Sternal wound management after bilateral internal thoracic artery grafting: a significant detail

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Provenance: This is a Guest Editorial commissioned by Section Editor Busheng Zhang, MD, PhD (Department of Cardiac Surgery, Shanghai Chest Hospital, Shanghai Jiaotong University, Shanghai, China).

Comment on: Taggart DP, Altman DG, Gray AM, *et al*. Randomized Trial of Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med 2016;375:2540-9.

Submitted Mar 16, 2017. Accepted for publication Mar 17, 2017.

doi: 10.21037/atm.2017.03.84

View this article at: http://dx.doi.org/10.21037/atm.2017.03.84

Introduction

Throughout the last 20 years, many—prospective and retrospective—observational studies have shown long-term survival benefits derived from the use of bilateral internal thoracic artery (BITA) grafts for myocardial revascularization (BITA grafting). Outcomes of large cohorts of BITA patients have been reviewed. Pooled analyses of these studies suggest that, at 10 years, there are approximately 20% fewer all-cause deaths with BITA grafting than with the standard model of myocardial revascularization, i.e., single internal thoracic artery (SITA) graft to the left anterior descending coronary artery (SITA grafting), and saphenous vein grafts (SVGs) for the remaining diseased coronary vessels (1-3). The benefits arise mainly from the higher late patency of internal thoracic artery (ITA) graft versus SVG, even for difficult subset of patients such as diabetics. In fact, the SITA graft has a 10-year rate of angiographic patency exceeding 90%, as compared with 50% for SVG, having the radial artery (RA) an intermediate performance (4-6). However, BITA grafts remain underutilized in coronary surgery, and routine use of BITA grafting is still far from coming in most worldwide institutions (7,8). Increased risk of postoperative complications, primarily sternal wound infection (SWI) and bleeding, longer duration of operation due to the time needing for the second ITA graft harvesting, as well as more complex surgical techniques limit a more extensive adoption of surgical strategies that require the simultaneous use of both ITAs. In lack of randomized evidence of long-term benefits, these issues are valid deterrents to discourage liberal BITA use (1-3,7-10).

Results at 5 years of The Arterial Revascularization Trial (ART)

On the basis of the above considerations, the interim analysis of clinical and safety outcomes at 5 years of ART that has been recently reported by Taggart and colleagues is welcome (11). Undoubtedly, these authors should be congratulated for their excellent and informative study.

This two-group, multicenter, randomized trial was initiated in 2004 and conducted in 28 cardiac surgical centers in seven countries. Its primary objective was to compare 10-year survival rates associated with BITA and SITA grafting. Secondary outcomes were the composite of death from any cause, myocardial infarction, or stroke, rate of repeat revascularization, safety outcomes (including bleeding and sternal wound complications), quality of life, costs, and cost effectiveness. Data were gathered at participating sites by means of annual telephone calls or hospital visits. Serious adverse events were reported by investigators on specific forms. Quality of life was assessed with the use of ad hoc well-codified questionnaires. The trial was sponsored by the University of Oxford. Trial

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management was provided initially by the Clinical Trials and Evaluation Unit at the Royal Brompton and Harefield NHS Foundation Trust in London and from 2014 by the Surgical Intervention Trials Unit at the University of Oxford (11-13).

Eligible patients were those with multivessel coronary disease who were scheduled to undergo coronary surgery (including patients requiring urgent surgery but not those with evolving myocardial infarction). Patients requiring only single grafts or concomitant valve surgery, as well as those with a history of coronary surgery, were excluded. Patients were randomly assigned, in a 1:1 ratio, to undergo SITA or BITA grafting.

The group that underwent SITA grafting received a SITA graft to the left anterior descending coronary artery plus supplemental saphenous vein or RA grafts to other coronary arteries. The group that underwent BITA grafting received both left and right ITA grafts to the two most important coronary arteries on the left side with supplemental saphenous vein or RA grafts to other coronary arteries (left-sided BITA grafting). Anastomosis of an ITA graft to the right coronary artery was not permitted because of concerns about inferior long-term patency. Surgeons could participate in the trial only if their experience included 50 or more operations using BITA grafts. Standard methods for anesthesia and myocardial protection were used according to local practice.

A total of 3,102 patients operated on between June 2004 and December 2007 were enrolled into the study; 1,554 patients were randomly assigned to the SITA group and 1,548 to the BITA group. The groups were well matched with respect to age, sex, race and ethnic origin, body mass index, systolic and diastolic blood pressure, smoking status, and coexisting conditions. In the SITA group, 96.1% of the patients received a SITA graft, and in the BITA group, 83.6% of the patients received BITA grafts. The rate of non-adherence to BITA graft surgery was higher than expected. Off-pump procedures were performed in 40.6% of patients. The mean number of grafts in each group was three. Medications at 5 years were well balanced between the two groups.

A total of 159 (5.1%) participants had unknown vital status at 5 years because of loss to follow-up or withdrawal from the trial. At 5 years of follow-up, there were 134 deaths (8.7%) in the BITA group and 130 deaths (8.4%) in the SITA group [hazard ratio (HR) with the SITA group as the control group throughout, 1.04; 95% confidence interval (CI), 0.81–1.32; P=0.77]. Results were similar after adjustment for age, sex, diabetes status, and ejection fraction (HR, 1.03; 95% CI, 0.81–1.32; P=0.80). For the composite of death from any cause, myocardial infarction, or stroke, there were 189 (12.2%) in the BITA group and 198 events (12.7%) in the SITA group (HR, 0.96; 95% CI, 0.79–1.17; P=0.69). Approximately half the deaths were classified as being cardiovascular, with a HR that was similar to that in the analysis of all-cause mortality. Subgroup analyses did not show any evidence of significant interactions.

The incidence of sternal wound reconstruction was 1.9% in the BITA group, as compared with 0.6% in the SITA group (relative risk, 2.91; 95% CI, 1.42–5.95; P=0.002), and all these events occurred in the first year after surgery. Sternal wound complications occurred in approximately twice as many patients in the BITA group as in the SITA group, whereas the rates of major bleeding events and the need for any repeat revascularization were similar in the two groups (just over 6% in each group). Angina status at 5 years showed similar results in the two groups, with approximately 70% of the patients who responded to the questionnaire reporting no chest pain. Mean quality-of-life scores at 5 years showed no between group differences for patients who provided data.

In a nutshell, in the ART, patients undergoing coronary surgery were randomly assigned to receive either SITA or BITA grafting. At 5 years of follow-up, there were no significant differences in clinical outcomes between the two groups. There was some early excess of sternal wound complications in the BITA group. Ten year follow-up is ongoing.

The absence of any midterm benefit from BITA over SITA grafting might have several explanations.

The rate of SVG failure within 5 years may not be high enough to have an obvious adverse clinical effect. There may not be a direct association between SVG failure and clinical events. Variation in surgeon's experience may have reduced the effectiveness of BITA grafting. There may be little difference between the effects of the two techniques on clinical outcomes, owing to better long-term SVG patency, asymptomatic SVG failure, and improved medical therapy.

According to Taggart and colleagues, the following limitations of the trial have to be considered: (I) this planned interim analysis of an ongoing trial does not provide definitive long-term evidence regarding the comparison between SITA and BITA grafting (which is still awaited); (II) at 5 years, the trial has less power to detect a difference in outcomes than is likely to be the case at 10 years, with consequent wide CI for

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the primary outcome; (III) more patients who were randomly assigned to BITA than to SITA grafting did not receive the assigned procedure (16.4% *vs.* 3.9%), and some expected loss to follow-up may reduce the power of the trial.

Comment

While I totally agree with the critical analysis by the authors, I have some comments in addition.

Generally, the standard model of myocardial revascularization does not provide the use of RA, but of SVGs alone in addition to the SITA graft to the left anterior descending coronary artery. In the ART, instead, some SITA patients have received a RA graft as well. Consequently, for these patients, the comparison was between surgery using two arterial grafts, ITA plus RA, and surgery using two arterial grafts, right ITA plus left ITA! (14-16).

In the ART, surgeons could adopt a variety of configurations for BITA grafting. Generally, BITA grafts are used in two configurations: (I) both ITAs retain their connection to the corresponding subclavian artery (BITA *in situ*, or double source configuration); (II) the right ITA is taken down and used as a free graft from the *in situ* left ITA (BITA Y-graft, or single source configuration). Although to date there is no evidence of superiority of the one configuration over the other (and the choice either of the one or the other configuration depends on the site of target coronary vessels, the length of BITA conduits, and ultimately the surgeon's preference), this aspect could have any impact on efficacy of revascularization.

There was a mean number of three coronary grafts per patient. It is not clear for me whether this number was the mean number of coronary anastomoses per patient as well. If yes, there could be some issues about the completeness of revascularization. If not, how many sequential anastomoses were performed?

When the analysis of the results at 10 years will be performed, these three points should be taken into account.

Indications to the use of off-pump surgery, important issues such as the use of the "skeletonized", "semi-skeletonized", or "pedicled" technique for ITA harvesting, and the relationship between these two aspects and the rate of sternal wound complications after surgery were addressed partially, in post hoc nonrandomized analyses (16-18). Actually, although pre-specified subgroup analyses were performed on the basis of surgery type, RA grafting, and number of grafts, I believe that the above reported specific issues remain unresolved.

Last but not least, insufficient data are recorded as the perioperative management of sternal wounds and the postoperative management of sternal wound complications.

In conclusion, I think that the use of BITA grafting is really a more complex technique that requires for surgeons specific skills and sufficient expertise, which are hardly obtained after only 50 procedures. Besides, a multidisciplinary, preoperative, intraoperative, and postoperative approach is needed to prevent and manage successfully sternal wound complications. Throughout the years, each centre should develop a specific program to control sternal complications after sternotomy. The program should be based both on the experience and expertise of the surgeons and the evidence of the literature (19). A definite program of prevention and treatment of SWIs after BITA grafting has been created and adopted at the Cardiovascular Department of the University Hospital of Trieste, Italy (*Table 1*) (9,20,21).

I think that Dr. David P. Taggart, his colleagues, and the ART Investigators should be congratulated for their excellent study.

Table 1 Perioperative patient management, surgical techniques, and sternal wound care at the Cardiovascular Department of the University Hospital of Trieste, Italy*

Measure	Trieste series
No. of patients	3,470
Study period	1999–2016 (18 years)
Selection criteria of the patients	All patients having multivessel coronary disease who require left-sided myocardial revascularization are candidates for BITA grafting; the sole exceptions being the cases in which one or both ITAs are unsuitable as coronary grafts, when there is an unexpected operative finding of severe cardiac dysfunction, or when rapid worsening of haemodynamics due to ischaemia requires immediate institution of cardiopulmonary bypass. Actually, there have been even some cases where a second ITA graft was harvested during cardiopulmonary bypass

Table 1 *(continued)*

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Table 1 *(continued)*

Measure	Trieste series
Rate of BITA use (%)	73.9 (3,470/4,694)
Use of prophylactic antibiotics	A first-generation cephalosporin (cefazolin) is chosen. Vancomycin is used if there is a severe allergy to β-lactam antibiotics, or in the event of mediastinal re-exploration; in the last case, the addition of an aminoglycoside is considered
Skin preparation	A careful skin preparation is performed with alcoholic iodine solution. Chlorhexidine-alcohol is used only for patients with iodine allergy. A microbial sealant that immobilizes bacteria is adopted
ITA-harvesting technique	Both ITAs are harvested as skeletonized conduits with low-intensity cautery and bipolar coagulation forceps, extending distally just to include either the superior epigastric or the musculophrenic artery. In the last few years, actually, there has been a trend to save at least one bifurcation and use Y-grafts
Use of off-pump and beating heart on-pump techniques	Off-pump and beating heart on-pump techniques are adopted only in the presence of a diffusely atherosclerotic ascending aorta (by intraoperative epiaortic scan)
Sternal closure	Standard single-loop sternal wiring technique has been used as a sternal closure method until 2009. Since 2010, double-loop sternal wiring technique is being adopted systematically. Bone wax is forbidden. Neither platelet gel nor topical antibiotics are used. Skin staples are used
Wound care	Traditional gauze dressings are applied immediately after the surgery to closed surgical incisions. The incision site is cleaned and dried to ensure proper fixation of the dressings. Patients are monitored daily for symptoms of wound infection. Wounds are inspected immediately after removal of the dressings (postoperative day 2), early before hospital discharge, and at postoperative day 30
Management of hyperglycemia	All diabetic patients are treated during operation and then in intensive care unit with a continuous intravenous insulin infusion in order to maintain serum glucose <180–200 mg/dL
Surgical strategy	Both ITAs are used as *in situ* grafts when possible (based on the double-source concept). The right ITA was preferentially directed to the left anterior descending coronary artery, and the left ITA to the posterolateral cardiac wall. Sometimes, the right ITA is taken down and used as a free graft from either the *in situ* left ITA (Y-graft) or (rarely) the proximal (aortic) end of a SVG. The anteaortic crossover right ITA bypass graft is protected by means of a pedicled flap taken from the thymic remnants. Additional coronary bypasses, usually for the right coronary artery, are performed with SVGs
Post-discharge surveillance of the surgical wounds	Post-discharge surveillance of the surgical wounds is performed for every patient in a specifically dedicated surgical outpatient unit. All the patients with a surgical site complication are referred to this outpatient unit, at any time after hospital discharge. All the data are recorded in a computerized data registry
Treatment	The negative pressure wound therapy is adopted for every patient with deep SWI and many patients with superficial SWI. When necessary, the surgical debridement is performed as soon as possible
Monitoring	A hospital committee for the control of nosocomial infections has been created to monitor any surgical infection, SWI in particular. A risk factors analysis for deep SWI, which complicates BITA grafting has been performed and a deep SWI risk score based on the results of this analysis (the Gatti score) has been generated

*, Ref. (9,20,21). BITA, bilateral internal thoracic artery; ITA, internal thoracic artery; SVG, saphenous vein graft; SWI, sternal wound infection.

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Gatti G. Sternal wound management after bilateral internal thoracic artery grafting: a significant detail. Ann Transl Med 2017;5(12):262. doi: 10.21037/atm.2017.03.84

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