Gen Thorac Cardiovasc Surg
DOI 10.1007/s11748-017-0807-8

CURRENT TOPICS REVIEW ARTICLE

Current trends in selection of conduits for coronary artery bypass grafting

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Received: 20 March 2016 / Accepted: 31 July 2017

Abstract The procedure of coronary artery bypass grafting continues to be the "gold standard" for patients with multivessel coronary artery disease and left main stenosis due to favourable long-term and consistent outcomes despite the advent of new generations of stents. But the targeted better long-term outcome of surgical revascularization over percutaneous interventions depends on several variables and aspects; one of them is the choice of conduits used to bypass the stenosed arteries. Coronary artery bypass surgery has been studied and debated for decades and the same applies to the selection of grafts. Current data provide significant benefits for patients who receive full arterial revascularization using both internal thoracic arteries and, if applicable, the radial artery. Unfortunately, the use of multiple arterial grafts is still not performed widely despite the evidence of superiority over multiple saphenous vein grafts that are still the most used grafts in cardiovascular procedures. In this review article, we present current trends and evidences for graft selection and give an overview of controversial data regarding the comparison of the radial artery and saphenous vein. Additionally, few words are spelt on alternative conduits.

Keywords Coronary artery bypass grafting · Internal thoracic artery · Radial artery · Vein graft · Patency rate

Introduction

Coronary artery bypass grafting (CABG) remains one of the most frequently performed procedures in cardiac surgery despite the latest technical advancements in percutaneous interventions (PCI). Operative revascularization continues to represent an effective therapy especially in terms of durability and long-term outcome. The ESC/EACTS 2014 guidelines still consider CABG as the gold standard for significant left main coronary artery (LMCA) disease in patients based on the Coronary Artery Surgery Study (CASS) registry. In addition, more recent evidence confirms a clear benefit of surgical revascularization over PCI in the follow-up data beyond 5 years [1–5] (Table 1).

Procedural details, surgical technique, disease progression and also the choice of the conduits are determinants of the faith in the revascularization site. The use of the left internal thoracic artery (LITA) to the left anterior descending artery (LAD) has been well studied and has demonstrated the best outcome in terms of reduced long-term mortality and morbidity when compared to other conduits. Nowadays it can be considered as a matter of non-controversial knowledge among cardiac surgeons and cardiologists that the most reliable coronary artery bypass conduit in terms of patency rate is the internal thoracic artery grafted to the LAD. Especially the combination of LITA to LAD because of the specific biological, anatomical features of this graft and the large run-off of the LAD potentiate the single benefits [6, 7]. One of the key questions, besides the use of the LITA, is the issue of which conduit is the next best choice for surgical revascularization and favourable outcome. Since the first coronary artery bypass operation, numerous conduits have been used with the aim to provide optimal long-term patency. In daily clinical practice, the saphenous vein and the radial arteries

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Published online: 09 August 2017

Table 1 Patency rate for the most commonly used bypass conduits

	Patency rates		
	1 year	5–10 years	10–20 years
IMA	>98%	95–99%	95–98%
Radial artery	n/a	82%	<80%
Saphenous vein graft	80–90%	50%	<40%
RGEA	93%	70%	n/a
Splenic artery	n/a	40%	n/a
Allografts and artificial grafts	<30%	n/a	n/a

IMA internal mammary artery, *RGEA* right gastroepiploic artery, *n/a* not available

are, next to the internal thoracic artery, the most frequently used conduits. Other conduits are nowadays less frequently used and depend more on individual conditions and institutional experience. The small diameter (<5 mm) of artificial grafts made polytetrafluoroethylene obsolete too because of the high risk of thrombosis but artificial grafts seeded with patients' own cells may have a future revival due to emerging technologies like induced pluripotent stem cells and novel materials [8].

Internal thoracic artery (ITA)

Gordon Murray, who studied the direct suturing of internal thoracic arteries and carotid arteries to the diseased left anterior descending artery already in 1953, was the first to show the efficacy of arterial grafts in the coronary circulation [9]. The landmark study by Loop and colleagues described that the routine use of the LITA rather than sole use of the saphenous vein for coronary artery bypass grafting (CABG) improves survival and reduces significantly the incidence of myocardial infarction, recurrent symptoms of angina and repeat interventions [7]. LITA has been established as the best graft to revascularize the LAD with the highest patency rate and the best survival following CABG. The unparalleled long-term patency that is considered as reference value and better clinical outcomes associated with the use of the LITA makes it the first choice for the anastomosis to the LAD in almost all patients regardless of age or pathology. There are only very few exceptions where the ITA cannot be used routinely like in emergency operations under reanimation, after chest wall radiation therapy with subclavian artery or ITA occlusion or if the patient is dependent on collateral circulation via the ITAs [10, 11]. But why is the ITA superior and shows such a high resistance to atherosclerosis? [12]. The answer lies in its unique biological and structural features. The endothelium is more resistant than that of a vein or more peripheral artery against harvest injury, stretch stress. The medial layer is thinner because fewer smooth muscle cells are present. The response to pulsatile mechanical stretch or disturbing flow is less; this anatomical structure changes from central to the periphery [13]. In addition, the ITA has significantly increased rates of nitric oxide production in both basal and directly stimulated conditions turning the vessel into a highly effective "NO-pump" for the grafted coronary artery. Finally, the endothelium is more resistant to reactive oxygen species and therefore less susceptible to damage by related biochemical processes provoked by pathophysiological state such as diabetes mellitus or external hazardous substances as for example smoking. Data from Mueller suggested that smoking induces the endothelial dysfunction by increasing damaging reactive oxygen species production and that the ITA is more resistant to them. Different levels of endogenous antioxidant enzyme activities and the degree of atherosclerotic changes might therefore modulate vasoreactivity and seem to be responsible for decreased graft patency of radial artery when compared with ITA in active smokers [14]. Vein grafts are definitely more susceptible to thrombosis and the development of intimal hyperplasia in response to endothelial damage and smooth muscle cell hyperplasia [15].

The IMA has been demonstrated to produce patency rates between 95 and 99% 10 years after CABG, and up to 95 and 98% after 20 years. Vein graft failure occurs in up to 30–40% after 10 years with significant atheroma in most of the remaining grafts and intima hyperplasia of smooth muscle cells present in almost all vein grafts [16, 17]. Studies have also shown that there is no decrease of ITA patency when sequential anastomoses have been performed. This superior patency translates logically into improved 10-year survival with lower incidence of myocardial infarction, hospitalization for cardiac events and need for reoperations and reinterventions [18, 19].

However, recent debates concentrate as to which arterial conduit is the next best choice after LITA to LAD when multiple revascularization is required. The right internal thoracic artery (RITA) and the radial artery (RA) have been considered to be the next logical steps to achieve full arterial CABG.

The strategy of full arterial revascularization suggests the use of multiple arterial grafts and no vein grafts to improve long-term patency and outcome. When scheduled for CABG, a majority of patients will need three to five distal anastomoses. The most commonly performed standard procedure worldwide is a single ITA for the LAD and two vein grafts for the circumflex artery and the right coronary artery. When compared with a vein graft, a single ITA graft to the LAD improves survival by 8% and reduces the frequency of late myocardial infarction, recurrent angina, and need for further cardiac interventions significantly. In contrast to these excellent results, up to 75% of

vein grafts are severely diseased during the same time period [16, 19, 20]. This means that 15 years after their first operation, 30% of patients may need redo-CABG [21]. In general, the use of bilateral internal thoracic artery (BITA) grafting rather than unilateral internal thoracic artery grafting has been associated with increased survival and fewer cardiac events [22, 23]. The work by Nasso found that myocardial revascularization with not only one but two arterial conduits in multivessel coronary disease offers improved survival as compared with a single arterial graft, independent of which conduit is used as a second arterial graft [24, 25]. However, recent studies concentrate on which arterial conduit is the next best choice after LITA for multiple revascularizations. The right internal thoracic artery (RITA) and the radial artery (RA) have been considered to be the logical conduits to revascularize the non-LAD coronary arteries.

Right internal thoracic artery versus radial artery as second conduit

With growing interest in full arterial revascularization and subsequent higher numbers of procedures, there is growing evidence supporting the superiority of the RITA over the RA. The radial artery was initially used for coronary revascularization by Carpentier and colleagues in 1971, and its use was abandoned because of an occlusion rate that was greater than that observed in saphenous vein grafts [26]. It took nearly 20 years until Acar demonstrated that the radial artery is a good alternative to other conduits [27]. Navia studied a propensity score-matched patient population ($n = 1700$) exclusively undergoing arterial revascularization in off-pump CABG surgery. In the propensity score-matched patient population, the incidence of reintervention/readmission (HR 0.40; 95% CI 0.18–0.88; $P = 0.02$) and combined end points (HR 0.54; 95% CI 0.32–0.92; $P = 0.02$) were significantly better in the BITA group as compared with the LITA plus RA group [28]. Another representative propensity score analysis by Ruttman compared morbidity and survival of two groups, BITA ± SVG and LITA + RA ± SVG [29]. Results showed significantly lower perioperative major adverse cardiac and cerebrovascular events, significantly higher event-free survival in the BITA ± SVG group compared to the LITA + RA ± SVG group. Interestingly no significant difference in sternal complications in the BITA ± SVG group compared to the LITA + RA ± SVG group was detected. In an earlier published retrospective analysis of prospectively gathered data on consecutive patients undergoing isolated CABG, Borger reported data divergent to the above study. The first section of the study compared outcomes for one arterial graft (LITA to LAD, $n = 2333$) versus two arterial grafts (LITA + RA or LITA + RITA, $n = 378$). The second section of the study compared outcomes for the RITA ($n = 132$) versus the RA ($n = 171$) as second arterial graft: by multivariable stepwise logistic regression, the use of one arterial graft was associated with an increased incidence of perioperative cardiac morbidity and mortality. Double-arterial graft patients had a non-significant trend toward increased intermediate-term actuarial survival ($P = 0.12$) and cardiac event-free survival ($P = 0.09$). The paper included a second analysis that compared preoperative demographics and revealed a higher incidence of diabetes (27 vs 11%, $P < 0.001$), peripheral vascular disease (16 vs 8%, $P = 0.03$), and elderly age (13 vs 2%, $P = 0.001$) in patients receiving an RA versus those receiving a RITA as the second arterial graft. Interestingly, the perioperative outcome analysis revealed a decreased intensive care unit stay in the RA versus RITA group. RITA patients had a significant higher incidence of sternal wound infection (5.3 vs 0.6%, $P = 0.01$, and tended to require more blood product transfusions (51 vs 40%, $P = 0.06$) [30]. The authors concluded that patients receiving an RA instead of an RITA have a lower incidence of sternal wound infection and decreased transfusion requirements, with no difference in perioperative or intermediate-term cardiac morbidity or mortality rates. The retrospective angiographic study performed by Khot demonstrated a significantly lower patency rate for RA when compared with ITA or even SVG at a mean follow-up of 565 days [31]. The following study by Tatoulis in the same year reported excellent outcomes ($n = 5766$) following use of RITA. The late patency (10 years) of RITA was excellent, with similar outcomes to LITA when grafted to identical territories. The results showed a significantly better patency of RITA compared to radial artery ($P < 0.01$) and SVGs ($P < 0.001$) [32].

Schwann found in a multi-institutional, retrospective analysis that RA and RITA multiarterial revascularization (MABG) equally improve long-term survival compared with single arterial coronary artery bypass grafting and thus should be embraced by the Heart Team as the therapy of choice in LITA-based coronary artery bypass surgery. Unadjusted 5-, 10- and 15-year survival rates were best in RITA-MABG (95.2, 89 and 82%), intermediate in RA-MABG (89, 74, 57%) and worst in SABG (82, 61 and 44%) cohorts (all $P < 0.001$). Late survival (16 years) was equivalent in the RA-MABG and RITA-MABG cohorts [68.2 vs 66.7%, $P = 0.127$, hazard ratio (HR) = 1.28 (0.96–1.71)] and both significantly better than SABG (61.1%) [33].

In summary the radial artery has some shortcomings when compared to the RITA like susceptibility to vasospasm and intimal hyperplasia, the need for a proximal anastomosis. Radial artery patency is significantly influenced by competitive coronary flow with at least 75%

coronary stenosis being the accepted cut-off and evidence showing improved RA graft patency with 90% stenosis [34]. There are some concerns about using the RITA regarding its length, the ability to use it to revascularize the circumflex system, and the potential risk for increased sternal complication in patients with chronic obstructive pulmonary disease, obesity and/or diabetes [35]. Skeletonization of the IMA has been shown to reduce this complication due to better preservation of sternal vascularization even in diabetic patients [33–35]. Furthermore, the skeletonized graft has increased luminal diameter, free flow and conduit length compared to a pedicled graft [36–38]. To further extend graft length, the RITA can be routed through the transverse sinus to reach circumflex artery targets as an in situ graft, or it can be used as T-graft or Y-graft from the LITA to allow grafting of the left coronary system with both internal thoracic arteries. The in situ patency of the right ITA is comparable to that of the left when directed to the same target vessels with respect to delicate preparation [39].

Radial artery versus saphenous vein

Despite a multitude of available data, the use of multiple arterial conduits for coronary revascularization remains a rare event (<10%) in the US and Europe [40, 41]. Multiple arterial conduits result in better long-term graft patency and improved patient outcomes for surgical revascularization. Some studies comparing the RA and SVG still show conflicting results. Some recent data show that RA has no significant benefit compared to SVG when global outcome is analyzed. Benedetto for instance demonstrated no advantages of using the RA when compared to SVG [42]. In a systematic review Athanasious reported no significant difference in early and late graft failure when comparing RA to SVG [43]. Hayward and colleagues have published the results of a prospective randomized trial comparing RA with SVG. Angiography performed at 5 years demonstrated no significant difference in patency between RA and SVG [44]. As BITA grafting has been associated with improved long-term outcomes after CABG a recent study by Mohammadi evaluated the early results and long-term survival among CABG patients who underwent in situ BITA grafting with the radial artery (RA) as an additional arterial conduit compared with those who underwent BITA with additional SVG. 1750 consecutive patients with triple-vessel disease or left main plus right coronary system disease underwent primary isolated in situ BITA grafting with at least one ITA to the LAD. Propensity score matching was used to create two comparable cohorts and the median follow-up was 8 years. There was no difference in operative mortality between matched BITA-RA and BITA-SVG (0.8 vs 0.4%, respectively; $P = 0.6$). 5-, 10-, and 15-year survival rates were 98.3, 92.0, and 92.0%, respectively, among BITA-RA patients, versus 96.5, 93.0, and 87.0% in the matched BITA-SVG group and late survival was also similar among the BITA-RA subgroups matched to BITA-SVG patients. The authors concluded that the use of the RA as an additional arterial graft in patients undergoing CABG with in situ BITA does not prolong late survival when compared with BITA patients who received additional SVG [45].

Tranbaugh published a retrospective cohort study with 1851 consecutive patients undergoing primary, isolated CABG with the LITA, RA, and saphenous vein showed a clear benefit of the radial artery. Overall RA ($n = 420$ grafts) patency was 82% and SVG ($n = 364$ grafts) patency, 47% ($P < 0.0001$). LITA ($n = 287$) patency was 85% and RITA ($n = 15$ grafts) patency was 80% ($P = 0.6$). Interestingly the RA patency was not different from LITA patency ($P = 0.3$). The authors concluded in this study that RA grafting is a highly effective revascularization strategy providing excellent short and long-term outcomes with very low rates of reintervention. RA patency is similar to LITA patency and is much better than SVG patency. They concluded that RA should be more frequently used in patients undergoing CABG [46].

In a meta-analysis by Cao, five relevant randomized controlled trials were included. Angiographic results indicated that the RA was significantly more likely to be completely patent and less likely to be associated with graft failure or complete occlusion at 4 years' follow-up and beyond when compared to the SVG [47]. Nevertheless, SVG is traditionally the most frequently used conduit for CABG. It is harvested via an 'open', 'bridging', or endoscopic technique. The superficial location of the vein and its length are considered to be largely responsible for its frequent use despite known limited long-term patency. On average 50% of SVG are partially or completely occluded by 10–15 years.

The harvested veins adapt to the higher arterial pressure by remodelling and intimal hyperplasia with smooth muscle cell growth dependent on the flow pattern. The vein segments have a higher susceptibility to atherosclerosis due to their wall structure, endothelium, intraluminal anatomy, response to arterial hypertension and flow dynamics secondary to the presence of reversed valve segments. The current literature leaves little space for vein grafts despite the high frequency of use [48].

Alternative conduits

The right gastroepiploic artery (RGEA) is another arterial graft that allows revascularization in the pedicled technique avoiding additional aortic manipulations [49]. Harvest of

this artery requires intra-abdominal entry or an extra-abdominal incision which increases operative time and may be associated with additional complications especially in unexperienced centers. On the other hand, data have been reported that show clearly no significant increase in surgical risk and bowel ischemia and a cumulative patency rate of the GEA graft of 98.5% at 1 month, 93.7% at 1 year, 86.2% at 5 years and 70.2% at 10 years [49, 50]. Some other reports revealed that the patency rate of RGEA is not better than that of the SVG; again additional findings have shown a patency rate of >82% for the RGEA and 85.7% for the IEA at the 5-year follow-up [51]. The use of splenic artery has been described when no other conduit is available but requires again opening of the peritoneal sac and can be used to anastomose branches of the right coronary and circumflex arteries. The spleen does not have to be removed as it is also supplied with blood from short gastric branches of the left gastric artery. The data on patency rates are very sparse but ranges at 40% after 10 years [52]. Other conduits include the subscapular artery, the inferior mesenteric artery, the descending branch of lateral femoral circumflex artery and the ulnar artery [53, 54].

Allografts and artificial grafts

The success with cryopreserved vein grafts, treated bovine internal thoracic artery is very limited. The same applies to expanded polytetrafluoroethylene grafts with patency rates below 30% at the 1 year follow-up making them, as alternative grafts, obsolete [55–58]. Prosthetic grafts as replacement strategy for autografts in patients lacking suitable bypass material are still very limited due to low patency rates, risk of infection and a high risk of thrombosis. Advances in vascular tissue engineering technology, e.g., cell sheets, scaffold-guided and decellularized conduit techniques with the aim to provide off-the-shelf living conduits with properties similar to those of native tissue have been extensively studied over the past decades. Vascular tissue engineering has become one of the fastest-growing areas of research. The serial clinical application has yet to happen but several serious and promising technologies are on the way [59].

Conclusion

The outcome for surgical coronary artery revascularization depends on multiple variables, but when long-term outcome is an issue, the choice of a conduit assumes major importance. Non-use of the ITA as a graft to the LAD is a strong negative procedural risk factor; even octogenarians have benefits from it [60]. The use of both ITAs has been shown to further improve outcomes compared to using a single arterial conduit. Multiple arterial revascularization further improves the long-term survival. The choice between radial artery and SVG has been controversial in the past and current studies prefer the use of the radial artery, especially to revascularize higher grade stenotic coronary. At least 50% of SVG are partially or completely occluded by 10–15 years especially if the vein quality is poor or traumatic handling during the harvesting process has damaged the endothelium. There is plenty of evidence that full arterial revascularization provides better long-term outcomes but still surgeons have to balance anatomical criteria, patient characteristics and conduit availability. Total arterial revascularization is achievable in a majority of patients but requires good planning in terms of graft selection and graft configurations [58]. The major drawback is the risk of sternal complications in patients with diabetes, obesity and pulmonary complications but it can be avoided by using skeletonization [61, 62]. The radial artery and the right gastroepiploic artery are more susceptible to spasm as they are arteries with substantial muscle layers while the ITA is less affected due to the specific "bio-functions" [63].

As described by Serruys et al. [64], stenting is still associated with a greater need for repeated revascularization over time. A recent editorial by Puskas relating to the "Society of Thoracic Surgeons' Workforce on Evidence Based Surgery Task Force's" presentation on "Clinical Practice Guidelines on Arterial Conduits for Coronary Artery Bypass Grafting" the matter of age is given special attention [65]. Interestingly, these recent guidelines do not report any age threshold for arterial revascularization. Of course the patient with very limited life expectancy will have less clinical benefit from arterial grafts regarding long term patency but will still profit from the other advantages of arterial conduit material. The need for individualized decision making is reflected by the missing age cut-off in the current guidelines [66]. Tranbaugh showed in an innovative approach very encouraging results for multiple arterial bypass grafting, supporting that arterial revascularization should be the routine in the majority of patients with left-sided target vessel stenosis of at least 70% and an age up to 80 years. The study presents Kaplan–Meier estimated survivals that analyzed the potential number of lives that could be saved based on a 20 and 80% rate of multiple arterial revascularization when directly compared to the average national rate of only 10%. This was applied to a hypothetical national sample of 200,000 similar patients. The 80% rate of multiple arterial revascularization has the enormous potential in this study to prevent more than 10,000 deaths annually and add >64,000 person-years of life over the course of 10 years [67]. These data are in

line with others recently published by Shi who found that a third arterial graft in patients receiving BITA is associated with a strong survival benefit [68]. Therefore, the aim of modern coronary artery bypass grafting should be a patient-specific tailored graft selection optimizing available conduits to provide good, long-term outcome, and prevent reintervention and complications. The modern cardiac surgeon has to embrace full arterial revascularization.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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