REVIEW TOPIC OF THE WEEK

The Choice of Conduits in Coronary Artery Bypass Surgery

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ABSTRACT

Coronary artery bypass grafting is the most common cardiac surgery operation performed worldwide. It is the most effective revascularization method for several categories of patients affected by coronary artery disease. Although coronary artery bypass grafting has been performed for more than 40 years, no detailed guidelines on the choice of coronary artery bypass grafting conduits have been published and the choice of the revascularization strategy remains more a matter of art than of science. Moreover, there is a clear contradiction between the proven benefits of arterial grafting and its very limited use in everyday clinical practice. In the hope of encouraging wider diffusion of arterial revascularization and to provide a guide for clinicians, we discuss current evidence for the use of different conduits in coronary artery bypass surgery and propose an evidence-based algorithm for the choice of the second conduit during coronary artery bypass operations. (J Am Coll Cardiol 2015;66:1729–37) © 2015 by the American College of Cardiology Foundation.

Although coronary artery bypass graft (CABG) has been performed for more than 40 years, no detailed guidelines on the choice of CABG conduits have been published to date. Moreover, current practice demonstrates a clear contradiction between the proven benefits of arterial grafting and the very limited use of arterial conduits in everyday clinical practice.

With the aim of encouraging a wider diffusion of arterial revascularization, and to provide a guide for clinicians, we herein discuss the current evidence basis for the use of different arterial conduits for CABG and propose an evidence-based algorithm for the choice of the second conduit during coronary operations.

SEARCH METHOD

In December 2014, the PubMed database was searched using the terms "radial artery," "gastroepiploic artery," and "internal thoracic artery" coupled with "coronary surgery," "myocardial revascularization," "coronary artery bypass," "CABG," and "patency." Relevant abstracts were reviewed and the related articles function was used for all included manuscripts. References for all selected studies were cross-checked. The present review focuses on data from randomized controlled trials (RCT), propensity-matched observational series, and meta-analyses. Unmatched observational series were considered only when data from RCT or propensity-matched studies were not available.

It is important to note that the quality and weight of the evidence for the various conduits is not the same. RCT and propensity-matched series include around 25,000 patients for bilateral internal thoracic arteries (BITA), 2,000 for the radial artery (RA), and a few hundred for the right gastroepiploic artery (GEA).

BILATERAL INTERNAL THORACIC ARTERIES

The survival benefits associated with the use of the left internal thoracic artery (ITA) to the left anterior descending (LAD) coronary artery were established in a landmark paper from the Cleveland Clinic almost 30 years ago (1). The improved outcome using the ITA is almost certainly due to its superior long-term patency. Several studies have reported substantially inferior patency rates with saphenous vein grafts (SVG), of which approximately 75% are occluded or significantly diseased at 10 years (2), in comparison to patency rates in excess of 90% for the ITA (3). Its peculiar morphologic features probably explain the superior patency of the ITA. The ITA has a discontinuous internal elastic lamina and a relatively thin media with multiple elastic laminae and the absence of a significant muscular component, which explains its reduced tendency for spasm and the development of atherosclerosis (4). Moreover, compared with all other arterial and venous conduits, it shows increased production of anti-inflammatory and vasoactive molecules, particularly nitric oxide (4).

The highest patency rates have been documented when the ITA (either in situ or as a Y or free graft) is placed to the left-sided coronary vessels (3). Inferior rates have been documented when the ITA is placed to the right coronary artery (probably due to size discrepancy and progression of disease at the crux, or to a lower amount of viable myocardium) (3).

Only 1 published RCT has compared outcomes between single ITA and BITA grafting. The ART (Arterial Revascularization Trial) recruited 3,108 patients in 7 countries. The primary outcome is 10-year survival, but an interim analysis at 1 year (a "safety" endpoint) reported excellent outcomes with both strategies. Mortality, stroke, myocardial infarction, and repeat revascularization were all under 2.5% (5).

While awaiting the outcome of the ART trial, there is currently a substantial body of circumstantial evidence to support the use of a second ITA, as it appears to offer an additional survival benefit over a single ITA graft. Indeed, more than a decade ago, a systematic review of matched cohorts of almost 15,000 CABG patients who received BITA grafts reported a significant reduction in the hazard ratio (HR) for mortality of 0.78 (6). In the past 2 years, 2 independent meta-analyses have supported this finding, not only in larger cohorts of patients, but also with longer-term follow-up. One study included 27 observational reports with over 79,000 patients (approximately one-quarter with BITA), and reported a significant reduction in long-term mortality with BITA (HR: 0.78; 95% confidence interval [CI]: 0.72 to 0.84; p < 0.00001) (7). Another study included 9 observational series of over 15,000 patients (approximately one-half with BITA), with follow-up duration exceeding a mean of 9 years, and reported a significant reduction in mortality with BITA (HR: 0.79; 95% CI: 0.75 to 0.84) (8). Importantly, no study has reported any detrimental effect of BITA on survival.

The major concern with the use of BITA grafts is the increased risk of sternal wound complications and mediastinitis. One of the largest meta-analysis on this issue showed that adding a second ITA to the ITA-LAD graft significantly increase the incidence of sternal complications (relative risk [RR] of a single ITA: 0.62; 95% CI: 0.55 to 0.71) (9). This risk is even higher in diabetics and in patients with pulmonary disease (9). In ART, the incidence of sternal wound complications increased from 0.6% in the single ITA group to 1.9% in the BITA group (i.e., an absolute difference of 1.3% or a number needed to harm of 78 patients) (5).

However, the incidence of serious wound problems can be significantly reduced by judicious patient selection and the choice of harvesting technique. Consideration should be given to avoiding BITA in patients with certain potentially morbid characteristics, especially if they occur simultaneously (diabetes, obesity, respiratory problems), and in patients receiving steroids or immunosuppression treatments. Moreover, 2 systematic reviews have both reported that skeletonization, rather than a pedicled harvesting technique, significantly reduces deep sternal wound infections, even in patients with diabetes (9,10). Importantly, the survival benefit of BITA grafting is seen in both nondiabetic and diabetic patients (11).

THE RADIAL ARTERY

Introduced in coronary surgery in the 1970s (12), the RA was "rediscovered" in the early 1990s (13). Concerns over vasospasm, due to the muscular nature of the RA wall, have been reduced after the demonstration of progressive morphofunctional remodeling of the artery toward an elastomuscular profile after implantation in the coronary circulation (14). This finding is probably the anatomic background for the demonstrated lack of utility of long-term antispastic therapy in patients with RA grafts (15), even though

such therapy is still widely adopted in the surgical community (16).

The largest angiographic series report an RA patency rate of 80% to 90% at 7 to 10 years follow-up (17). The severity of the stenosis of the target vessel is a key factor in determining RA patency. There is general agreement that the RA should be used only to bypass a vessel with >70% stenosis, and there is evidence that a 90% stenosis limit ensures an even better RA patency rate, especially on the right coronary system (18,19). The site of proximal anastomosis and the harvesting technique (open vs. endoscopic) do not affect RA patency rates, whereas there is some evidence that skeletonization of the artery can lead to better perfect patency rates (20).

The RA is the arterial conduit for which there is the most evidence derived from RCT. In fact, 4 RCT have compared the RA with either SVG or the right internal thoracic artery (RITA) (18,21–23) (Table 1). All studies that extended the follow-up beyond the first post-operative year showed significantly better patency rates for the RA over the SVG, and in 2 studies, a tendency toward a lower incidence of clinical events was also found for RA patients.

A number of meta-analyses pooled data from these RCT and large observational studies to compare the RA and the SVG (24–29). Again, all studies with a mean follow-up time extending beyond the first postoperative year reported significant benefits in terms of graft patency for the RA (Table 2). The only meta-analysis to include clinical outcomes found reduced cardiac death, myocardial infarction, and repeat coronary procedures, in addition to better late graft patency for the RA (odds ratio [OR]: 0.72, 0.68, 0.27, and 0.52, respectively) (28).

Only 1 RCT compared the RA and the RITA: the RAPCO (Radial Artery Patency and Clinical Outcomes) trial found no difference in the patency of the 2 conduits and a nonsignificant tendency to better event-free survival for the RA at the 6-year follow-up (Table 1) (23). Observational studies addressing this are discordant and usually have major methodological or sample-size limitations (Table 3) (30–33). The only comparative meta-analysis with clinical endpoints reported comparable mortality, but reduced cardiac events (myocardial infarction, heart failure, ischemia) for the RA (RR: 0.49; 95% CI: 0.28 to 0.87; p = 0.014) (25). Furthermore, a comparative network meta-analysis of angiographic studies showed that the RITA was associated with a nonsignificant 27% absolute risk reduction for late functional graft occlusion when compared with the RA (29).

Compared with the RITA, the RA seems a better choice in patients at risk for post-operative sternal complications (diabetes, obesity, chronic pulmonary disease). Indeed, harvesting of the RA is extremely safe and well tolerated, even by complex and fragile patients (25) and (unlike the RITA) does not affect sternal vascularization and healing. Two recent propensity-matched comparisons of patients at risk of sternal complications who received the RA or RITA as the second conduit reported clear clinical benefits with use of the RA (31,34). Furthermore, a recent substudy of the RAPS (Radial Artery Patency Study) focusing only on diabetic patients reported a very strong protective effect against graft occlusion with use of the RA (35), making the use of this conduit in diabetics particularly attractive. Very limited

TABLE 1 RCT Comparing the RA With Other Conduits

First Author or Study Acronym (Ref. #)	Number of Patients/ Grafts	Mean Follow-Up (yrs)	Conduits Compared With the RA	Main Findings
Goldman et al. (21)	757	1	SVG	No difference in patency
RSVP (22)	142	5	SVG	Better patency for the RA (p = 0.004)
RAPS (18)	561	7.7	SVG	Better patency for the RA (p = 0.002) Tendency to lower incidence of adverse clinical events for the RA
RAPCO (23)	649	6	SVG and RITA	No difference in patency and clinical outcome between RA, RITA, SVG Tendency to lower reintervention on target vessel for RA vs. SVG and better event-free survival for RA vs. RITA

RA = radial artery; RAPCO = Radial Artery Patency and Clinical Outcomes; RAPS = Radial Artery Patency Study; RITA = right internal thoracic artery; RSVP = Radial Artery Versus Saphenous Vein Patency; SVG = saphenous vein graft.

TABLE 2 Meta-Analysis Comparing the RA With Other Conduits

First Author (Ref. #)	Number of Patients/ Grafts	Mean Follow-Up (yrs)	Conduits Compared With the RA	Main Findings
Benedetto et al. (24)	936	1.8	SVG	No difference in patency
Hu and Zhao (25)	3,889	1-6	SVG and RITA	Better patency and reduced wound complication for RA vs. SVG (p < 0.05) Comparable survival and patency for RA and RITA, reduced cardiac events for RA vs. RITA (p = 0.014).
Athanasiou et al. (26)	1,157	>5	SVG	Better patency for the RA (p = 0.003)
Cao et al. (27)	1,708	>4	SVG	Better patency for the RA (p = 0.0001)
Zhang et al. (28)	1,860	1-7.7	SVG	Better patency and lower need for repeat coronary procedures for RA vs. SVG (p = 0.0002 and 0.0008 respectively)
Benedetto et al. (29)	2,780	1-7.7	SVG and RITA	SVG associated with a 2-fold increased risk of complete graft occlusion vs. RA after 4 yrs (OR: 2.64; 95% CI: 1.60-4.35) No difference in patency between RA and RITA.

CI = confidence interval; OR = odds ratio; other abbreviations as in **Table 1**.

TABLE 3   Observational Studies Comparing the Different Arterial Conduits

First Author (Ref. #)	n	Conduits Compared	Mean Follow-Up	Main Findings
Caputo et al. (30)	661	RA vs. RITA	18 months	Better survival (HR: 0.25) and event-free survival (HR: 0.37) for the RA
Tranbaugh et al. (31)	1,056	RA vs. RITA	9 yrs	Better survival and event-free survival for the RA (see text)
Ruttmann et al. (32)	554	RA vs. RITA	57 months	Better survival (HR: 0.23) and event-free survival (HR: 0.18) for the RITA
Raja et al. (33)	1,020	RA vs. RITA	8 yrs	Higher rate of late death (HR: 1.9) and repeat revascularization (HR: 1.5) for the RA
Hirose et al. (36)	197	RA vs. GEA	2.3 yrs	Comparable operative mortality and freedom from cardiac event
Di Mauro et al. (37)	295	RA vs. GEA	131 months	Comparable early and late survival and event-free survival
Pevni et al. (50)	477	GEA vs. RITA	67 months	Comparable survival and event-free survival
Hwang et al. (51)	210	GEA vs. RITA	5 yrs	Comparable clinical outcome and patency rate

GEA = gastroepiploic artery; HR = hazard ratio; other abbreviations as in **Table 1**.

evidence is available regarding the comparison between the RA and the GEA (**Table 3**) (36,37).
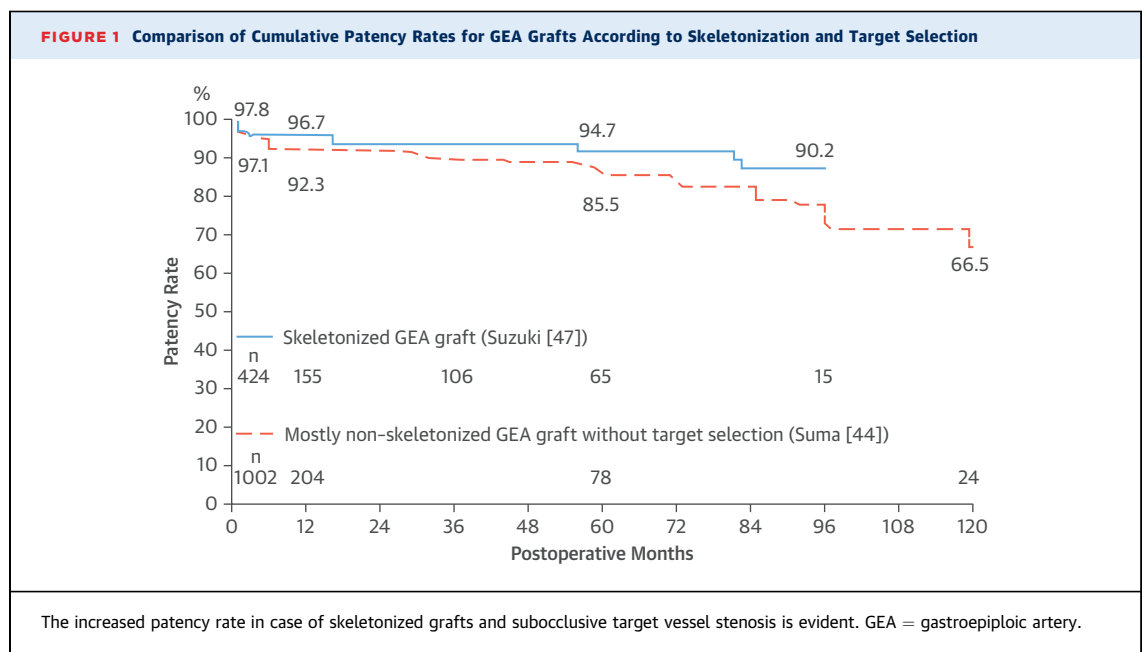
RIGHT GASTROEPIPLOIC ARTERY

Pym et al. (38) and Suma et al. (39) first independently reported systematic use of the GEA graft for CABG in 1987. Since then, GEA grafts have been widely applied in clinical practice. Very few CABG candidates have contraindications to GEA harvesting (40); the conduit has a low incidence of severe atherosclerosis (41) and good flow capacity (42). The biological and physiological profile of the GEA has now been extensively studied (43), and the use of this artery does not increase perioperative risk (44).

The most favorable target for the in situ GEA graft is the distal right coronary artery, but the conduit can be used also for the distal circumflex system. A subocclusive (>90%) stenosis of the target coronary artery is essential to maximize patency rates and avoid spasm and eventual failure due to chronic competitive coronary flow. This concern is formally recognized in the 2011 ACCF/AHA Guideline for Coronary Artery Bypass, in which arterial grafting of the RCA is contraindicated (Class III, Harm) in patients with less than critical (i.e., >90%) stenosis of the native vessel (45).

In 1 of the largest GEA series published to date, the cumulative patency rate of the artery was 97.1% at 1 month, 92.3% at 1 year, 85.5% at 5 years, 80.9% at 7 years, and 66.5% at 10 years after surgery (46). This relatively low patency rate at late periods has improved by using a skeletonized GEA graft only to target vessels with >90% stenosis. Using this approach, Suzuki et al. (47) have reported 97.8%, 94.7%, and 90.2% cumulative patency rates in the early post-operative period and at 5 and 8 years after surgery, respectively (**Figure 1**).

Two recent series reported that use of the GEA, instead of the SV, to graft the right coronary artery in patients having BITA to the left coronary system leads to a significant increase in late survival (48,49).

FIGURE 1   Comparison of Cumulative Patency Rates for GEA Grafts According to Skeletonization and Target Selection

The increased patency rate in case of skeletonized grafts and subocclusive target vessel stenosis is evident. GEA = gastroepiploic artery.

However, other studies have not confirmed this finding, and a recent network meta-analysis of RCT comparing all conduits used in coronary surgery found the GEA to be associated with the highest risk of functional and complete graft occlusion (29). Of note, a major bias in the current literature is that the majority of published series report use of the GEA as a pedicled, rather than as a skeletonized graft; skeletonized harvest of the artery has been shown to significantly improve its patency (47). Very few studies have compared the GEA with the RITA (Table 3) (50-52).
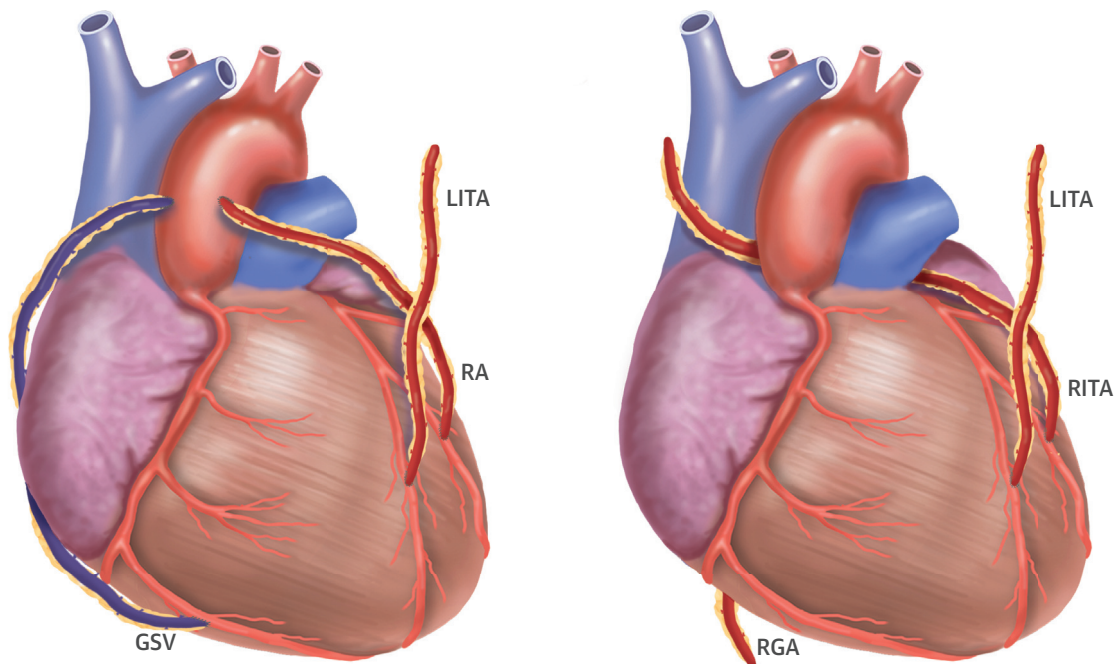
COMMENTS

CABG is the most common cardiac surgery operation performed worldwide. It has been shown to be the most effective revascularization method for several categories of patients affected by coronary artery disease. Long-term conduit patency is the key factor for the success of the procedure (2). Yet, to date, no precise guidelines on graft selection exist, and the choice of revascularization strategy remains more a matter of art than of science. Although several arterial and venous conduits have been proposed during the last 5 decades, only 4 have stood the test of time: the ITA, the RA, the GEA, and the great saphenous vein.

Currently, the clinical benefits of using the left ITA to bypass the LAD artery are well established, and this graft represents the cornerstone of modern coronary artery surgery. Robust evidence suggests that the use of an artery, rather than a vein, to graft to the second target vessel is associated with further improvement in late outcome (6-8,53). The benefits of a second arterial graft apply also to high-risk patients, such as those with reduced ventricular function or unstable angina (54,55), and become evident within the first post-operative decade (although the survival advantage tends to increase with time) (53,56). The location of the second arterial conduit and the use of sequential technique do not modify the extent of the survival advantage (57,58).

In sharp contrast with these data, there is evident reluctance toward a wider adoption of an arterial revascularization strategy in the surgical community. A recent analysis of the STS (Society of Thoracic Surgeons) database showed that, in the United States, slightly more than 5% of CABG cases receive a second

CENTRAL ILLUSTRATION The Choice of Conduits for CABG: Modern Coronary Artery Surgery

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Possible graft configurations using multiple arterial conduits. CABG = coronary artery bypass graft; GEA = gastroepiploic artery; GSV = great saphenous vein; LITA = left internal thoracic artery; RA = radial artery; RGA = right gastroepiploic artery; RITA = right internal thoracic artery.

arterial conduit (59). A similar situation exists both in Europe and in Asia. In the mostly European SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) trial (60), a second arterial graft was used in 26.2% of patients in the registry and in 35.3% in the randomized trial and the rate of BIMA utilization in a 2009 report of the Australasian Society of Cardiac Surgery was 12.6% (61).
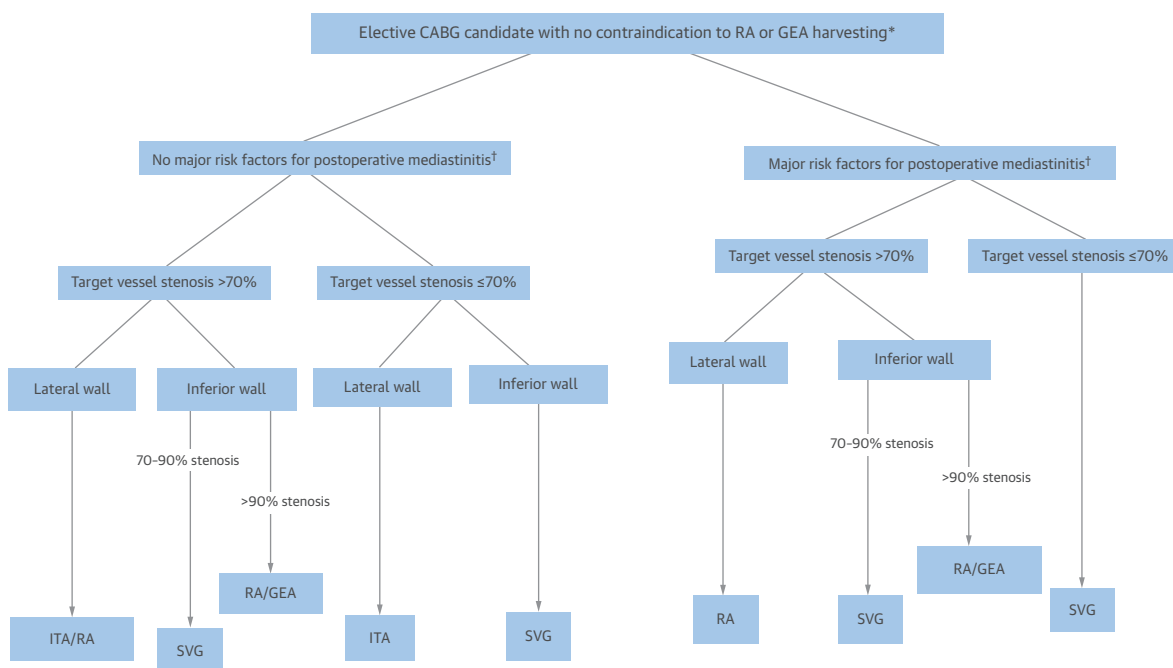
The reasons for this low use of arterial grafts are complex and multifactorial. More than a decade ago, a survey among U.K. surgeons reported that the low use of BITA grafts was because of the perceived concerns of increased technical difficulty and enhanced risk of post-operative complications (62). These concerns are heightened by the trend toward employment of surgeons by hospitals and hospital networks. In this scenario, short-term "quality metrics," including avoidance of deep sternal wound infection, may be drivers of surgical decision making because they directly affect the financial status of the employer institutions (presently, the cost of treatment of sternal complications after CABG is not reimbursed by U.S. Medicare/Medicaid, as they have

been designated "never events" by the U.S. Center for Medicare & Medicaid Services).

However, the ART trial showed that the use of a second ITA graft did not increase mortality or other major morbidity, with the exception of sternal wound complications, and added only 23 min to the duration of surgery, in comparison with the use of a single ITA graft (5). Moreover, the use of the RA, instead of the RITA, eliminates the risk of mediastinitis from the equation and can safely extend the use of a second arterial conduit to the considerable number of patients at risk of respiratory or sternal wound complications (31,34). Yet, the RA is used in not more than 12% of all CABG procedures worldwide (59,60).

The evidence presented earlier indicates that modern coronary artery surgery should entail the use of multiple arterial grafts, at least in the absence of major clinical or anatomic contraindications, and substantial efforts should be made to increase the adoption of arterial conduits during CABG procedures (**Central Illustration**). The RA and RITA should be considered similar alternatives for the anterolateral wall; the RA should be preferred in cases at risk for sternal complications and the RITA in patients

FIGURE 2   Algorithm for Graft Selection for the Second Target Vessel in Elective CABG Patients Without Contraindications to RA and GEA Harvesting

Composite and elongated grafts are not considered. *In the case of contraindications to RA or GEA harvesting, SVG should be used. †Defined as: obesity, diabetes, and severe chronic lung disease, especially in combination. CABG = coronary artery bypass graft; GEA = gastroepiploic artery; ITA = internal thoracic artery; RA = radial artery; SVG = saphenous vein graft.

without ulnar compensation. Due to its superior diameter and length, the RA permits the performance of sequential anastomoses and is able to reach even very distal vessels; however, it requires a sub-occlusive target stenosis. RITA is probably less sensitive to competitive coronary flow and more appropriate in case of less severe coronary stenosis. The skeletonized in situ GEA can be considered to graft to the distal branches of the right coronary artery when critically stenosed (>90%). The use of the great saphenous vein should be limited only to cases in which an arterial conduit is not indicated for clinical or technical reasons.

On the basis of the evidence reviewed in this study, we propose an algorithm for the choice of the second conduit in stable CABG candidates without contraindications to RA or GEA harvesting (**Figure 2**). In this algorithm, we have taken into account the most important technical, anatomic, and angiographic determinants of arterial conduit patency, as well as the clinical characteristics of the patient. Due to the major impact on post-operative mortality, special relevance has been given to minimization of the risk of post-operative mediastinitis. In view of its strong influence on graft outcome, the severity of target vessel stenosis (in relation to its location) has been the other determinant of our tree's branch points.

As arterial grafts are live conduits and tend to react much more than venous grafts to native competitive flow, a functional characterization of the target vessel lesion is of paramount importance when using an arterial revascularization strategy. In the future, the use of fractional flow reserve to plan the conduit's configuration, instead of angiography, will allow a more physiological integration of graft and coronary flow and is likely to result in enhanced long-term patency and clinical outcomes.

Less art, more science…

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