Multiarterial grafting: Why is it so hard to convince the masses of the benefits?

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We will go to the moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills.

—President John F. Kennedy, 1962

Perplexingly, the debate of single arterial grafting (SAG) versus multiple arterial grafting (MAG) and total arterial grafting (TAG) has continued. This is despite strong historical and contemporary case series, registry data, and meta-analyses that have demonstrated the benefits of bilateral internal thoracic artery and MAG strategies.[2-9]

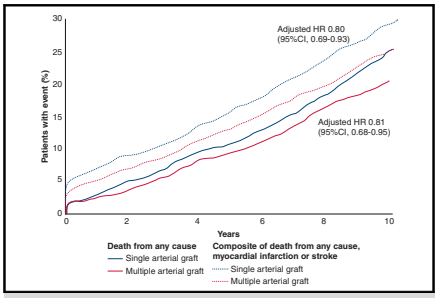
In a recent editorial, Taggart[10] (a dedicated anaortic MAG surgeon) highlighted 3 main reasons he believed that the wider surgical community has been reluctant to move away from a single left internal thoracic artery (LITA)-to-left anterior descending (LAD) and vein grafts to other targets:

1. Lack of supportive evidence from randomized trials to support a change in practice
2. Potential for an increased risk of morbidity and mortality (in particular, deep sternal wound infection)
3. Perceived increased technical complexity of using MAG strategies

However, we believe these reasons can be countered by the current evidence available.

First, the results of the largest randomized study comparing bilateral internal thoracic artery (BITA) to single internal thoracic artery (SITA), the arterial revascularization trial (ART),[11] have indicated that using an intention-to-treat basis, the ART did not demonstrate a difference in death or a composite of death, myocardial infarction, or stroke at 10 years. Although this appears to support the SAG strategy, almost 40% of participants had actually received a different therapy to the one proposed in the trial, including a 14% crossover rate from BITA to SITA. Also, 22% of the patients in the SITA group had received a radial artery (RA) and 4% had received BITA grafting. Therefore, the as-treated data are arguably more relevant, and, although lacking the robustness of randomization, the groups remained well matched. In those who had received MAG (either LITA and RA or BITA) versus SAG, MAG resulted in a significant reduction in both mortality at 10 years (18.6% vs 23.1%; adjusted hazard ratio [HR], 0.81; 95% confidence interval [CI], 0.68-0.95) and the composite endpoint (23.6% vs 28.9%; adjusted HR, 0.80; 95% CI, 0.69-0.93; Figure 1, *A*).[1]

The high crossover rate could be explained by surgeon experience and, possibly, surgeon preference. The trial authors reported a wide variation in individual surgeon



As-treated analysis of MAG versus SAG in the ART trial.[1]

CENTRAL MESSAGE

Multiple arterial grafting strategies are supported by an increasing amount of robust evidence and are safely applicable to most patients after adequate subspecialized training.

This Invited Expert Opinion provides a perspective on the following paper: *J Am Coll Cardiol.* 2019;74(18):2238-2248. https://doi.org/10.1016/j.jacc.2019.08.1043.

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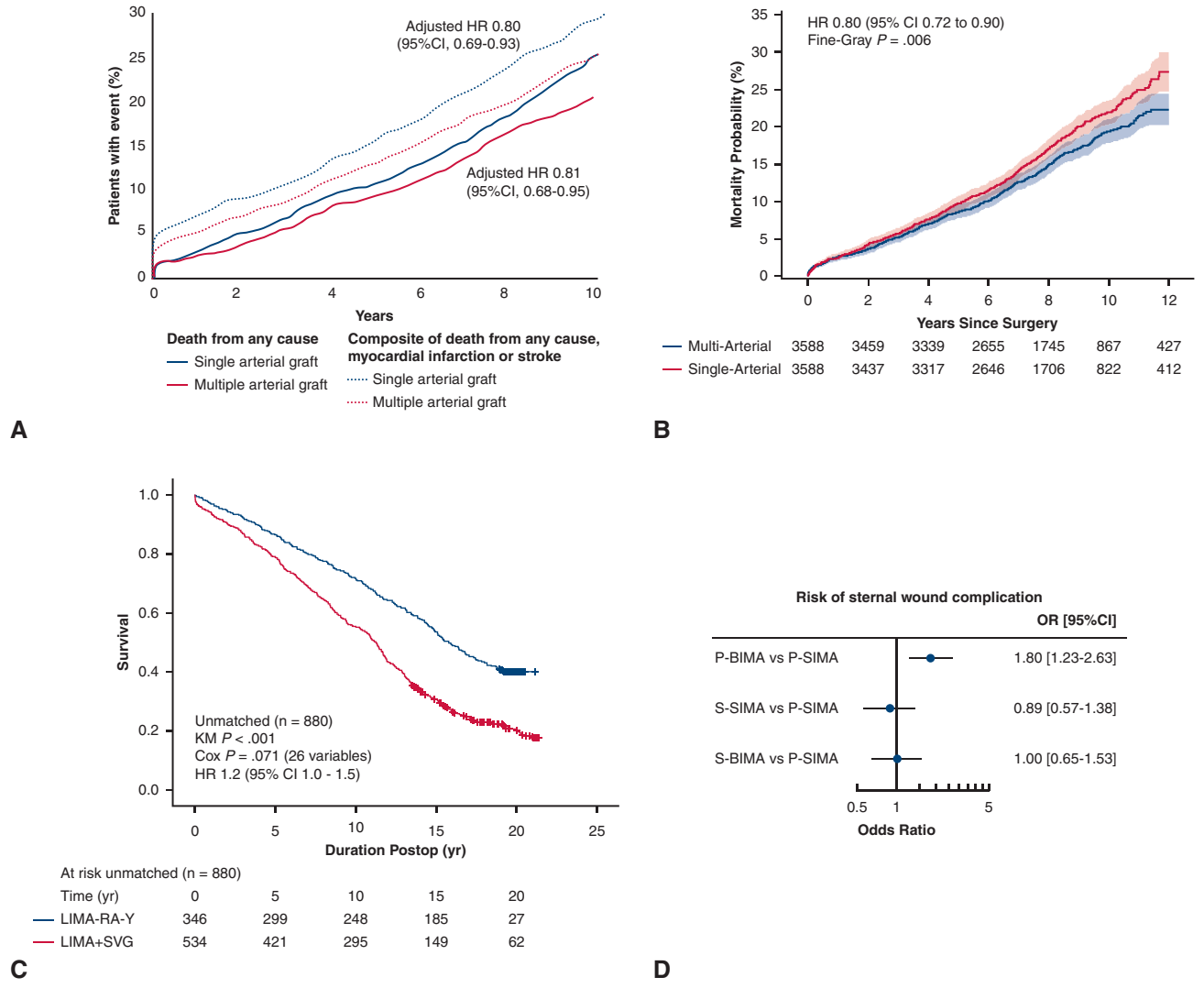

FIGURE 1. A, As-treated analysis of multiple arterial grafting (MAG) versus single arterial grafting (SAG) in the arterial revascularization trial.[1] B, Ten-year mortality of MAG versus SAG from a large registry-based series.[12] C, Survival at 21 years of left internal thoracic artery (LITA)- radial artery (*RA*) Y-graft versus LITA (originally left internal mammary artery) plus saphenous vein graft (*SVG*).[13] D, Effect of skeletonization on sternal wound infection risk during bilateral internal thoracic artery (BITA) and single internal thoracic artery (SITA) grafting.[14] *HR*, Hazard ratio; *CI*, confidence interval; *KM*, Kaplan-Meier; *LIMA*, left internal mammary artery; *OR*, odds ratio; *BIMA*, bilateral internal mammary arteries; *SIMA*, single internal mammary artery.

crossover rate (≤100%) and that the surgeons who had performed more operations in the trial appeared to have had lower crossover rates. This is not a new phenomenon—randomized trials in cardiac surgery have previously been hampered by (a lack of) surgical experience.[15,16] Should a minimum level of experience or demonstration of proficiency be required to participate in these trials or should alterative trial designs be tested[17] (eg, expertise-based randomization)? This presents a detractor for the surgical community relying solely on the existing randomized data to support a change in practice. A second large trial (ROMA [randomization of single vs multiple arterial grafts]), comparing a SITA plus a vein graft versus MAGs (a second ITA or RA to graft the main target vessel of the lateral wall), is currently underway.[18] The results are expected in 2025.

Significant observational data are also available to support the use of MAG strategies. Most recently, a large study by Chikwe and colleagues[12] compared SAG and MAG using propensity-score matching and patients from the New Jersey State Open Heart Registry (n = 26,124; 3588 matched pairs). The findings were compelling, with the use of MAG associated with lower 10-year mortality (15.1% vs 17.3%; $P = .01$; Figure 1, *B*), myocardial infarction (HR, 0.81; 95% CI, 0.69-0.95), and reintervention rate (HR, 0.81; 95% CI, 0.67-0.99). Another

recent propensity-matched study by Royse and colleagues[19] demonstrated reduced survival with the use of any saphenous vein graft (SVG). These findings are consistent with other historical and contemporary reports,[1-9,13] including a large retrospective review from the Cleveland Clinic, which showed a significant long-term survival advantage when the second ITA was deployed to a non–LAD coronary artery supplying an important amount of myocardium (determined by the vessel length, >75% terminal reach to the cardiac apex).[20]

Finally, a recent meta-analysis by Gaudino and colleagues[21] compared drug-eluting stents versus coronary artery bypass (MAG and SAG) for the primary outcome of long-term mortality and the secondary endpoints of operative mortality, perioperative stroke, and follow-up repeat revascularization. Overall, a MAG strategy was ranked as the best treatment for both primary and all secondary endpoints.

The right internal thoracic artery (RITA) is not the only second arterial graft. The RA could have some advantages over the RITA, including that the left RA can be taken simultaneously with the LITA and eliminates any increased risk of sternal wound infection related to BITA grafting. A recent network meta-analysis by Gaudino and colleagues[22] simultaneously compared the RA, RITA, and SVG as the second conduit. The use of an SVG resulted in greater long-term mortality than the 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). Additionally, no difference was found in mortality or major morbidity between the RITA and RA. The long-term superiority of a LITA/RA Y-graft configuration compared with a SAG strategy has also been reported by Royse and colleagues.[13] Using propensity-score matching, the investigators demonstrated a survival advantage at ≤21 years for the LITA/RA total arterial strategy (Cox proportional HR, 1.3; 95% CI, 1.0-1.6; $P = .038$; Figure 1, *C*).

The current European Guidelines on Myocardial Revascularization advocate a MAG strategy for all patients with a life expectancy >5 years.[23] One could argue that patients with a life expectancy <5 years should not be offered coronary artery bypass grafting (CABG) if percutaneous intervention is feasible and that all remaining patients should receive MAG. The European guidelines have also advocated an "aortic no-touch" (anaortic) approach for all patients at high risk of stroke or those with ascending aortic disease—which will include most, if not all, elderly patients. Anaortic surgery uses ITA inflow to allow for construction of composite grafts that will facilitate complete revascularization; thus, anaortic surgery lends itself well to a MAG approach.[24]

Second, the argument that the use of BITA will be associated with increased deep sternal wound infection has also not been borne out in large case series[25,26] nor from a post hoc analysis of the ART[14] when a fully skeletonized technique has been used. The latter study demonstrated the importance of skeletonization, which minimizes surgical trauma and maintains the sternal blood supply and venous drainage, by demonstrating that pedicled BITAs resulted in increased risk but not when skeletonized compared with a pedicled SITA (Figure 1, *D*).

A pragmatic approach to BITA use should be considered for morbidly obese and/or patients with poorly controlled diabetes. However, this should not preclude these patients from receiving MAG or, indeed, TAG. The use of a LITA/RA composite graft will achieve complete revascularization in most patients with a normal length arm and anything less than gross cardiomegaly. This strategy also lends itself to an anaortic approach, which has been shown to significantly reduce all-cause mortality and neurologic and other morbidity.[27]

We believe argue that it is "surgical inertia" that accounts for the vast majority of surgeons not adding a BITA graft to their patients' grafting strategy. The harvesting of a BITA must be performed sequentially, in contrast to an SVG or a RA, which can be harvested simultaneously. It would seem that the argument of increased sternal wound complications might, in part, explain the avoidance by surgeons to extend the length and complexity of an operation that otherwise might result in prolongation of life expectancy and freedom from morbidity. In reality, once surgeons have become accustomed to the refined technical skills required and free themselves from the LITA-to-vein mindset, the additional deployment of a second skeletonized ITA as a composite graft (tandem or Y) will usually not prolong the overall surgical time for >30 minutes (with no effects on the bypass or cross-clamp time). We would argue that this extra time is a valuable investment to allow the crafting of a more refined treatment regimen.

The compelling evidence of the benefits of the RA,[28] and the potential equivalence to the RITA as a second conduit,[22] also counter the concern regarding an increased risk of sternal wound infection from RITA harvest. The harvesting of the RA is straightforward and simple.

Finally, the argument of "increased complexity" as a reason to continue with SAG is perplexing. The first LITA (originally left internal mammary artery) to the LAD was performed in the 1960s,[29,30] with the landmark 1969 series by Favaloro[31] of SVG aortocoronary grafting, establishing CABG as a viable therapy for coronary artery disease. Data from the Cleveland Clinic on the benefits of

SITA in the 1980s established the LITA as the mainstay of CABG.[32] Data from the Cleveland Clinic and from Gabriele D'Annunzio University in Chieti reported by Calafiore and colleagues[33] have also highlighted the benefits of BITA over SITA grafting in the 1990s.

Coronary artery disease is the number one cause of death in the world,[34] and coronary artery surgery has remained the most common cardiac surgical procedure performed by adult cardiac surgical units and (usually) by most surgeons performing adult cardiac surgery. It has also remained a superior intervention to percutaneous coronary intervention for multivessel disease,[35,36] which contrasts with recent data on other common surgical procedures such as aortic valve replacement. However, CABG often does not receive the attention that it deserves. This has been evident at local levels, with surgeons and units seeing CABG as a commodity item, and at the wider level, with industry and conference attention given to structural heart, aortic surgery, and other aspects of cardiac surgery, exceeding that of CABG.

The paradigm shift must start from the origin of surgical training. Cardiothoracic surgery is a technically demanding surgical specialty, and advanced coronary surgery requires a versatile mindset combined with impeccable technical skills and endless dedication. To facilitate the transition to more technically demanding strategies, cardiothoracic surgeons in training should familiarize themselves from the outset with time-efficient skeletonized harvesting, manipulation of arterial conduits, construction of composite grafts, and quality assessment using transient time flowmetry.

Mirroring the transition to minimally invasive valve surgery, advanced coronary training courses and proctoring by MAG experts should be available to surgeons willing to increase their skills and develop an advanced coronary program, including MAG, TAG, and anaortic surgery.[37] Surgeons such as Dr Teresa Kieser have mastered the skeletonized technique and her lectures are well illustrated with excellent technical videos, all available online.

National society quality bundles should capture the rate of MAG, TAG, and/or anaortic strategies. Also, contraindications to their use should be documented, especially for young, nondiabetic, nonobese patients, and when aortic calcification is present.

Mack and Taggart[38] have advocated for CABG to become a subspecialty interest; however, the sheer volume of patients requiring CABG could make this an unwieldy solution. We would argue that a stepwise approach to MAG with an increased adoption of the RA and then the RITA as a graft to allow surgeons to familiarize themselves would be a good place to start. Adding a second ITA or an RA is not technically onerous.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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