Bilateral internal thoracic artery grafting: an update

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Contributions: (I) Conception and design: Both authors; (II) Administrative support: MFL Gaudino; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: C Spadaccio; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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Abstract: The use of bilateral internal thoracic artery (BITA) grafting in coronary artery revascularization has been at the center of debate in recent years. Despite compelling evidence from a large body of observational studies advocating the clinical and angiographic advantage of BITA over standard single ITA and saphenous vein grafting, the largest randomized controlled trial (RCT) currently available, the Arterial Revascularization Trial (ART), reported neutral results. Methodological flaws might have affected the reliability of both the randomized and observational data currently available. However, this apparent contradiction has generated a significant degree of controversy, with the surgical community demanding for additional evidence to clarify the benefit and role of multiple arterial grafting in coronary artery bypass grafting (CABG). In this review we examine the evidence on BITA acquired before ART, the results and potential limitations of the trial and discuss pending questions and future perspectives taking into consideration the current state of the knowledge about CABG.

Keywords: Bilateral internal thoracic arteries; coronary artery bypass grafting; clinical outcomes; multiple arterial grafting; patency rate

Received: 29 January 2020; Accepted: 22 April 2020; Published: 25 December 2020.
doi: 10.21037/amj-20-13
View this article at: http://dx.doi.org/10.21037/amj-20-13

Introduction

The use of multiple arterial grafts in coronary artery revascularization (CABG) has been at the center of debate in the recent years (1). While the use of left internal thoracic artery (LITA) to graft the left anterior descending artery is widely accepted, the clinical benefit of the use of a second arterial graft, such as the right internal thoracic artery (RITA), radial artery (RA) or right gastro-epiploic artery (RGEA) remains controversial.

A compelling body of observational and randomized evidences in the last two decades has pointed at the safety and survival benefit of multiple arterial coronary artery bypass grafting (MA-CABG) with different conduit configurations (2-5). The American (6) and European (7) guidelines, as well as position paper from the Society of Thoracic Surgery (8), encourage the use of MA-CABG in younger patients on prognostic grounds.

However, in the recent years the results of the Arterial Revascularization Trial (ART), the largest randomized trial comparing the use of bilateral internal thoracic arteries (BITA) with standard single ITA+ saphenous vein grafting (SVG), dispelled the majority of the evidence accumulated in the past 20 years with a neutrality verdict. Methodological flaws, treatment allocation biases and unmeasured confounders might have affected both this randomized trial and previous observational studies (9). However, inevitably, the ART trial marks a watershed in the debate on MAG, influencing to some extent the surgical practice.

In this review we examine the evidence on BITA grafting acquired before ART, the results and potential limitations of

ART and discuss pending questions and future perspectives taking into consideration the current state of the knowledge about CABG.

What is known about BITA grafting?

Patency

The postulated reason for the survival advantage of MA-CABG is the increased patency rate associated to arterial grafts in comparison to SVG. Large observational series have shown 15-year patency rate of >95% for LITA and >90% for RITA (10). Conversely, angiographic studies on SVG have shown a 5- and 10-year patency rate as low as 75% and 60%, respectively (11-13). In the randomized PREVENT IV (Project of Ex Vivo Vein Graft Engineering via Transfection IV; N=1,828) a 75% patency rate was reported at angiographic follow-up 12–18 months after the procedure (14).

Observational data have been confirmed by two randomized controlled trials (RCTs) that specifically investigated the patency rate of RITA and SVG. The patency of RITA did not statically differ compared with SVG at 1 year (97.9% in the SVG group versus 96.9% in the RITA group; P=0.36) (15). However, the superiority of RITA over SVG was evident at longer follow-ups (95% versus 90% patency rate for RITA versus SVG respectively, P=0.001) (16).

In a network meta-analysis including 9 angiographic RCTs the risk of late graft failure (>4 years) was significantly higher for SVG than RITA [odds ratio (OR), 4.07 (95% CI, 1.28–20.88)] or RA [OR, 2.94 (95% CI, 1.36–9.00)] (17). In view of these results it is possible to hypothesize that the increasing attrition rate of SVG after the procedure might explain the patency difference at different follow-up times (18).

Of note, radial artery (RA) has also been associated with patency rates of >90% at 10 years (11) and >85% at 20 years (19) when grafting coronaries with high degree stenosis, supporting the idea that the intrinsic biology of arterial and venous conduits may play a role in the patency outcomes. Reports from basic science studies suggests that the endothelium of arterial grafts is capable of releasing cytokines and other biological mediators exerting anti-inflammatory and anti-thrombotic effects (20,21). Also, structural proteomic analysis of ITA tissue shows specific expression of proteins involved in angiogenesis, vascular smooth cells trafficking, extracellular matrix composition, coagulation, and other crucial cellular responses (22,23). It has been hypothesized that the ITA graft might function as a "drug delivery device" (22) triggering the generation of a microvascular network of neo-capillaries via the paracrine release of growth factors diffusing from the grafted region to more distant territories (21,24). These basic science findings of a pro-angiogenetic effect are in agreement with the recently proposed concept of "surgical collateralization" to explain the survival benefit of CABG over percutaneous interventions (25). However, these hypotheses on the protective effect exerted by arterial grafts remain speculative and a causative link between the improved patency rate, reduction of native atherosclerosis progression and clinical outcomes still has to be firmly established (18,26).

Clinical outcomes

Systematic reviews and meta-analysis comparing clinical outcomes comparing standard and MA-CABG have repeatedly reported the survival advantage of bilateral ITAs versus single ITA (3,4,27-30). Buttar *et al.* showed in the BITA group reduced perioperative mortality (1.2% *vs.* 2.1%; P=0.04), and improved long-term survival [hazard ratio (HR), 0.78; P<0.00001] in a large meta-analysis of 29 observational studies including 89,399 patients (30). Also, rates of target vessel-revascularization (4.8% *vs.* 10%; P=0.005) and cerebrovascular events (1.3% *vs.* 2.9%; P=0.0003) were significantly reduced, the latter probably as a result of minimization of aortic manipulation or simply due to selection bias with lower-risk patient receiving BITA (30) (*Table 1*).

However, a significantly increased rate of deep sternal wound infection (DSWI) remained the Achilles' heel of BITA-CABG (1.8% *vs.* 1.4%; P=0.0008). This risk has fueled concerns in the surgical community and limited the use of BITA-CABG especially in diabetic patients (41).

Recently, the results of 3 meta-analyses have shown that if skeletonized technique is used during ITA harvesting, the risk of DSWI in diabetic patients with BITA is similar to single ITA (39,42,43). Zhou and colleagues, in a pooled analysis of 129,871 diabetic patients, reported the risk of DSWI in the BITA group to be higher than in the LITA group (3.26% for BITA *vs.* 1.70% for LITA; P<0.001) but this difference failed to reach statistical significance when skeletonization was taken into account (2.46% for LITA versus 2.48% for BITA; P=0.84) (*Table 1*) (39).

In a small study in which 48 patients were randomized to skeletonized or pedicled BITA harvesting, nuclear imaging

Table 1 Randomized clinical trials and meta-analyses on bilateral internal thoracic artery grafting*

Author	No. of patients/studies	Type of outcome	SITA *vs.* BITA	BITA *vs.* RA	SITA/BITA *vs.* MA	Notes
Randomized trials						
Myers 2000 (31)	162	Clinical	No difference			Follow-up: median 90 months; preliminary feasibility study
Muneretto 2003 (32)	200	Clinical			Similar mortality, lower graft failure, MI, angina	>70 years; follow-up: 15 months
Gaudino 2005 (16)	60	Clinical; angiographic	Improved event free survival; improved patency *vs.* SVG			Follow-up: Mean 52 months; also RA showed excellent clinical outcomes and patency rates
Stand-in-Y 2009 (33)	850	Clinical	Improved event-free survival; no differences in the overall survival			Follow-up: mean 2 years; underpowered
ART 2019 (34)	3,102	Clinical	No difference in mortality and event free survival			Follow-up: 10 years
Le 2015 (35)	58	Clinical; angiographic			No difference in short term, stroke, DSWI; no differences	Pilot feasibility study; follow-up: 6 months
RAPCO 2019 (unpublished)	619	Clinical; angiographic		Favor RA in survival; 90.4% for RA versus 82.9% for RITA, P=0.03; equal patency rate 8.0% for RA, 11.2% for RITA, P=0.19		Follow-up: 10 years
Meta-analysis						
Taggart 2001 (3)	15,962/7	Clinical	19% in favor of BITA			All studies, all patients
Rizzoli 2002 (29)	15,299/7	Clinical	21% in favor of BITA			Excluded high-risk patients, diabetics and emergencies; follow-up: 10 years
Weiss 2013 (27)	79,063/27	Clinical	22% in favor of BITA			All studies all patients; follow-up: 7.6 years
Takagi 2014 (28)	70,897/20	Clinical	20% in favor of BITA			Adjusted studies, all patients
Yi 2014 (4)	15,583/9	Clinical	21% in favor of BITA			Adjusted studies, all patients

Table 1 (*continued*)

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Author	No. of patients/studies	Type of outcome	SITA *vs.* BITA	BITA *vs.* RA	SITA/BITA *vs.* MA	Notes
Benedetto 2015 (17)	2,780/9 RCT	Angiographic		No statistically significant difference (27% absolute risk reduction for graft occlusion)		Follow-up: ranging from 1–7.7 years; graft occlusion rate in SVG: 4-fold > RIMA, 3-fold > RA
Benedetto 2016 (36)	15,374/8 PSM	Clinical		Favor BITA in long-term survival [HR, 0.75 (95% CI, 0.58–0.97)] and freedom from repeat revascularization [HR, 0.37 (95% CI, 0.16–0.85)]		No difference in DSWI if skeletonized technique is used
Buttar 2017 (30)	89,399/29	Clinical	22% in favor of BITA			Weighted average follow up: BITA 8.6 years, SITA 7.0 years
Yanagawa 2017 (37)	130,305/25; 4 RCT; 15 matched/adjusted; 6 unmatched/unadjusted				Favor MA over BITA and SITA; longer survival 0.85 (95% CI, 0.73–0.99)	
Gaudino 2017 (38)	10,287/8 PSM	Clinical			Favor MA over BITA; longer survival [HR, 0.8 (95% CI, 0.75–0.87)]	Follow up: 37.2–196.8 months; no difference in intraoperative mortality; no influence of sex and diabetic mellitus
Zhou 2019 (39)	129,871/18; 1 RCT; 17 obs	Clinical	Risk of DSWI similar in BITA if skeletonized technique used			Diabetic patients
Gaudino 2019 (40)	149,902/34; 4 RCT 31 obs	Clinical		No difference in short and long-term mortality, perioperative stroke, perioperative MI		Trend in higher DSWI if pedicled technique

*, randomized clinical trials and meta-analyses investigating comparisons between single internal thoracic artery (SITA), bilateral thoracic artery (BITA), and multiple arterial (MA) grafting. DSWI, deep sternal wound infection; MI, myocardial infarction; PSM, propensity score matched; obs, observational; RA, radial artery; RCT, randomized controlled trial.

showed increased sternal perfusion at 3 months follow-up as well as reduced postoperative pain and dysesthesia without influencing the distal conduit flow with skeletonized harvesting (44).

A substudy of the ART trial showed a significant risk of DSWI when both ITAs were harvested in pedicled fashion (OR, 1.80; 95% CI, 1.23–2.63). However, in the skeletonized BITA group the risk of DSWI was similar to the one of a single pedicled ITA and no additional risk reduction was shown if skeletonization was applied in the context of a single ITA-CABG (45).

Before ART, two RCTs comparing LITA *vs.* BITA have been reported. While one was a feasibility study (31), the largest, Stand-in-Y Mammary study, included 850 patients randomized to single LITA or 3 different configurations for MA-CABG. Despite being underpowered to detect survival difference, the study showed that BITA was associated with an improved event-free survival at 2 years. However, no differences in the overall survival was found (*Table 1*) (33).

ART

ART is a multicentre international randomized study designed to compare all-cause mortality (primary outcome) among patients receiving elective CABG with BITA or LITA. It included 3,102 patients during a 3-year recruitment phase (June 2004–December 2007) and involved 28 centers from 7 countries (34).

At the end of the 10 years follow-up in the intention-to-treat analysis no difference among the two groups was found for survival and event-free survival. However, during the trial an unexpectedly high crossover rate from BITA to single ITA (14%) and a significantly frequent use of another arterial conduit, the RA, in both groups, introduced a significant confounder. Out of 1,554 patients 1,330 actually received a single ITA graft. For this reason, an "as treated" analysis has been also performed in which patients undergone MA-CABG (i.e., BITA or LITA-RA) were compared to single ITA patients. This analysis revealed a significantly reduced risk of mortality and major adverse events in the MA-CABG group [adjusted HR, 0.81 (95% CI, 0.68–0.95)] and [adjusted HR, 0.80 (95% CI, 0.69–0.93)], respectively. This retrospective "as treated" analysis, despite supported by a balanced allocation and risk adjustment among the groups, still shares the limitations of an observational study. Especially in the context of surgery, such studies have been shown to be affected by intrinsic selection biases and unknown confounders regardless of the statistical method utilized (9).

Several observations must be made about the discrepant neutral conclusion of ART including careful data interpretation.

Firstly, the trial was powered to detect a 20% relative difference and a 5% absolute difference in all-cause mortality, but sample size was calculated based on studies published in 70s, 80s and 90s included in large meta-analysis published almost 20 years ago (3). This is clearly not representative of the advances in operative techniques, secondary prevention and postoperative care prevalent during the era in which ART was conducted. Indeed, the control event rate was lower than expected and similar to the theorized rate in the treatment group.

A considerable part of the LITA arm (23%) received a RA graft. The use of RA has been associated with better clinical outcomes and patency rate in comparison to SVG in randomized studies and in recent large patient-level meta-analysis (5,11,17,46) thus representing a significant confounder in the interpretation of the results. In support of this idea, a post hoc analysis of the trial showed that independently of the group, the use of RA was associated with a significant lower incidence of major adverse events (47).

The unexpected rate of crossover between the arms of the study might also be considered an important limitation. Crossover was higher in the BITA group (16.4% *vs.* 3.9% in the LITA group) and the possibility of an intraoperative conversion from the randomly allocated BITA to LITA ranged between 0% and 100% among the 131 surgeons involved in the study (48). Beside the dilution of the treatment effect, the high crossover rate might also suggest lack of confidence with the use of BITA among the recruited operators. This achieves additional significance in light of the recent demonstration of a volume-outcome relationship in BITA-CABG so that more experienced high-volume surgeons have better short and long-term outcomes and mortality (49,50). Interestingly a similar trend was found in the context of ART where surgeons who recruited >50 patients in the trial had better survival and outcomes with BITA (34).

Another finding potentially responsible for diluting the treatment effect could be the high adherence to guideline-directed medical therapy (81% of patients on aspirin, 74% on β-blockers, and 90% on statins at 10 years).

Lastly, is important to notice that ART trial did not include angiographic outcomes therefore conclusions on the patency rate and speculations regarding the potential survival benefits associated with one or the other approach

cannot be made.

Pending questions about BITA grafting after ART

RITA or RA?

After the controversial results of the ART trial, several questions remain unanswered. One of the main recognized biases in ART was the frequent use of RA in both LITA and BITA arms. It should be noted that when the trial was conducted, the definitive evidence on the superior clinical outcomes of RA over SVG was not yet available (5) and the erroneous allocation of LITA-RA grafts to the single arterial group might have significantly narrowed any potential differences in clinical outcomes between the LITA and BITA groups.

It is therefore reasonable to question how RITA and RA compare and which should be preferentially used to supplement LITA in MA-CABG.

The latest report on the 10 years results of the RAPCO trial (still unpublished) has shown equivalent graft failure rates (8.0% for RA, 11.2% for RITA; P=0.19) but improved survival in the RA group (90.4% for RA *vs.* 82.9% for RITA; P=0.03). No other randomized evidence specifically investigating these aspects is available at the moment, however a meta-analysis of clinical outcomes including 15,374 patients from 8 propensity score-matched studies comparing RITA and RA as second conduit (BITA *vs.* LITA+RA) showed superior long-term survival [HR, 0.75 (95% CI: 0.58–0.97)] and freedom from repeat revascularization [HR, 0.37 (95% CI, 0.16–0.85)] in the BITA group, with similar perioperative mortality and incidence of sternal wound complication when the skeletonized harvesting technique was adopted (36). In a more recent network meta-analysis including 4 randomized trials, 31 observational studies and a total of 149,902 patients, both RITA and RA confirmed superiority to SVG in terms of long-term survival (RA incidence rate ratio, 1.23; 95% CI, 1.12–1.34 and RITA incidence rate ratio, 1.26; 95% CI, 1.17–1.35), but no significant difference in short and long-term mortality, perioperative stroke, perioperative myocardial infarction was found among the two arterial conduits. However, a trend towards higher incidence of DSWI was found in the RITA group (OR, 1.39; 95% CI, 0.92–2.1) with the risk being more significant if pedicled harvesting technique was used (40) (*Table 1*).

If RITA equally compares with RA on hard outcomes as survival and cerebrovascular events, then the main potential limitation to consider is the risk of DSWI. In a large meta-analysis of observational studies a relative increase risk of DSWI of 38% was reported in the BITA group [1.6% LITA *vs.* 2.05% BITA; relative risk, 1.38 (95% CI, 1.29–1.45)], with obesity, diabetes mellitus and chronic obstructive pulmonary disease being the main non-technical determinants of this complication (51). On the other hand, harvesting technique has also been repeatedly reported to be another factor and skeletonization is recommended as a strategy for reducing DSWI risk (45,49).

In large state registry report from 126 centers in California BITA was associated with similar survival rates but increased DSWI risk when compared to RA [7-year mortality rates 10.3% *vs.* 10.7% for BITA and RA, respectively; HR, 1.10 (95% CI, 0.89–1.37); DSWI risk 2.29% in BITA versus 1.22% in RA risk difference, 1.07% (95% CI, 0.15–2.07)] (52).

In a more recent report from the Society of Thoracic Surgeons database including 1,493,470 patients, it was shown that BITA had a slightly increased operative mortality risk [risk-adjusted OR, 1.14 (95% CI, 1.00–1.30; P=0.05)] and a significant increase in sternal complications in comparison to standard LITA + SVG procedure [risk-adjusted OR, 2.09 (95% CI, 1.80–2.43); P<0.001]. Notably, when RA was used as second arterial graft (LITA+RA) and compared to standard fashion LITA+SVG CABG no increased intraoperative mortality or DSWI risk was shown [mortality OR 1.01 (95% CI, 0.89–1.15; P=0.85); risk of DSWI OR 0.97 (95% CI, 0.83–1.13; P=0.70)] (50). In this study the presence of a U-shaped volume outcome relation was more clearly associated with BITA rather than LITA+RA grafting. This was in agreement with the large meta-analysis of an operator volume-outcome relation for long-term mortality and DSWI that suggested better results for surgeons who were more experienced and performing larger number of cases (49).

The perceived technical challenge and the lack of familiarity or confidence of surgeons in performing BITA grafting might be also at the root of the discrepancy noted between ART and RADIAL analysis outcomes particularly as from an angiographic perspective the two conduits are comparable (17). RA is more surgeon-friendly (53) and adherence to RA use might have been higher than with RITA, as confirmed by the lower crossover rate in the studies included in the RADIAL analysis when compared to ART.

In conclusion, the question on the best second arterial conduit still requires a definitive answer. However,

considering the patency equivalence (16,17) and the more solid evidence on clinical benefit in favor of RA, this conduit should perhaps be preferred in addition to LITA in patients with longer life expectancy and according to surgeon experience. However, additional evidence is required and presently individualized decision making remains the mainstay in the choice of the graft to be used (54).

Use of total arterial grafting

The addition of a third arterial conduit is also a debatable issue (55-62). A study dating back to 2003, randomizing 200 patients of >70 years to either total arterial or standard LITA+SVG revascularization showed similar mortality at 15 months, but demonstrated lower rates of graft failure, return of angina or new myocardial infarction for total arterial grafting group. Authors found that SVG was an independent determinant of graft failure and return of angina (32). Interestingly in a more recent large retrospective database from the Australian and New Zealand Society of Cardiothoracic Surgeons Society including >50,000 patients, the use of any SVG determined a reduction in survival up to 12.5 years following CABG [HR, 1.24 (95% CI, 1.18–1.30)] (63).

Conversely, in a small pilot randomized study of 58 patients designed to ascertain trial feasibility Le *et al.* found no differences in short term mortality, myocardial infarction, stroke, and DSWI between total arterial and standard single ITA CABG and no improved graft patency in the total arterial grafting group at 6 months follow-up (35).

More recently, a meta-analysis including unadjusted studies showed longer survival rates in patients receiving total arterial revascularization in comparison to single or double arterial grafting [incident rate ratio, 0.85 (95% CI, 0.73–0.99); P=0.04] (37). These results were confirmed by another meta-analysis pooling only propensity matched studies (8 studies; 10,287 matched patients; 5,346 two arterial grafts; 4,941 three arterial grafts; mean follow-up time, 37.2–196.8 months) which showed that the addition of third arterial conduit was associated with better long-term survival [HR, 0.8 [95% CI, 0.75–0.87)] regardless of the diabetic status and with no increased intraoperative mortality (38).

In a propensity-matched analysis of the Ontario state registry patients receiving three arterial grafts did not suffer increased rates of major adverse cardiac and cerebrovascular events, death, myocardial infarction, stroke, or repeat revascularization in comparison to 2 arterial conduits at a mean follow-up of 4.2 years [HR, 1.08 (95% CI, 0.94–1.25)] (64) (*Table 1*).

Finally, a recent meta-analysis investigated the best conduit to complete the revascularization of the right coronary in patients receiving BITA grafting to the left system. Authors compared both RA and right gastroepiploic artery to SVG showing better long-term mortality when using an arterial conduit (either RA or RGEA) (HR=0.58, 95% CI, 0.43–0.80; P<0.001) (65).

Future perspectives: the ROMA trial

The methodological limitations, hidden confounders and treatment allocation biases are probably at the base of the apparent neutral findings of ART, meaning that the original question posed by the trial is still not answered. To address the unanswered question, a novel trial, Randomized comparison of the clinical Outcome of single versus Multiple Arterial grafts (ROMA), has been designed (66).

ROMA has a different methodology. It has been designed as randomized multicenter event-driven trial with a sample size of 4,300 patients and will be preceded by a pilot phase to assess adherence to protocol and crossover rates. The aim will be to compare the mid-term and long-term clinical outcomes of single versus MA-CABG.

Differently from ART, the primary outcome is represented by major cardiovascular and cerebrovascular events, age cut-off will be 70 years and the surgeons will be allowed to use a second arterial conduit (including RITA or RA) only in the MA-CABG group, thus minimizing the risk of allocation bias seen in ART (1). Enrollment of patients commenced in January 2018 and is ongoing and the results are eagerly awaited considering both its scientific relevance and the significant clinical, social and economic implications of CABG. Also, ROMA would hopefully address the controversy regarding the use of RITA or RA.

The response of the surgical community to BITA grafting and real-life scenario

The lack of definite evidence from randomized studies and the contradictory evidence from majority of observational studies undoubtedly have discouraged the surgical community to adopt BITA grafting. However, data antecedent to the ART had already suggested a degree of reluctance to embrace MA-CABG.

In the previously mentioned report from the Society of Thoracic Surgeons database a second arterial conduit was

Table 2 Barriers to universal adoption of bilateral internal thoracic arteries (BITA) grafting

Lack of solid and unequivocal evidence
Perceived technical challenge
Prolonged operative time
Fear of increased mortality/morbidity and complications affecting quality metrics (deep sternal wound infection)
Steep learning curve
Difficulty to establish training for residents

used in 11.4% of the cases. Out of these, only 4.9% of the cases were performed using BITA (53). In another registry from 126 nonfederal units in California only 9.9% of the cases employed a second arterial conduit and its use decreased from 10.7% in 2006 to 9.1% in 2011 (P<0.0001) (52).

Similarly to USA, data from Canada showed that out of 50230 patients operated between October 2008 to March 2016, only 3044 (6.1%) and 8253 (16.4%) patients received 3 and 2 arterial grafts, respectively (64).

Use of a second arterial conduit or total arterial revascularization strategy is ranging between 20–30% in Europe (67), while in Japan the reported usage is 22.7% according to the Japanese Association of Thoracic Surgery (68).

The technical challenges, the prolonged operative time and the perceived increased risk of postoperative complications, rather than the actual lack of definitive evidence have been acknowledged as the main deterrents for UK surgeons to use BITA in an old survey study (69). Despite abundant literature evidence, factors such as the fear of complications, especially related to sternal wound, potentially affecting early quality metrics, the longer learning curve and the lack of specific training are still conspiring against the use of BITA (*Table 2*).

On the other hand, conflicting scientific evidence has contributed to fuel confusion and left the greatest part of decision-making in CABG to surgeons' individual interpretation or experience. Indeed, if on the one hand, many surgeons declined adoption of BITA grafting as supported by the neutral results of ART, then on other hand, the ones that have already embraced this approach for long time were legitimate to continue their practice and even push the boundaries of its application towards different high-risk subgroups of patients, as shown by the most recent "post-ART era" literature (70). This conundrum shows that, despite a general adherence to the guidelines, the real-life practice is often multifaceted and inevitably influenced by surgeons' experience or predilection. In this context, an interesting real-life analysis of the CABG situation has been recently proposed by Butt *et al.* Despite the intrinsic limitations of their study, these authors reported a 40% re-hospitalization rate at 1 year after CABG with 70% of the cases due to cardiac causes (71). This study triggered reflections on the actual efficacy of CABG as it is currently performed (72).

Although CABG is considered the "entry-level" of cardiac surgery, progressive refinement of the techniques is required to improve outcomes, including arterial grafting to secure longer patency rate, or anaortic approaches to reduce cerebrovascular events. This demands for special training and skills as demonstrated by the volume-outcomes relationships in BITA grafting (49) and in off-pump surgery (73). To this extent, it has been suggested that in order to improve outcomes, CABG should move from the status of a "generalist" procedure to a subspecialty with a dedicated team, training and scientific network (74). A preliminary report on the adoption of a programmatic specialization in CABG produced significantly better outcomes including improved survival, reduced complications, shorter operative time and increment in the use of BITA (75). Implementation of such programs is promising and might signify a step-change in CABG practice with emergence of more robust evidence on MA revascularization.

Conclusions

The use of BITA is advocated by a large body of evidence from observational studies but not fully supported by the largest currently available RCT. Although methodological flaws in THE existing evidence have hindered the universal adoption of BITA grafting, yet the idea of clinical and angiographic superiority of arterial conduits over SVG is also supported by additional robust evidence from trials on RA as well as basic science studies. The ongoing ROMA trial may shed new light on this controversy and assist the surgical community to make a more informed choice of the best revascularization strategy.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Shahzad G. Raja) for the series "Coronary Artery Bypass Grafting" published in *AME Medical Journal*. The article has undergone external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://amj.amegroups.com/article/view/10.21037/amj-20-13/coif). The series "Coronary Artery Bypass Grafting" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/amj-20-13
Cite this article as: Spadaccio C, Gaudino MFL. Bilateral internal thoracic artery grafting: an update. AME Med J 2020;5:39.