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Total arterial coronary grafting: outcomes, concerns and controversies

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Abstract

Choice of conduit remains the Achilles heel of coronary artery bypass grafting. Conduit choice is crucial as it is deemed to influence the long-term outcomes. While the important survival advantage of a left internal mammary artery graft over vein grafts is universally accepted, controversy reigns supreme regarding the next best conduit. There is plenty of evidence to suggest that arterial grafts are not only superior in terms of patency and survival, but they also protect the native coronary arteries against further progression of atherosclerotic disease. Total arterial coronary grafting, utilizing various configurations of bilateral internal mammary arteries, radial artery and occasionally right gastroepiploic artery is a safe and reproducible strategy. However, concerns about additional operative time, enhanced technical complexity, graft spasm with hypoperfusion, competitive flow, increased risk of bleeding, deep sternal wound infection, and most importantly lack of randomized trial data have prevented the universal adoption of total arterial coronary grafting. This review evaluates the currents outcomes of total arterial coronary grafting and summarizes the concerns and controversies associated with this strategy.

Keywords: Coronary artery bypass grafting, bilateral internal mammary artery grafting, multiple arterial grafting, total arterial grafting, total arterial revascularization

INTRODUCTION

Coronary artery bypass grafting (CABG) remains, more than five decades after its introduction into clinical practice, the most scrutinized surgical procedure and a therapeutic intervention of paramount importance for patients with coronary artery disease[1]. The choice of the graft conduit for CABG has significant impact both on the short- and long-term outcomes. The patency of a coronary conduit is fundamentally related with a smooth postoperative course, improved long-term patient survival and enhanced freedom from re-intervention[2]. Long saphenous vein has been the most commonly used conduit in CABG. However, progressive saphenous vein graft (SVG) failure remains a major impediment to the long-term success of CABG[3]. Total arterial coronary grafting also known as total arterial revascularization (TAR) is a logical solution to deal with late vein graft atherosclerosis, and occlusion.

RATIONALE

Arterial coronary grafts are relatively resistant to atheromatous changes and have better patency rates, resulting in less recurrent angina, fewer myocardial infarctions and reoperations and better survival than with SVGs[4]. Hence it is logical to use arterial grafts instead of SVGs. Multiple large studies have documented better long-term outcomes for CABG with two internal mammary arteries (IMAs) over one[5-7]. Arterial grafts (unlike SVGs) also synthesize and release nitric oxide and other favorable vasoactive agents that protect the coronary artery downstream from development of further atheromatous changes[8].

CURRENT UTILIZATION RATES

Utilization rates of TAR are variable. It is estimated that about 20% CABG procedures in Europe utilize TAR while utilization rates are up to 80% at some centers in Australia. On the other hand, in North America almost 5% of patients undergoing CABG receive TAR[9-11]. This large variation in practice can be partially attributed to the paucity of evidence from adequately powered randomized controlled trials (RCTs) with long-term follow-up. Furthermore, increasingly complex patient profiles and enhanced scrutiny facing the cardiac surgeons in an era of public reporting of surgeon-specific mortality data may also impact adoption rates of TAR.

CONFIGURATIONS

The deployment of arterial grafts and their configuration is generally dictated by the availability of conduits, the degree of stenosis in the native coronary arteries and the technical expertise of the surgeon. There are numerous potential configurations that can be achieved during TAR highlighting the fact that that there is no single operation that is suitable for every patient - it is not a case of "one size fits all" as would be the scenario for the use of a single internal mammary artery and supplemental vein grafts[12].

Bilateral internal mammary arteries

Several configurations have been used to accomplish TAR of left-sided coronary system with bilateral internal mammary arteries (BIMA) only[13]. These include *in situ* right internal mammary artery (RIMA) to the left anterior descending (LAD) artery and the left internal mammary artery (LIMA) to circumflex marginal branches[14] [Figure 1], routing the RIMA through the transverse sinus in a retroaortic course[15] [Figure 2], and free RIMA grafts anastomosed proximally either to the LIMA[16] [Figure 3] or to the ascending aorta[17]. Table 1 summarizes the pros and cons of these configurations.

Radial artery

The radial artery can be combined with BIMA to achieve TAR. The radial artery from the aorta to the posterior descending artery (PDA) is an attractive approach in the presence of 80% or more stenosis in the right coronary artery (RCA) or ideally if the RCA is completely blocked thereby reducing competitive flow [Figure 4]. An alternative strategy, especially if a no touch aortic technique is indicated, is to use the main body of the RIMA to construct a composite left-sided graft while anastomosing the radial artery to the proximal *in situ* RIMA[12]. The RIMA will frequently fail to reach the PDA even after full

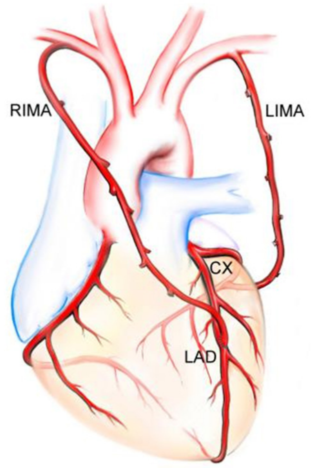

Figure 1. *In situ* right internal mammary artery (RIMA) to the left anterior descending (LAD) artery and the left internal mammary artery (LIMA) to circumflex (Cx) marginal branches. (Figure courtesy Marcie Bunalade)

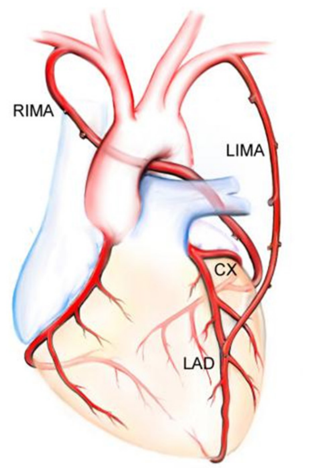

Figure 2. *In situ* left internal mammary artery (LIMA) to the left anterior descending (LAD) artery and the *in situ* right internal mammary artery (RIMA) through the transverse sinus in a retroaortic course to the circumflex (Cx) marginal branches. (Figure courtesy Marcie Bunalade)

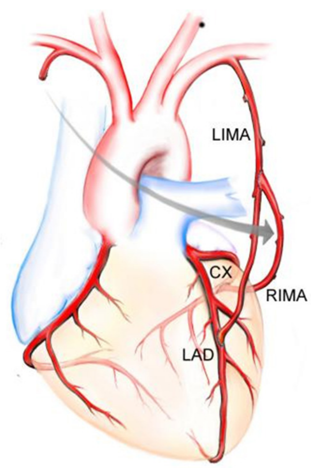

Figure 3. Composite Y graft with free right internal mammary artery (RIMA) connected proximally to the left internal mammary artery (LIMA) with LIMA anastomosed to the left anterior descending (LAD) artery and RIMA anastomosed to the circumflex (Cx) marginal branches. (Figure courtesy Marcie Bunalade)

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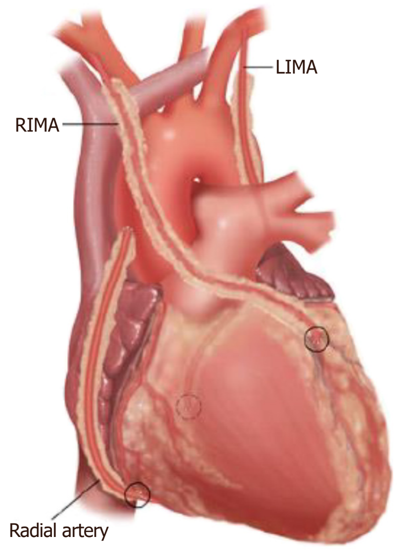

Figure 4. Radial artery from the aorta to the posterior descending artery with *in situ* right internal mammary artery (RIMA) anastomosed to the left anterior descending artery and *in situ* left internal mammary artery (LIMA) anastomosed to the circumflex marginal branches. (Figure courtesy Marcie Bunalade)

Table 1. Configurations of bilateral internal mammary arteries

Configuration	Pros	Cons
Retroaortic *in situ* RIMA via transverse sinus to circumflex marginal branches with *in situ* LIMA to LAD	The LAD is revascularized by the *in situ* LIMA, which is well accepted as a gold standard technique The left coronary system is perfused by 2 *in situ* IMAs It avoids the difficulties of anastomosing a thin-walled vessel, such as the free RIMA, to a thick-walled vessel, such as the aorta There are no grafts crossing the midline behind the sternum, and both IMAs are in a safe position, which decreases the risks in case of mediastinal revision or reoperation It offers the possibility to easily apply the no-touch principle by using different composite graft configurations.	The inability to control bleeding from retroaortic RIMA branches Aortic compression of the *in situ* RIMA, and compromised graft patency because of undetected kinks, graft overstretching, rotation, and spasm of distal RIMA
Retrosternal crossover *in situ* RIMA to LAD with *in situ* LIMA to circumflex marginal branches	This strategy is easily reproducible and technically less demanding The LAD is grafted by an intact *in situ* IMA, complete left-sided IMA grafting is readily achieved, and the principle of multiple-origin blood supply is maintained The additional length obtained by harvesting the IMA as a skeletonised vessel enables better selection of the LAD anastomotic site and precludes the use of the more distal vasospastic RIMA segments	The potential risk of damage to the artery during repeat sternotomy
Composite LIMA-RIMA T or Y grafting	The composite anastomosis is ideally matched and avoids the problems of proximal anastomoses to the aorta The aortic "no touch" technique reduces the risk of stroke and is particularly useful in off pump surgery A greater length of RIMA is available for more extensive myocardial revascularization, perhaps avoiding the use of a third conduit	Single source blood supply with steal phenomenon, competitive flow, and hypoperfusion syndrome as potential disadvantages
Right internal mammary artery for grafting the right coronary system	The aortic "no touch" technique reduces the risk of stroke and is particularly useful in off pump surgery	Gross mismatch between RCA and RIMA sizes Usage of the distal part of the pedicled RIMA to graft PDA increases the risk of vasospasm

LIMA: left internal mammary artery; PDA: posterior descending artery; RCA: right coronary artery; RIMA: right internal mammary artery

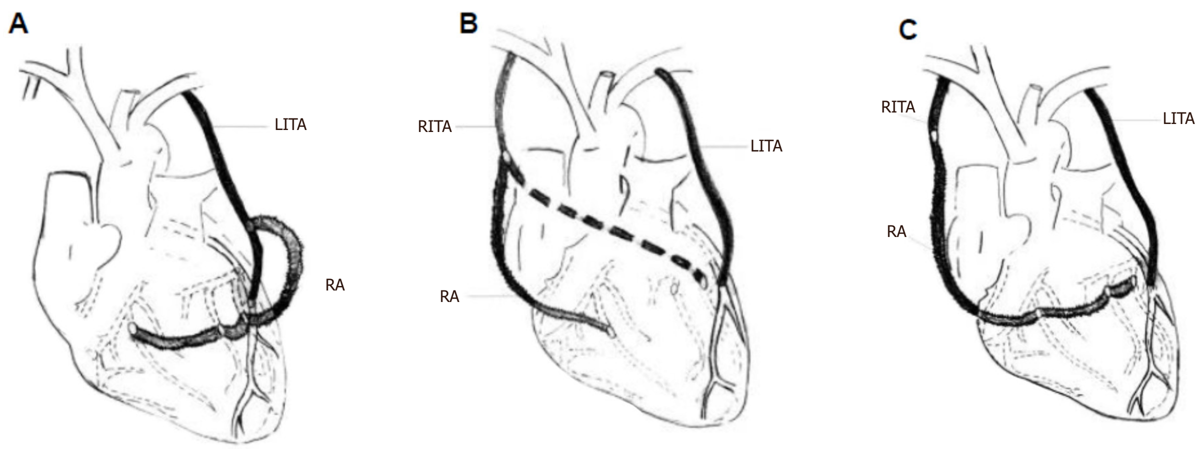

Figure 5. Composite configurations of radial artery. A: Radial artery (RA) Y or T graft from the in situ left internal mammary artery (LITA) anastomosed to the circumflex marginal branches and distal branches of right coronary artery; B: RA Y or T graft from the in situ right internal thoracic artery (RITA) anastomosed to the distal branches of right coronary artery; C: Extension of RITA with RA. (Figure courtesy Marcie Bunalade)

skeletonization and can be lengthened with recycled LIMA or radial artery [Figure 5]. The RIMA should not be anastomosed to the main RCA because of the possibility of competitive flow due to size disparity and ultimately evolution of progressive disease at the crux[12].

Right gastroepiploic artery

The right gastroepiploic artery can be combined with *in situ* RIMA to the LAD and LIMA to the obtuse marginal. Right gastroepiploic artery is particularly useful for grafting an occluded dominant ungrafted RCA or one with a failed graft in the presence of patent grafts to the left side. Grafting of the PDA can be achieved off-pump through a reasonably small incision via the lower sternum.

OUTCOMES

Perioperative outcomes

The perioperative outcomes of TAR are similar to those of conventional CABG. Majority of the studies report 1% mortality and a 1%-3% rate for stroke, intra-aortic balloon pump use and myocardial infarction[18-21]. There is increasing acceptance that TAR should be offered only to younger patients (usually now perceived as less than 70 years old), predominantly with preserved ventricular function and absence of significant co-morbidity, as they are more likely to benefit from the superior long-term patency of the arterial grafts[12]. However, TAR in combination with off-pump CABG can also be offered to the elderly to allow a true "no touch aortic technique" where there is robust evidence for a reduction in the risk of most major complications and, in particular, stroke[22]. There is evidence from RCTs that TAR with composite grafts is a safe and useful procedure in the elderly[23-25].

Long-term outcomes

The added value of TAR in CABG becomes particularly apparent when assessing long-term results. Tavilla *et al.*[26] recently reported 20-year outcomes of TAR using BIMA and gastroepiploic artery as *in situ* grafts in patients with 3-vessel disease. The Kaplan-Meier estimated survival probabilities were 73.9% (95%CI: 67.2%-79.5%) and 63.5% (95%CI: 55.7%-70.4%) for overall survival and 57.9% (95%CI: 50.7%-64.5%) and 47.9% (95%CI: 40.1%-55.3%) for freedom from major adverse cardiac events at 15 and 20 years respectively. The respective estimated cumulative incidences at 15 and 20 years were 7.0% (95%CI: 3.5%-10.6%) and 7.8% 95%CI: 4.0%-11.6%) for myocardial infarction, 8.6% (95%CI: 4.7%-12.5%) and 9.3% (95%CI: 5.2%-13.3%) for percutaneous reintervention, 7.0% (95%CI: 3.5%-10.5%) and 7.0% (95%CI: 3.5%-10.5%) for reoperation, 8.6% (95% CI, 4.7%-12.6%) and 12.9% (95% CI, 7.6%-18.2%) for cardiac death, and 10.8% (95% CI, 6.5%-15.2%) and 15.2% (95% CI, 9.8%-20.6%) for death from other causes.

Tatoulis and colleagues[27] in a mulitcentre analysis compared outcomes in patients who underwent TAR (n = 12,271) with outcomes in those who did not (n = 21,910). They determined the impact of TAR on 10-year all-cause late mortality by propensity score analyses in 6,232 matched pairs. The 30-day mortality was 0.8% (96/12,271) for TAR patients and 1.8% (398/21,910) for non-TAR patients (P < 0.001). Late mortality was 7.5% (918/12,271) for TAR patients and 8.9% (1,952/21,910) for non-TAR patients (P < 0.001). The mean follow-up time was 4.9 years. In the propensity-matched cohort, the perioperative mortality was 0.9% (53/6,232) for TAR patients versus 1.2% (76/6,232) for non-TAR patients (P < 0.001). Kaplan-Meier survival in the matched cohort at 1, 5, and 10 years was 97.2%, 91.3%, and 85.4% for TAR patients and 96.5%, 90.1%, and 81.2% for non-TAR patients (P < 0.001). Late mortality was 8.0% (n = 500) for TAR patients and 10.0% (n = 622) for non-TAR patients (P < 0.001). Stratified Cox proportional hazards models showed lower risk for all-cause late mortality in the TAR group (TAR:HR 0.80, 95% confidence interval 0.71 to 0.90, P < 0.001).

A systematic review and meta-analysis of 130,305 patients from 4 smaller shorter follow-up RCTs, plus 15 matched/adjusted and 6 unmatched/unadjusted larger longer follow-up observational studies suggested that TAR may improve long-term survival compared with conventional CABG by 15%-20% even when compared with two arterial grafts[28].

CONCERNS

Single blood source

The composite grafting technique has the disadvantage of complete reliance of the coronary bypass flow on the flow of the proximal IMA. Multiple clinical and experimental studies have assessed the adequacy of the IMA as the sole blood source in composite arterial grafting[29,30]. Sakaguchi and colleagues[30], utilizing positron emission tomography, demonstrated that the composite Y graft was not as efficient as independent grafts for increasing the coronary flow reserve soon after bypass grafting. However, most investigations have reported that the flow reserve of the proximal IMA is adequate as a blood source of composite grafts in TAR. Affleck *et al.*[31], in an effort to determine the constraint posed by a single source inflow recorded intraoperative flow in each limb of the T graft before and after distal anastomoses in 204 patients. They also compared flow capacity with completion coronary flow. Free flow for the radial arterial limb was reported as 161 ± 81 mL/min, the IMA limb as 137 ± 57 mL/min (combined 298 ± 101 mL/min) compared with simultaneous limb flow of 226 ± 84 mL/min resulting in a flow restriction of 24% ± 14%. Completion coronary flow was 88 ± 49 mL/min for the radial artery, 60 ± 45 mL/min for the IMA, and 140 ± 70 mL/min for both limbs simultaneously to give a flow reserve (*vs.* simultaneous free flow) of 160% or 1.6. This flow reserve of 1.6 compares favorably with an IMA flow reserve of 1.8 at 1-month postoperatively and 1.8 for both the IMA T graft and the IMA/radial artery T graft at 1-week postoperatively as reported by Wendler and associates[32].

Graft spasm and hypoperfusion

Hypoperfusion syndrome, associated with a high mortality, is a recognized sequela of vasospasm of arterial grafts. Spasm of the proximal IMA in case of composite grafting may result in hypoperfusion of the whole left coronary system and may lead to calamitous consequences[30]. Similarly, the radial artery and gastroepiploic artery with an enhanced spasmodic tendency, owing to preponderance of smooth muscle, predispose to a risk of hypoperfusion due to spasm of these vessels if used to construct a composite graft[33].

In practice however, 1% to 2% of the patients undergoing composite arterial grafting experience perioperative hypoperfusion resulting in myocardial ischemia, infarction, low output states, or even extreme hypotension[33,34]. Injury to the conduit during harvest, technical errors in the anastomosis, linear tension on the conduit, angulation at anastomotic site, and unresolved harvest spasm are recognized reasons for hypoperfusion syndrome[33,34]. Preoperative angiographic evaluation of the quality of the IMA conduit and the subclavian artery, careful conduit harvesting and meticulous construction of anastomoses, insertion of 1.5-mm flexible probe into the IMA and the radial artery after harvesting, and flow measurement using transit time Doppler flow meter after completion of anastomosis are some of the strategies which can mitigate the risk of perioperative hypoperfusion[33,35].

Competitive flow

Another concern is the augmented risk of competitive flow in the composite graft in comparison with the individual bypass graft. Competitive flow reduces the antegrade flow especially in the diastole, and the phasic delay in pressure wave in the IMA causes a retrograde flow in the early systole[33]. This oscillating flow pattern in the competitive scenario influences the endothelium. The release of nitric oxide and prostacyclins is affected leading to string sign, which is considered a physiologic vasoconstriction of the arterial graft. String sign is associated with moderate stenosis in the target coronary artery[29,35] and results in failure of the arterial graft[35,36].

In the composite graft, the mechanism of competitive flow is more intricate than that in the individual graft. In addition to the relation between the graft and its target coronary branch where competitive flow occurs, the interactions of all anastomosed branches within the composite graft, the phasic delay between the *in situ* grafts, and the whole graft arrangement in the patient contribute to this phenomenon. Therefore, avoidance of competitive flow and graft occlusion relies on both adequate surgical strategy and maneuver[33,35]. It is perhaps wise to avoid using composite grafts on moderately stenotic coronary arteries particularly moderately stenotic branch in the RCA territory which is the most important predictor of competitive flow and graft occlusion[33,35].

Deep sternal wound infection

Deep sternal wound infection (DSWI) is a dreadful complication of TAR, especially when BIMA is part of the revascularization strategy. The Arterial Revascularization Trial reported a 1.3% increase in the incidence of sternal wound reconstruction associated with the BIMA[37]. Different techniques of harvesting the IMA may influence these results. DSWI can be reduced to less than 1% by avoiding BIMA usage in morbidly obese patients (body mass index above 35), insulin-dependent diabetic patients, and those with severe chronic obstructive airways disease, and by appropriate timing of prophylactic antibiotics, including redosing after 4 h, tight blood glucose control intraoperatively and for 48 h, alcohol-based antibacterial preparation, and Vancomycin paste to the sternal edges[27].

Skeletonized technique of IMA harvesting has been shown to conserve considerable collateral flow to the sternum by sparing some of the sternal and intercostal branches that originate from the IMA as a common trunk[38,39]. This technique is claimed to reduce the risk of sternal wound complications by improving wound healing, especially when both left and right IMAs are harvested, due to preservation of sternal blood supply[40].

Other concerns

Harvesting additional arterial conduits takes an additional 20 to 30 min. However, the avoidance of a proximal anastomosis (*in situ* RIMA), and the use of sequential anastomoses and “Y” grafts, result in shorter aortic clamp and bypass times, which may benefit myocardial protection and blood element preservation[27].

Another concern is the potential risk of increased bleeding. A trend towards a higher rate of re-exploration for bleeding in the TAR patients is reported[41], suggesting the need for extra attention during hemostasis when using 3 arterial conduits.

The single most important and perhaps greatest issue in encouraging adoption of TAR has to be a consideration of data quality. As it has occurred in other areas to which changes to long-standing and previously well-established practices have been recommended, skepticism may well override reason in the absence of "gold standard" prospective RCTs[42]. The arena of TAR unfortunately has not enjoyed the benefit of great amounts of such data. As a consequence, even cursory reviews of the available retrospective data readily identify "easy targets" of dissonant data typical of retrospective studies that offer a ready opportunity for disproving the conclusions of these studies[42].

CONTROVERSIES

Are three arterial grafts better than two?

Whether the addition of a third arterial conduit (mainly radial artery) to BIMA is associated with better survival than BIMA plus SVGs remains a controversial area, with published literature reporting conflicting results[41,43-51] [Table 2]. Luthra *et al.*[50] in a retrospective, single-center, propensity-matched study compared the impact of a third arterial or venous conduit to the right circulation on early and intermediate survival after CABG in patients with at least two arterial grafts to the left circulation. They failed to demonstrate a significant difference in early or intermediate survival in the propensity-matched groups (venous *vs.* arterial, 99.2% *vs.* 99.2%; P = 1.000 at 1 year; 85.2% *vs.* 88.8%; P = 0.248 at 5 years and 69.2% *vs.* 88.8%; P = 0.297 at 7 years). Similarly, Formica and associates[51] comparing the use of radial artery as a third arterial conduit versus SVG failed to show long-term survival benefit of addition of third arterial graft to BIMA. One possible explanation for these contradictory findings is that the survival benefit provided by the use of a third arterial graft is lower when compared with the use of the first or second arterial conduit as most of these single-institutional studies, with small sample sizes, were underpowered to detect moderate differences in survival[52]. Interestingly, a meta-analysis of these studies reported that the use of a third arterial graft is not associated with an increase in the operative risk but rather with a 24% survival benefit at a mean follow-up of 77.9 months[52]. Clearly, there is a need for an RCT, preferably multi-institutional, with a large sample size to address this controversy.

Are all configurations of total arterial grafting equal?

The optimal conduit choice and configuration in achieving TAR remains controversial, with uncertainty regarding the individual prognostic impact of IMAs and supplemental arteries. Shi and associates[53], in a multicentre propensity matched study showed that all configurations of TAR are not equivalent. They compared long-term survival after TAR using single IMA and BIMA supplemented with radial arteries and reported that the use of BIMA as *in situ* or free conduits is associated with greater survival and seems to offer a prognostic advantage over the use of only a single IMA supplemented by radial arteries. Similar findings were reported by Navia and colleagues[54].

The recently published 10-year final analysis of the Arterial Revascularization Trial (ART), comparing single IMA with BIMA, failed to show significant between-group difference in the rate of death from any cause in the intention-to-treat analysis[55]. One plausible explanation offered by the authors for this outcome was that 14% of the patients who had been randomly assigned to the BIMA group actually underwent single IMA grafting, and 22% of those who had been randomly assigned to the single IMA group also received a second arterial graft in the form of a radial artery graft. The use of radial artery grafts in ART may be a key confounder, because it is likely to preferentially benefit the single IMA group by the addition of an arterial graft to the second most important coronary artery. When data from patients were analyzed according to the actual receipt of two or more arterial grafts, as compared with a single arterial graft (the as-treated analysis), there appeared to be a meaningfuifference in mortality in favor of multiple arterial grafts[53]. It is anticipated that the Randomized Comparison of the Clinical Outcome of Single versus Multiple Arterial Grafts (ROMA) trial[56] will address this controversy.

Table 2. Key studies comparing impact of three arterial grafts versus two arterial grafts on long-term survival

Author	Year	Study type	PSM Numbers 2-Art	3-Art	Follow-up Duration (months)	Improved survival
Benedetto *et al.*[41]	2016	PSM	275	275	2-Art = 126 ± 58.8 3-Art = 126 ± 54	No
Di Mauro *et al.*[43]	2008	PSM	590	295	2-Art = 88 3-Art = 128	No^
Glineur[44]	2013	PSM	203	93	2-Art = 196.8 ± 74.4 3-Art = 192 ± 64.8	Yes
Grau *et al.*[45]	2015	PSM	183	183	NR (max 14 y)	Yes
Locker *et al.*[46]	2012	PSM	NR 1029*	NR 155*	Mean: 91.2 ± 55.2 Median: 87.6	Yes
Mohammadi *et al.*[47]	2016	PSM	249	249	2-Art = 97.8 (IQR, 0.03-22.6) 3-Art = 97.2 (IQR, 0.02-17)	No
Nasso *et al.*[48]	2012	PSM	3584	3584	Mean: 37.2	No
Shi *et al.*[49]	2016	PSM	262	262	2-Art = 144 ± 60 3-Art = 144 ± 60	Yes
Luthra *et al.*[50]	2018	PSM	167	167	Max: 7 y	No
Formica *et al.*[51]	2019	PSM	190	190	Max: 18.5 y (IQR, 5.6-13)	No

*Non-propensity matched cohort; ^Increased mortality and cardiac death with addition of third arterial conduit (gastroepiploic artery)
Abbreviations: 2-Art: 2 arterial grafts; 3-Art: 3 arterial grafts; IQR: interquartile range; NR: not reported; PSM: propensity score matched

CONCLUSION

TAR, with its well-recognized benefits of enhanced long-term survival and freedom from re-intervention and cardiac events, is an attractive revascularization option for patients with multi-vessel coronary artery disease. However, the universal adoption remains extremely low due to lack of evidence from RCTs, relatively greater technical complexity and length of the procedure, the perceived increased risk of DSWI and other complications, and the prolonged interval before survival benefits are derived from this strategy. If TAR is to gain popularity then compelling data from RCTs is the single most important strategy to improve uptake of this technique.

DECLARATIONS

Authors' contributions

The author contributed solely to the article

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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