mortality [19,26,43]. For most it requires a stepwise, incremental approach and also comfort with flow delivery which is gained by routine intraoperative flow measurement and appreciation of arterial conduit physiologic response to flow demand by vasodilation and remodeling [32].

ALL ARTERIAL

The epitome of multi-arterial grafting is all arterial grafts which for most patients mean three conduits which is my goal to age 75, more or less, depending on my estimation of life expectancy and specific contraindications to harvesting a given conduit. Few reports address the age issue but are supportive [18,48]. Most arterial conduits are of good quality at advanced age although the RA may be atherosclerotic or have medial calcification to a greater extent; the GEA and its parent vessels may manifest atherosclerotic progression. The ITA's are usually well preserved but in type 1 diabetes intimal disease may be present. BITA harvest in the past has been associated with a greater occurrence of sternal infection which has been abolished by skeletonization and avoidance of obese diabetic females, those with obstructive pulmonary disease or sternal radiation and reoperative CAB [48,49]. In patients with an absolute or relative contraindication to BITA harvest the RA or GEA are appropriate alternatives.

COMPLETENESS OF REVASCULARIZATION

Debated since the early years of CAB the consensus definition is one graft per system with the caveat that more than one graft to the LAD system had negative value [50]. In most reports off-pump CAB is associated with fewer grafts but this has not translated into greater early or late mortality or morbidity [51]. In their efforts to achieve 'more complete' revascularization surgeons have historically bypassed all vessels with 50% or greater stenosis and a lumen of 1.5 mm or

greater which in part reflects a philosophy or mindset of 'to do a better job.' That is why many patients with triple vessel disease have four or more grafts. On occasion I have regretted bypassing secondary or smaller vessels when left ventricular function was severely impaired preoperatively and the operation lengthened by my decision which may have contributed to less than optimal intraoperative myocardial preservation. Hybrid revascularization is an option today and allows the surgeon to avoid anatomically difficult access or to limit the duration of myocardial preservation when desirable [52].

MEDIASTINAL WOUND INFECTION

Historically and to the present one of the greatest concerns is the complication of mediastinal wound infection which is associated with significant morbidity and mortality. Harvest of the LITA, whether pedicle or skeletonized, does not significantly increase this complication. Diabetes has long been associated with this complication as has obesity, chronic obstructive pulmonary disease, poor left ventricular function and thoracic radiation therapy. Sternal blood flow is reduced by ITA harvest and to a greater degree with pedicle harvest rather than skeletonization. The combination of diabetes and obesity has been particularly associated with this complication and surgeons have learned to avoid BITA harvest in these at risk patients which has led to selection and for good reason. Sternal infection has been significantly reduced by skeletonization, patient selection and attention to technique with minimal use of cautery which will damage small and collateral arterial vessels. Sternal infection in one large (n=1,079) observational series with pedicle ITA harvest occurred in 1.2% and was 2.54% (7/276) in diabetics versus 0.75% (6/803) in non-diabetics [53]. Meta-analysis has demonstrated the value of skeletonized BITA harvest in reducing sternal infection and in single institution experiences the incidence was about 1.0% [21,49,54].

CONDUIT PATENCY

Patency of the ITA's is equivalent with the only difference being the targets. The RA and GEA have similar patency to

10 years which is somewhat inferior to the ITA's but not too far behind when non-LAD targets are compared. The ITA's have not developed atherosclerosis to 25 years and beyond while only a few angiograms of the RA and GEA have been at 15 years, but do not reveal atherosclerosis. There is no doubt in my mind that patency of the RA and GEA is better than SV although only recently has this been documented [12]. The problem has been comparison of these two grafts to SV grafted to the right coronary which in many instances did not have a flow restrictive lesion (90%) so that competitive flow caused the arterial grafts to close whereas VG patency is not influenced by a lesser stenosis.

CONCLUSION

Five year results from the SYNTAX study support the advantage of CAB over PCI for patients with moderate/severe CAD (SYNTAX score of 23–32 and 33 or more). Survival benefit for CAB over PCI is also demonstrated in patients with risk factors for perioperative mortality. Diabetics receive greater benefit from CAB both early and late. The value of SYNTAX cannot be overstated in that it has fostered the 'heart team' approach, created guidelines for management of CAD and achieved mutual cooperation between interventional cardiologists and cardiac surgeons.

The fundamental difference between the two approaches is that a bypass treats two-thirds of the vessel, not just the 'culprit' lesion, and by doing so anticipates new lesions developing proximal to the graft. An added benefit is the apparent ability of an arterial bypass to modulate coronary atherosclerosis distal to the bypass. Bypass conduits are not perfect but their failure rate is less than for stents and reflected in re-intervention rates, MI and angina. It is also evident that arterial conduits have better patency than VG's and particularly as they age and veins develop the disease they are treating. Arterial conduits have been demonstrated to be atherosclerosis free beyond 25 years for the ITA and to 15 years for the RA while the GEA is comparable but if *in situ* is vulnerable because it is a 4th order branch.

Devastating is stroke as a complication of CAB or PCI. It is clear that aortic manipulation causes perhaps 50% of strokes related to CAB. Off-pump technique alone does not

consistently reduce this complication which occurs from manipulation of the aorta. Aortic cannulation and cross clamping, as opposed to partial clamping which is commonly used in off-pump, is associated with a stroke rate of <1% when no grafts are attached to the aorta or the anastomosis accomplished without clamping [11,19,26]. The alternative is off-pump without aortic clamping to reduce perioperative stroke to the level seen with PCI.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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