Long-term clinical outcome and graft patency of radial artery and saphenous vein grafts in multiple arterial revascularization

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ABSTRACT

Objective: The long-term benefits of multiple arterial revascularization (MAR) in coronary artery bypass grafting remain uncertain. The aim of this study was to investigate the clinical outcome, graft patency, and need for subsequent target revascularization of radial artery (RA) versus saphenous vein graft in patients undergoing MAR in both patient- and graft-specific analyses.

Methods: Between 2001 and 2016, we followed 1654 patients over a median of 7.4 years in a prospective, longitudinal study. Major adverse cardiac and cerebrovascular events, graft patency, and need for revascularization were assessed through clinical manifestation, coronary angiography, or coronary computed tomography and analyzed with propensity score–adjusted Cox regression, general estimating equation, and competing risk models.

Results: Bilateral internal thoracic artery (BITA) grafting was performed in 910 patients (55.0%), and 744 patients (45.0%) received a left internal thoracic artery graft together with at least 1 RA graft. Patients receiving BITA, of whom 187 received an additional RA, showed improved survival (hazard ratio, 0.57; 95% confidence interval [CI], 0.38–0.86; P = .009), major adverse cardiac and cerebrovascular event–free survival (hazard ratio, 0.33; 95% CI, 0.23–0.46; P < .001), and lower need for repeat revascularization (subhazard ratio, 0.59; 95% CI, 0.39–0.90; P = .015). In a subgroup of 512 patients, comparing 419 RA with 487 saphenous vein grafts, RA grafting showed a lower risk for graft occlusion (odds ratio, 0.59; 95% CI, 0.47–0.73; P < .001) and target revascularization (subhazard ratio, 0.58; 95% CI, 0.43–0.78; P < .001).

Conclusions: MAR with BITA and RA grafting revealed to be the recommended strategy in coronary artery bypass grafting to achieve long-term beneficial results. The use of saphenous vein graft showed less favorable outcomes regarding target-vessel revascularization.

Perspective

MAR with BITA and RA grafting revealed to be the recommended strategy in CABG to achieve long-term beneficial results. The use of SVG showed less-favorable outcomes regarding long-term patency and the need for target-vessel revascularization.

See Commentaries on pages 451 and 453.
The potential advantages of CABG surgery with more frequent use of arterial grafts has been reported while simultaneously dramatic improvements in percutaneous stent technologies (percutaneous coronary intervention [PCI]) have led to a substantial proportion of patients known to benefit from surgery being treated with stents. Moreover, PCI has become the mainstay for the treatment of CABG-related graft failure.

In addition, computed tomography angiography (CTA) technology has evolved to be a valuable, less-invasive tool to investigate both native coronary arteries and graft patency among patients with or without previous revascularization.

Most outcome studies after MAR evaluate crude survival with relatively short-term follow-up—and in the light of PCI treatment of graft failure—may only imprecisely reflect outcome and graft patency among patients undergoing MAR. Repeat revascularization after CABG also may occur in de novo lesions, and CABG-related graft occlusion may not necessarily mandate repeat revascularization. In contrast, a major adverse cardiac and cerebrovascular event (MACCE) may not automatically be related to graft failure. To answer these questions, this longitudinal follow-up study was implemented among patients undergoing MAR.

Therefore, the aim of this study was to investigate the clinical outcome, graft patency, and need for subsequent target revascularization of RA and SVG among patients undergoing MAR in a large prospective follow-up study. Because of its clinical importance, we also investigated BITA versus LITA grafting in this study.

**METHODS**

**Study Population**

In this prospective longitudinal outcome study, 1654 consecutive patients who underwent first, nonemergent MAR at the Innsbruck Medical University were followed for a median of 7.4 years between August 2001 and August 2016 (Table 1). Inclusion, exclusion criteria, and endpoint definitions for this study have been described previously. All patients gave informed consent, and permission for this study was obtained from the local institutional review board (approval: 21.2.2001, UN4232). In addition, we participate in the RADIAL (Radial Artery Database International ALliance) conducting research related to the RA.

**Diagnostic Procedures and Endpoint Definitions**

Patient data including baseline characteristics such as obesity, hypertension, diabetes, or smoking habits as well as operative data were prospectively collected in full accordance with the standards of the Quality Control Working Group of the Austrian Society of Cardiothoracic Surgery. Survival, MACCE-free survival, freedom from angina, and repeat revascularization were routinely obtained in 4- to 5-year intervals. MACCes were defined as combined endpoints including acute myocardial infarction (AMI), stroke, cardiac-related death, and repeat revascularization. Coronary angiography (CA) reports in patients who underwent repeated cardiac catheterization or CTA were obtained and evaluated. In case of death, the autopsy reports (if available) were obtained to discriminate cardiac from noncardiac death causes. Late death was supplemented from routine anniversary follow-up supplemented with the Social Security Death Index.

CA and CTA procedures during follow-up were reviewed and evaluated by board-certified cardiologists/radiologists (Table 2). CTA was performed using a 64-slice CT system of multiple slices according to international standardized scan parameters. An iodine contrast agent was injected intravenously and triggered into arterial phase to evaluate bypass graft patency on axial images and multiplanar reformations. In patients with repeated coronary diagnostic procedures during follow-up, only the first examination after CABG was selected.
for graft patency analysis. When CTA was followed by a confirming CA investigation, the result was taken from the CA examination. The CA/CTA findings were categorized according to Khot and colleagues as (1) occluded, (2) severely diseased (≥70% stenosis or string sign), or (3) patent.

Graft-specific information included the native target-vessel stenosis, graft type (LITA, right internal thoracic artery [RITA], RA, SVG) and information as whether the target-vessel had been subjected to previous PCI. Additional information included the proximal graft configuration—either in situ grafting or y-configurations to other arterial or venous conduits.

In patients with sequential grafting, each graft anastomosis and corresponding target-vessel was analyzed as separate graft. In addition, therapeutic interventions of each graft target—either by successful or attempted PCI or repeat CABG—were documented to evaluate the need for target-vessel revascularization.

### Statistical Analysis

Categorical variables are presented in percentages and corresponding numbers. Continuous variables are summarized with means and standard deviations. Dichotomous variables are reported as n (%). LITA, Left internal thoracic artery; RA, radial artery; SVG, saphenous vein graft; BITA, bilateral internal thoracic artery; CAD, coronary artery disease; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; EuroSCORE, European System for Cardiac Operative Risk Evaluation.

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**TABLE 1. Preoperative characteristics of patients receiving first, nonemergent MAR by the use of BITA and LITA + RA from 2001 to 2016**

<table>
<thead>
<tr>
<th></th>
<th>LITA + RA ± SVG (n = 744 patients)</th>
<th>BITA ± RA ± SVG (n = 910 patients)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>638 (85.8%)</td>
<td>805 (88.5%)</td>
<td>.1</td>
</tr>
<tr>
<td>Age, y</td>
<td>60.2 ± 8.1</td>
<td>59.2 ± 9.0</td>
<td>.019</td>
</tr>
<tr>
<td>Positive family history regarding premature CAD</td>
<td>335 (45.0%)</td>
<td>549 (60.3%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.7 ± 4.0</td>
<td>27.3 ± 3.9</td>
<td>.055</td>
</tr>
<tr>
<td>Obesity (BMI ≥30 kg/m²)</td>
<td>180 (24.2%)</td>
<td>211 (23.2%)</td>
<td>.63</td>
</tr>
<tr>
<td>Previous smoking</td>
<td>327 (44.0%)</td>
<td>447 (49.1%)</td>
<td>.036</td>
</tr>
<tr>
<td>Current smoking</td>
<td>143 (19.2%)</td>
<td>189 (20.8%)</td>
<td>.39</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>192 (25.8%)</td>
<td>188 (20.7%)</td>
<td>.013</td>
</tr>
<tr>
<td>Insulin-dependent diabetes</td>
<td>42 (5.6%)</td>
<td>44 (4.8%)</td>
<td>.46</td>
</tr>
<tr>
<td>COPD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>160 (21.5%)</td>
<td>252 (27.7%)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>120 (16.1%)</td>
<td>162 (17.8%)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>36 (4.8%)</td>
<td>82 (9.0%)</td>
<td></td>
</tr>
<tr>
<td>Preoperative creatinine, mg/dL</td>
<td>1.0 ± 0.48</td>
<td>0.9 ± 0.60</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Preoperative hemodialysis</td>
<td>5 (0.7%)</td>
<td>14 (1.5%)</td>
<td>.10</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>91 (12.2%)</td>
<td>104 (11.5%)</td>
<td>.63</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>45 (6.0%)</td>
<td>58 (6.4%)</td>
<td>.79</td>
</tr>
<tr>
<td>Previous cerebrovascular event</td>
<td>22 (3.0%)</td>
<td>37 (4.1%)</td>
<td>.23</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>135 (18.1%)</td>
<td>329 (36.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>123 (16.5%)</td>
<td>232 (25.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Left main disease (≥50%)</td>
<td>202 (27.2%)</td>
<td>377 (41.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Isolated left main disease</td>
<td>74 (9.9%)</td>
<td>84 (9.2%)</td>
<td>.63</td>
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<tr>
<td>Severity of CAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>297 (39.9%)</td>
<td>170 (18.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>447 (60.1%)</td>
<td>740 (81.3%)</td>
<td></td>
</tr>
<tr>
<td>Received procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LITA + RA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LITA + RA ± SVG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BITA only</td>
<td>133 (14.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BITA + SVG</td>
<td>227 (30.5%)</td>
<td>590 (64.9%)</td>
<td></td>
</tr>
<tr>
<td>BITA + RA</td>
<td>517 (69.5%)</td>
<td>187 (20.5%)</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, % of stroke volume</td>
<td>54.8 ± 10.9</td>
<td>56.7 ± 10.3</td>
<td>.001</td>
</tr>
<tr>
<td>Impaired left ventricular function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (35 to &lt;48%)</td>
<td>141 (19.0%)</td>
<td>129 (14.2%)</td>
<td></td>
</tr>
<tr>
<td>Severe (&lt;35%)</td>
<td>32 (4.3%)</td>
<td>26 (2.9%)</td>
<td>.006</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>2.9 ± 3.3</td>
<td>2.4 ± 2.7</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Continuous variables are reported as mean ± standard deviation. Dichotomous variables are reported as n (%). LITA, Left internal thoracic artery; RA, radial artery; SVG, saphenous vein graft; BITA, bilateral internal thoracic artery; CAD, coronary artery disease; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; EuroSCORE, European System for Cardiac Operative Risk Evaluation.
deviations or medians and ranges, respectively. Differences in the characteristics between the treatment groups were assessed using χ² tests (categorical variables) and Mann–Whitney U or t test (continuous variables) as appropriate and reported using standardized differences.

The statistical analysis consisted of a patient-wise analysis (BITA vs LITA) of time-related events (overall survival, MACCE-free survival, and repeat revascularization) in the whole cohort and a graft-wise analysis (RA vs SVG) of graft patency and target revascularization in a subset of 512 patients including 57 patients with cardiac-related deaths as competing events. For both the patient-wise and graft-wise analysis, a separate propensity score was estimated with the use of logistic regression analysis. For the patient-wise analysis, a propensity score was constructed considering the following patient characteristics that potentially influence the decision to perform BITA grafting rather than LITA grafting: sex, age, diabetes, creatinine (mg/dL), hemodialysis, chronic obstructive pulmonary disease severity class, previous and current smoking, severity of coronary artery disease (either 2- or 3-vessel disease), previous cerebrovascular event, previous AMI, previous PCI, left main disease (>70% stenosis), ejection fraction (%), and a positive family history according to the definitions of the Framingham Offspring Study. These variables were univariably tested as already outlined, and variables showing a P value less than .2 were selected to generate the propensity score. For the graft wise analysis, the same covariates (P <.2) were used to generate a propensity score representing the decision for RA versus SVG grafting. Graft- and target vessel–specific variables were not included in the propensity score; the respective variables were included as covariates in the graft-wise outcome models.

In the patient-wise multivariable analyses, Cox proportional hazards regression modeling and competing risk analysis (for repeat revascularization) were used to estimate the clinical outcomes regarding cumulative survival, MACCE-free survival, and repeat revascularization comparing the use of BITA versus LITA using the propensity score as a covariate. Hazards ratios (HRs), subhazard ratios (SHRs), and their corresponding 95% confidence intervals (95% CIs) were calculated and displayed. The assumption of proportional hazards was assessed graphically using log-log plots and did not contradict the application of the Cox model.

In the graft-wise multivariable analyses, a general estimating equation (GEE) model according to Zeger and Liang was fitted to compare RA and SVG regarding graft patency. With the GEE model, it is possible to account for multiple grafts and repeated graft patency evaluations within patients and within follow-up time. For this purpose, different correlation structures with similar results were assumed. The reported model assumes an unstructured correlation structure.

Model covariates included target vessel–specific parameters, namely graft territory (either circumflex or right coronary artery), target-vessel stenosis (%), previous PCI of the corresponding target vessel, and whether a CA or CTA investigation was performed. The GEE model was further adjusted for follow-up time and the propensity score containing clinical characteristics as outlined above and whether grafting was part of a BITA or LITA procedure. With the GEE model, odds ratios and corresponding 95% CIs were estimated.

Finally, as part of the graft-wise analyses, a competing risk model was applied to estimate relative risks for target-vessel revascularization comparing RA versus SV grafting. As outlined for the GEE model, covariates were the graft-specific variables with the exception of CA/CTA and a propensity score representing patient characteristics. The competing risk model was used to estimate the cumulative incidence function of RA and SVG for the need of target-vessel revascularization; SHRs and their corresponding 95% CIs were calculated and displayed. Robust standard errors were used to account for the correlated (within patients) graft data.

Competition risk analysis was performed using Stata statistical software, version 14 (StataCorp College Station, Tex). Data documentation and all other statistical analyses were performed using IBM SPSS Statistics for Windows 24.0 (IBM Corp., Armonk, NY).

RESULTS

Patient-Wise Comparison: BITA Versus LITA

A total of 1654 patients undergoing first, nonemergent MAR were included; of these patients, 910 patients
received BITA/C6RA/C6SVG, and 744 patients (45.0%) received LITA + RA/C6SVG. The vast majority of patients underwent on-pump CABG (1606 patients, 97.1%), 90.9% of RITA grafts were used as in situ configurations (828 of 910 patients). Table 1 displays the preoperative characteristics of the study cohort. Perioperative in-hospital mortality was 1.7% (13 patients) in the LITA + RA group and 0.7% (6 patients) in the BITA group (P = .04).

Propensity score-adjusted Cox regression and competing risk analysis identified BITA grafting to be associated with improved long-term survival (HR, 0.57; 95% CI, 0.38-0.86, P = .009), MACCE-free survival (HR, 0.33; 95% CI, 0.23-0.46, P < .001), and lower need for repeat revascularization (SHR, 0.59; 95% CI, 0.39-0.90, P = .015). Overall survival at 1, 5, and 10 year(s) was 99.1%, 97.8%, and 92.5% among patients receiving BITA and 98.3%, 94.8%, and 87.1% in patients receiving LITA + RA, respectively. Figure 1 displays MACCE-free survival. MACCE-free survival was 98.1%, 95.2%, and 92.2% in patients receiving BITA and 92.5%, 85.5%, and 76.9% in patients receiving LITA. Repeat revascularization at 1, 5, and 10 year(s) after CABG was 1.0%, 4.3%, and 8.2% in patients receiving BITA and 2.9%, 7.7%, and 13.9% in patients receiving LITA + RA.

Graft-Wise Comparison: RA Versus SVG

A subgroup of 455 patients underwent coronary diagnostic procedures (CA/CTA) after MAR. Video 1 shows the open harvesting of a radial artery. Patient characteristics of this subgroup are shown in Table 2. Of these, 311 patients (68.5%) received LITA + RA/C6SVG, 114 patients received BITA/C6SVG (25.1%), and 29 patients received 3 arterial conduits (6.4%). Regarding graft configurations, 98.9% of all investigated LITA and 78.6% of RITA grafts were in situ. Furthermore, 98.6% of all RA and 99.2% of all studied SVG grafts were used as single anastomosis conduits. Table 3 displays the indications and outcome of repeat coronary diagnostic investigations. Angina was the most common indication for repeat diagnostic investigations (97.7%). However, 7.7% of patients in the BITA/C6 group and 6.7% of patients in the LITA/C6 group underwent repeat diagnostic investigations for other indications (e.g., chest pain without diagnostic evidence of coronary artery disease).

FIGURE 1. Kaplan–Meier-estimated cumulative MACCE-free survival in patients with multiple arterial revascularization. Comparison of BITA (green) versus LITA (blue); log-rank: P < .001. MACCE, Major adverse cardiac and cerebrovascular event; LITA, left internal thoracic artery; BITA, bilateral internal thoracic artery; CABG, coronary artery bypass grafting.

frequent indication for CA/CTA among 205 patients (45.1%), 86 patients were asymptomatic (18.9%), and 24 patients received CA/CTA before scheduled noncoronary surgery. AMI was present among 97 patients only (24.1%). Among 174 investigations (38.3%), CA/CTA revealed normal findings, in 42.3% (192 patients) disease or occlusion of at least 1 conduit was diagnosed. Progression of native coronary artery disease independent from CABG graft supply was present among 76 patients (16.7%), and complications resulting from previous PCI were found among 12 patients (2.6%). In 60.8% of all diagnostic procedures, findings resulted in conservative or optimal medical treatment (OMT), 37.0% received repeat revascularization by PCI and 10 patients underwent repeat CABG.

GEE modeling based on 419 RA grafts and 487 SVGs revealed RA grafting to be associated with significantly lower risk for graft disease/occlusion (odds ratio, 0.59; 95% CI, 0.47-0.73, P < .001; see Table 4). At a mean of follow-up of 6.5 years, graft occlusion was estimated 26% for RA and 43% of SVG.

Competing risk analysis identified RA grafting associated with lower need for subsequent target-vessel revascularization (SHR, 0.58; 95% CI, 0.43-0.78, P < .001; see Table 5). Figure 2 displays the cumulative incidence function of RA versus SVG regarding repeat target-vessel revascularization.

**DISCUSSION**

Our study analyzed graft patency among 1654 patients at risk with a median follow-up of 7.4 years undergoing first, nonemergent MAR. We were not only able to analyze crude endpoints but also investigated graft patency among patients undergoing CA/CTA during frequent follow-up. Both the individual and the graft-specific analysis showed conclusive and reproducible results. The use of RITA as second conduit was associated with improved survival and lower rate for future cardiovascular events compared with LITA + RA. However, a long-term benefit of the RA over SVG has been a matter of debate due to the lack of
sufficient in-depth studies with follow-up periods beyond 5 years, not considering that repeat revascularization might not always be related to CABG-related graft failure. \(^1\)\(^3\)\(^8\)\(^9\)

In our study, RA grafting was associated with significantly greater graft patency and lower need for target-vessel revascularization even after adjustment for relevant clinical conditions and target vessel–specific parameters such as target-vessel stenosis, graft territory, or previous target-vessel PCI. Furthermore, stratified for the indication for repeated CA/CTA, the divergence between RA and SVG patency was even greatest in patients with AMI. Therefore, these results implicate a strong need for the use of more arterial grafts especially of RITA and additional RA as a third graft of choice. \(^1\)

The results of our study are almost identical to our very recently published meta-analysis of randomized controlled trials comparing RA versus SVG performance for CABG. \(^2\)

In this study with comparable numbers of conduits, the incidence of adverse cardiac events was significantly lower in association with RA grafts. Moreover again, the use of RA was associated with lower risk for repeat revascularization at 5 years’ follow-up. Both studies—from patients recruited in randomized clinical trials and from the actual all-comer patients—showed reproducible treatment effect using the RA rather than SVG, indicating clinical translation from randomized trials to daily, real-world settings. However, after 5-year follow-up, the working group meta-analysis has not yet shown a survival benefit of RA grafting. Tranbaugh and colleagues \(^2\) compared the outcome of 1560 propensity-score matched LITA + RA ± SVG patients with conventional CABG and found significantly lower mortality in the RA group. Their 10-year survival in the LITA + RA ± SVG group was identical to the overall survival of our LITA + RA ± SVG patients. In symptom-driven CA after a mean follow-up of 4.3 years, unadjusted RA graft patency was significantly greater compared with SVG.

Locker and colleagues \(^2\) investigated the very long-term survival among patients receiving either conventional CABG or MAR in a large population of 8622 patients. They observed a significant survival benefit of MAR at 10 and 15 years compared with a matched population receiving conventional CABG. Furthermore, the results were reproducible for both sexes and older patients, concluding that MAR should be proven among greater-risk subgroups. Another multicenter study has investigated the merit of MAR with crude survival ascertained by the Social Security Death Index only and have found a significant greater survival among patients undergoing MAR. \(^2\)

Current randomized trials have shown intermediate RA results only and our long-term investigation demonstrates significant advantage of the RA over SVG especially beyond 5 years after CABG among a population receiving MAR only. SVG patency exponentially declined after 6 to 7 years of follow-up, and therefore most current outcome studies may be more likely to display technical errors rather than any long-term graft degeneration.

Another study conducted by the Cleveland Clinic investigated all CA procedures after CABG involving at least 1 RA but could not relate this to any clinical outcome regarding the whole patient population at risk. \(^1\) Although they found an increased failure rate among RA grafts compared with SVG, a number of potential facts need to be acknowledged. (1) The mean follow-up time from CABG to CA was only 1.6 years; therefore, corresponding graft patency in this study may almost exclusively display early technical graft failure rather than any long-term merit of RA and SVG. (2) Sequential grafting was extensively performed among 42% of all RA grafts but only in 18% of SVG adding competitive flow, especially for the RA. (3) Only 11.7% of investigated RITA grafts remained in situ, in contrast to 78.6% of our studied RITA grafts, where our results showed significantly greater potency for in situ-grafted RITA. (4) As this study was a graft/anastomoses-specific analysis, adjustment for vessel-specific parameters was not performed.

In our study, a very homogenous surgical technique was applied, namely the vast majority of patients were operated on-pump with predominantly in situ RITA configurations and single anastomoses of non-ITA conduits. Moreover, the recently published 5-year results from the ROOBY-FS (The Department of Veterans Affairs “Randomized On/Off Bypass”) trial demonstrated greater rates of death and MACCE events in patients undergoing off-pump coronary revascularization; therefore, based on the low frequency

**FIGURE 2.** Cumulative incidence of repeat target-vessel revascularization of RA (subhazard ratio, 0.58; 95% confidence interval, 0.43-0.78; \(P < .001\)) versus SVG in propensity score–adjusted competing risk analysis. CABG, Coronary artery bypass grafting.
of off-pump surgery among patients undergoing MAR, this parameter may be ignorable as a possible confounder.\textsuperscript{25}

CTA has become a reasonable tool for coronary diagnostics within the past decade and is gaining increasing importance in the long-term surveillance after CAGB. The high accuracy of CTA allied to the greater vascular complication rate during CA in CAGB patients in contrast with the low need for repeat revascularization among nonischemic patients suggests that CTA investigations should be used more frequently.\textsuperscript{10,11,26,27}

In our analysis, RA patency was superior to SVGs, and this effect was independent of age, indicating that even older patients may profit from additional arterial grafts. These findings are supported by Benedetto and Codispoti,\textsuperscript{28} who reported that additional RA grafting improved all-cause mortality in patients undergoing CAGB up to the age of 70 years.

Furthermore, as women demonstrated lower graft patency among non-ITA grafts, it could be argued that women may be more likely to benefit from both ITAS and RA. Dimitrova and colleagues\textsuperscript{29} found a significant survival benefit at 15 years among women receiving RA instead of SVG. Moreover, MAR is less likely performed among women and patency rates of arterial grafts were not significantly different between sexes but SVG patency was lower in women.\textsuperscript{30}

The greater risk of sternal wound complications has prevented a more common use of BITA. However, the sternal wound complication rate was even lower among patients undergoing BITA compared with LITA + RA \pm SVG in our series (2.1\% vs 4.0\%, \( P = .02 \)). This ongoing step-wise decline of sternal complications is explainable as follows: first, the use of skeletonized grafts in BITA; second, the use of augmented and parasternal wires providing greater stability; and third, the administration of teicoplanine, which has significantly reduced the incidence of sternal complications.\textsuperscript{31} Moreover, recently we have introduced prophylactic negative pressure wound therapy (Kerlix; Acelity, San Antonio, Tex) among patients undergoing BITA. As we have seen improved results with the use of RITA and RA together with a declining sternal complication rate, we have switched to an almost-obligatory use of BITA grafting at our center.\textsuperscript{13,31}

There are several limitations—one might argue that SVGs have solely been grafted to tertiary important vessels and this may be responsible for the lower patency rates of SVG. However, we have clearly shown in a second analysis using target-vessel revascularization as primary endpoint that SVG-grafted targets were more likely to undergo repeat target revascularization compared with RA, underlining at least comparable importance of the SVG-grafted targets. The longer follow-up of patients in the LITA + RA \pm SVG group compared with BITA group is a further limitation for the interpretation of the findings. However, even despite shorter follow-up in the BITA group, there is a clear difference between early- and long-term outcome, supporting the benefit of BITA. Moreover, we cannot account for missing covariates.

Another annotation has to be mentioned—namely that during this very long period—we have gained increasing confidence to provide patients more likely with BITA. According to a stepwise modification of our surgical technique, we were able to lower sternal complications to a nearly never-happens event.

The additional use of RITA and RA is associated with a lower need for future revascularization procedures in the long-term follow-up after CAGB. In the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial at 5 years, it has been clearly shown that early repeat revascularization was an independent predictor of future death and MACCE events.\textsuperscript{32} There has been a shift in CAGB surgery toward patients in their 50s and 60s—as older patients will be more likely to be treated by culprit lesion or multiple-vessel PCI—and these patients require an “insurance for life.” If CAGB surgery wants to survive in an era of multivessel PCI with lacking realistic long-term studies—we have to implement MAR as treatment of choice.

Graft occlusion, however, is a multifactorial phenomenon based on intrinsic factors such a competitive flow, thrombosis, oxidative stress, and endothelial dysfunction.\textsuperscript{33,34} Extrinsic OMT is the second mainstay after CAGB. As 92\% of our presented MAR patients received frequent controls by a cardiologist, we are confident that the vast majority of our patients received OMT.

In conclusion, both the clinical and conduit-related outcomes of this large long-term investigation provide clear answers to 2 important issues in CAGB. The results clearly indicate that the use of both in situ ITAs is advantageous and that the use of RA grafting demonstrates superior graft patency with lower need for target revascularization compared with SVG.

Conflict of Interest Statement
Authors have nothing to disclose with regard to commercial support.

References
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