Coronary Artery Bypass Grafting with Arterial Conduits in the Elderly
Where Do We Stand?

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Summary
Although improved long-term outcomes obtained with the use of arterial grafts for coronary revascularization in comparison with the traditional association of a single arterial and saphenous vein grafts have been demonstrated in the overall population, the efficacy of this newer technique in the elderly is difficult to prove because their shorter life expectancy due to advanced heart disease, associated with severe comorbidities. Moreover, more widespread use of this technique is limited by the concerns on the potential morbidity, particularly the longer time required to perform the operation and the possibility of deep sternal wound infection in case of bilateral internal thoracic artery harvesting due to the decreased blood supply to the sternum and surrounding tissues.

The review of the recent literature indicates that the use of bilateral internal thoracic arteries in very elderly patients should not be considered routinely. It seems reasonable to avoid it in octogenarians in the presence of well-known predictors of sternal complications such as diabetes, morbid obesity, and severe chronic lung disease.

There is also still controversy about the superiority of the radial artery over the saphenous vein graft as a second or third conduit for surgical myocardial revascularization, although the majority of recent studies seem to support more liberal use of the radial artery as second arterial conduit in the elderly. Although a clinical benefit of arterial graft revascularization cannot be formally excluded for elderly patients, the increased complexity of this technique suggests that careful clinical judgment is necessary to select grafts for individual patients.

Key words: Coronary artery disease, Old patients, Arterial grafts

Nowadays a growing number of patients are older at the time of coronary artery bypass grafting (CABG) and present with a clinical history characterized by more comorbidities than in the past. However, despite the increasing proportions of elderly patients with a worse risk profile for elective CABG, mortality in elderly patients over recent decades has dramatically declined. In fact, recent studies on elderly patients operated with CABG reported a 30-day mortality rate ranging between 3.7 and 16.8%, a 1-year mortality between 8% and 10.8% and a 5-year mortality ranging from 28.4% to 31%.

It is well recognized that octogenarians have a higher risk of post-operative complications, require greater clinical and economic resources, and have worse but acceptable short and long-term survival in comparison with younger patients. However, improvements in technical management, particularly the development of innovative extracorporeal circulatory systems, the use of off-pump CABG and the increased use of pedicled arterial conduits have been proven effective in improving outcomes, although they have not completely eliminated the morbidity in this high-risk population.

Although improved long-term outcomes obtained with the use of arterial grafts for coronary revascularization in comparison with the traditional association of a single arterial and saphenous vein grafts have been demonstrated in the overall population, the efficacy of this newer technique in the elderly remains difficult to verify because their shorter life expectancy due to advanced heart disease, associated with severe comorbidities. Moreover more widespread use of this technique is limited by concerns on the potential morbidity, particularly the longer time required to perform the operation and the possibility of deep sternal wound infection in case of bilateral internal thoracic artery harvesting due to the de-
The aim of this study was to review the recent literature reporting the results of coronary revascularization by CABG obtained with arterial conduits in elderly patients.

**Bilateral Internal Thoracic Artery Revascularization in the Elderly**

The choice of strategy for surgical treatment in elderly patients is a controversial issue. It is unclear whether the use of bilateral internal thoracic artery (BITA) grafts is associated with better outcomes than the traditional use of single internal thoracic artery (SITA). Several studies have been published reporting better outcomes after use of BITA grafts, although these studies were not specifically designed to study the efficacy of this technique in elderly patients. In fact, few studies investigating the feasibility of using BITA grafts in an aged population have been reported recently.

A recent systematic review and meta-analysis on the feasibility and efficacy of coronary revascularization with BITA grafts in the elderly has been published. This study showed that in an aged population, the incidence of deep sternal wound infection was 2.4% in the BITA cohort versus 1.3% in patients who received a SITA graft, confirming that BITA harvesting carries a higher risk of deep sternal wound infection. Although perioperative mortality, the incidence of myocardial infarction, and postoperative respiratory failure were comparable in both cohorts, the stroke rate was lower in the BITA cohort (1.1% versus 1.6%), although without a statistically significant benefit. Moreover it remains unclear whether BITA is the best choice for elderly patients in the long term as the only randomized controlled trial to date evaluating long-term survival (the Arterial Revascularization Trial) is still ongoing. This trial was designed with the aim of confirming potential improved survival rates with BITA grafting. One-year results showed that BITA grafting is routinely feasible although only 10-year results will determine whether BITA grafting gives better survival rates and decreased need for repeat revascularization.

Another reason why the advantages of using BITA grafts in extremely elderly patients are not sufficiently recognized is that older age patients have a relatively short life expectancy which leads to a poor prognosis in the follow-up after cardiac surgery. Kieser et al. showed that use of BITA grafts has not demonstrated to be beneficial in patients aged > 70 years. Similarly, Benedetto, et al. showed that BITA provided a survival benefit related to patient age at the time of CABG, although this benefit progressively declined with age, with no evidence for longer survival after BITA for patients older than 69 years. The authors speculated that the risk of death from noncardiac causes due to increasing age is responsible for the shorter life expectancy of these patients.

Gatti, et al. reported the results of a retrospective no-propensity matched study designed to investigate potential differences in terms of early mortality and perioperative complications after BITA grafting in octogenarians in comparison with standard revascularization. During the follow-up, the authors reported no significant differences between the two groups of patients either in overall survival or in freedom from cardiac and cerebrovascular death. Statistical analysis showed that diabetics, chronic dialysis and congestive heart failure were predictors of decreased overall survival, and also predictors of increased cardiac and cerebrovascular death. They concluded that left-sided BITA grafting may be used routinely in the octogenarians without any increase of hospital mortality and perioperative complications other than sternal wound infection. However, they confirmed no demonstrable benefits in terms of late outcomes.

Mohammadi, et al. published a study on early and long-term results of BITA grafting in a wide series of patients undergoing CABG. They found that advanced age, chronic obstructive pulmonary disease, and insulin-treated diabetes mellitus have a negative impact on late survival among patients with BITA grafts. Previously, in another study, they performed a prospective follow-up study of 1277 BITA patients and 9566 SITA patients. BITA grafting was associated with a significantly lower risk of early mortality, although this survival benefit seemed to be lost in patients older than 60 years of age.

Hashimoto, et al. investigated differences in the outcome between use of BITA and SITA grafts in octogenarians undergoing isolated CABG. They found that early outcomes were similar, including hospital death or deep sternal infection. Although the rate of MACCE was lower in the BITA group than in the SITA group, there was no significant difference in overall survival between two groups at 5 years. The explanation was that mean age of patients in this study was 82.7 ± 2.6 years, and thus the life expectancy in this population was not long enough to show a significant difference in survival between the two groups. However, lower rates of MACCE and cardiac events after coronary revascularization permitted lower rates of hospitalization and lower healthcare costs.

On the other hand, other studies showed better results with the use of BITA. Kinoshita, et al. and Medalion, et al. reported that use of BITA grafts improved late survival and freedom from cardiac events in patients aged > 70 years and > 65 years, respectively.

In spite of the fact that advantages of using BITA grafts in elderly patients are not sufficiently recognized probably because of their relatively short life expectancy, a limitation of these studies is that the authors did not report average life expectancy of the similar elderly control population in respective study regions in order to confirm the benefit in patient cohorts with similar age, operated on CABG with multiple arterial grafting. However, recently some studies are starting to report long-term outcomes of elderly patients after CABG. Pettinari, et al. have recently published the results of their study designed to compare outcomes in propensity score-matched patients aged 70 years or older using a BITA with patients using SITA graft. After the propensity score matching, 892 patients per group were selected. Survival at 3 months was similar in both groups but at 10 years was 38.9% in the SITA group and 57.5% in the BITA group (P = 0.02). The rates of stroke, myocardial infarction, and sternal wound complications were all similar between the SITA
and BITA groups. The authors concluded that the use of BITA grafting in elderly patients improves the 10-year survival rate, with similar postoperative morbidity. Similarly, Medalion, et al.43) reported that in a population of patients aged 70 years or more, ten-year survival (mean follow-up 8.17 ± 4.45 years) in the internal thoracic artery + saphenous vein graft group was significantly lower than in the bilateral internal thoracic artery grafting and internal thoracic artery + radial artery groups, further supporting the use of arterial grafts in elderly patients. Quality of life of elderly patients was not investigated in the majority of these studies. However, improvement in quality of life had previously been demonstrated in elderly patients receiving arterial grafts CABG.44) Berreklouw and colleagues45) reported that 47.5% of patients with BITA grafts versus 35.4% of patients with SITA grafts had an ischemic event-free existence after 13 years (P < 0.001). Muneretto, et al.,46) in a prospective randomized group of 188 patients older than 70 years randomized to either total arterial grafting or SITA grafting, found that recurrent angina occurred in 11.1% of the SITA/vein group versus 2.1% of the total arterial group.

Table I summarizes the results of the recent literature on BITA grafting in elderly patients.

### Radial Artery in the Elderly

Controversy still exists about the superiority of the radial artery (RA) over the saphenous vein graft (SVG) as a second conduit for surgical myocardial revascularization, particularly in the elderly. Several studies have reported a benefit derived from a revascularization obtained with left internal thoracic artery (LITA) + RA grafts in terms of intermediate and late survival after CABG, when compared with the conventional LITA + SVG approach for multivessel coronary revascularization.47-49) However, the limitation of these studies was that their design included relatively younger patients receiving RA as a second conduit. Surgeons are still often hesitant to use RA grafts in elderly patients, because of the perceived unfavorable risk/benefit ratio in this age group.

Muneretto, et al.,42,43) published the results of a prospective trial enrolling 160 patients older than 70 years randomized to the use of RA or SVG as a second conduit. The RA group reported better results in terms of angiographic patency and lower recurrence of angina after a mean follow-up of 16 months. The limitation of this study was that the authors did not assess the impact of RA on late death because of the short follow-up and the small sample size of the study population.

In a prospective randomized trial, Hayward and Buxton40) found no difference in terms of patency rate and late survival in patients older than 70 years receiving RA or SVG as a second conduit. The RA group reported better results in terms of angiographic patency and lower recurrence of angina after a mean follow-up of 16 months. The limitation of this study was that the authors did not assess the impact of RA on late death because of the short follow-up and the small sample size of the study population.

In a prospective randomized trial, Hayward and Buxton40) found no difference in terms of patency rate and late survival in patients older than 70 years receiving RA or SVG as a second conduit for CABG. Habib, et al.40,41) published data supporting the widespread use of the RA as a second arterial conduit in the elderly, irrespective of sex. Their data showed a clinically significant improvement in intermediate (1-5 years) and late (> 5 years) survival with multiple arterial grafts in female and male patients and in the elderly, for both the septuagenarian and octogenarian subgroups. The authors found that the choice of the RA as the second arterial conduit seems to be asso-
associated with low associated perioperative risks, particularly the potential for sternal healing complications due to BITA harvesting. These results were finally confirmed by Shi, et al., in a multicenter study enrolling 8 centers. After propensity score matching, among patients 70 years and older (327 matched pairs), despite similar 30-day mortality, patients who received RA exhibited improved survival at 15 years in comparison to those who received SVG.

On the other hand, Benedetto, et al., conducted a recent study aimed to investigate any survival benefit from use of the RA in comparison to SVG, stratified to patients’ age. After propensity matching, the sample size consisted of 809 matched pairs. Survival was comparable at 1, 3, 5, and 10 years between groups. RA use was associated with a lower risk for late death (hazard ratio [HR], 0.75; 95% confidence interval [CI], 0.57-0.98; \( P = 0.03 \)). Significantly, survival advantage from RA was maximum in patients 60 years and younger and gradually declined with increasing age, until it was no longer present in patients older than 70 years. The authors concluded that the use of the RA as a second conduit improves all-cause mortality in patients undergoing primary isolated CABG up to the age of 70 years and that the survival benefit is lost in a more elderly population.

Table II summarizes the results of the recent literature on RA grafting in elderly patients.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>Patients No.</th>
<th>Mean age</th>
<th>Early mortality (%), FU (years)</th>
<th>Late survival, MACCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muneretto(^{42})</td>
<td>Prospective randomized</td>
<td>RA ( n = 80 )</td>
<td>&gt; 70</td>
<td>3.8 versus 5, ( P = NS )</td>
<td>16 ± 3 months</td>
</tr>
<tr>
<td>Hayward(^{43})</td>
<td>Prospective randomized</td>
<td>RA ( n = 113 )</td>
<td>&gt; 70</td>
<td>5.5</td>
<td>( P = 0.98 )</td>
</tr>
<tr>
<td>Habib(^{44})</td>
<td>Retrospective</td>
<td>RA ( n = 607 )</td>
<td>75.3</td>
<td>2.3 versus 2.3, ( P = NS )</td>
<td>70.9% versus 50.5%</td>
</tr>
<tr>
<td>Shi(^{46})</td>
<td>Retrospective</td>
<td>RA ( n = 3320 )</td>
<td>68 ± 9.7</td>
<td>1.5 versus 3.2, ( P' = 0.004 )</td>
<td>51 ± 1.1</td>
</tr>
<tr>
<td>Benedetto(^{47})</td>
<td>Retrospective</td>
<td>RA ( n = 936 )</td>
<td>65 ± 10</td>
<td>2.0 versus 1.9, ( P = NS )</td>
<td>6.4 ± 4</td>
</tr>
</tbody>
</table>

SVG indicates saphenous vein graft; RA, radial artery; FU, follow-up; and MACCE, major adverse cerebral cardiovascular events.

On the other hand the use of BITA grafting enhances technical options that may reduce or avoid aortic manipulation in the presence of an atherosclerotic ascending aorta. The use of the no-touch aorta technique has been demonstrated to reduce the incidence of stroke, especially in the hostile aorta. Moreover, selective use of off-pump CABG (OPCABG) and minimized extracorporeal circulation systems in this high-risk population can reduce multi-organ morbidity and post-operative systemic inflammatory response syndrome. However a retrospective analysis of the results of the Australian and New Zealand Society of Cardiac and Thoracic Surgeons’ (ANZSCTS) database for elderly patients undergoing isolated CABG surgery compared the on-pump coronary artery bypass (ONCAB) \( n = 11676 \) with OPCABG \( n = 1021 \) technique. The authors showed that high-risk patients were more prevalent in the ONCAB group. Moreover OPCAB patients received fewer distal anastomoses than ONCAB patients and OPCAB did not offer a significant advantage over ONCAB with regards to 30-day mortality, stroke, or long-term survival. Although late better outcomes of BITA grafting in the elderly are not completely confirmed, the reported lower rates of MACCE and cardiac events after coronary revascularization with arterial grafts could lead to lower rates of re-hospitalization and lower healthcare costs, which are beneficial in the aging population.

However, the choice of the best option in coronary revascularization of patients aged 80 years or older must also take into account the impact of percutaneous coronary intervention (PCI), which has been shown to be associated with good early and intermediate results in octogenarians. Recent 2014 ESC/EACTS Guidelines on myocardial revascularization made no recommendations for the treatment of coronary artery disease in this subset of high risk patients. Moreover, there are few data in the literature because meta-analyses have rarely been performed on the elderly population, and clinical prospective randomized trials or multicenter studies did not generally study elderly patients, or included only a small proportion of these patients. The evidence for the optimal revascularization procedure in octogenarians is thus reported mainly from observational studies, mostly single-center series comparing PCI and CABG with SITA grafting.

It remains a matter of debate whether the use of bi-
lateral IMA further displays the superiority of CABG over PCI, because no study has been specifically designed with this aim in the elderly population. Recently, Raja, et al.66 reported the results of their retrospective single center study comparing SITA grafting or multiple arterial grafting versus PCI with DES/BMS in a large population with a mean age of 65 years. Propensity score adjusted analysis was performed to investigate the potential survival advantage of multiple arterial grafting over PCI. At a mean follow-up of 4.9 years, in this real-world study multiple arterial grafting improved late survival and provided greater freedom from repeat revascularization than conventional CABG with SITA and PCI with DES or BMS. Similarly, Habib, et al.67 reported that multiarterial surgical revascularization, compared with either BMS-PCI or DES-PCI, resulted in substantially enhanced death and reintervention-free survival, but in this study too, the mean population age was younger than 70 years. So, despite these favorable outcomes, the clinical advantage reported by multiple arterial grafting over PCI cannot be extrapolated to elderly patients.

Hybrid revascularization obtained with minimally invasive LITA grafting on the LAD and PCI/stenting of the other arteries during hospitalization may be a valuable option for elderly patients because it has been demonstrated that it makes the procedure less invasive, reduces short-term mortality, and achieves excellent long-term results, in comparison with conventional CABG.68,69 However the evaluation of this method raises the question of whether it is preferable to pursue less invasive surgical revascularization, at the cost of a partial revascularization, rather than complete grafting with arterial conduits in these elderly patients. No comparison study has been published with this aim so it is only possible to partially extrapolate to the elderly the results obtained from studies on unselected patient populations.

The ARTS-II trial reported that survival in patients with multivessel disease with partial revascularization did not differ among patients who received PCI and CABG. However, PCI patients reported a worse rate of MACE (mostly due to repeat revascularization) and a significantly lower survival, particularly in the subgroup of PCI patients with higher SYNTAX tertile.56 The limitation of this trial was that it did not include elderly patients. On the other hand, Hannan et al. demonstrated in a large-scale analysis (n = 21,945), that patients who received a partial revascularization, completed with PCI, had a worse survival rate than those with complete revascularization. These results have not been confirmed in patients older than 80 years.69 On the other hand, other authors56 reported that complete revascularization did not improve long-term survival for either CABG or DES treatment in patients affected by multi-vessel disease.

These mixed results do not give a clear picture. Physicians should evaluate sensibly a tailored approach combined with PCI, is a good alternative if the goal is to improve the quality of life and exertional capacity, without focusing on long-term results.

Conclusion
These mixed results on early morbidity and long-term survival, indicate that the use of BITA grafting in very elderly patients should not be considered routinely. It seems reasonable to avoid BITA in octogenarians in the presence of the well-known predictors of sternal complications such as diabetes, morbid obesity, and severe chronic lung disease.

There is also still controversy about the superiority of the RA over the SVG as a second or third conduit for surgical myocardial revascularization, although the majority of recent studies seem to support more liberal use of the RA as a second arterial conduit in the elderly.

Although a clinical benefit of arterial graft revascularization cannot be formally excluded for elderly patients, the increased complexity of this technique suggests that careful clinical judgment is necessary to select grafts for individual patients, until well-powered randomized controlled trials are designed with the aim of evaluating functional and symptom outcomes as a measurement of treatment effect (e.g., QOL, independent living scores, angina burden) in addition to the usual hard endpoints such as mortality or myocardial infarction.

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Conflict of interest: None declared

References


