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Elfriede Ruttmann, Nikolaus Fischler, Adel Sakic, Orest Chevtchik, Hannes Alber, Roland Schistek, Hanno Ulmer and Michael Grimm

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Second Internal Thoracic Artery Versus Radial Artery in Coronary Artery Bypass Grafting

A Long-Term, Propensity Score–Matched Follow-Up Study

Elfriede Ruttmann, MD; Nikolaus Fischler, MD; Adel Sakic, MD; Orest Chevtchik, MD; Hannes Alber, MD; Roland Schistek, MD; Hanno Ulmer, PhD; Michael Grimm, MD

Background**—**The best second arterial conduit for multiple arterial revascularization (MAR) is still a matter of debate. Previous studies on the benefit of either using the radial artery (RA) or the right internal thoracic artery (RITA) in coronary artery bypass grafting are not conclusive. The aim of our study was to compare the perioperative and long-term outcome of either RA or RITA grafts as second conduits for MAR.

Methods and Results**—**A consecutive series of 1001 patients undergoing first nonemergent coronary artery bypass grafting receiving either RA or RITA as second graft for MAR between 2001 and 2010 were studied. There were 277 patients receiving a RITA and 724 patients receiving a RA in addition to a left internal thoracic artery (LITA). Concomitant saphenous vein grafts (SVG) were grafted in addition as necessary. Propensity score–matched analysis was performed to compare the 2 groups, bilateral ITA±SVG (BITA±SVG group) and the LITA+RA±SVG group relative to overall survival and major adverse cardiac and cerebrovascular events–free survival. Hazard ratios and their 95% confidence intervals were estimated by COX regression stratified on matched pairs. The incidence of perioperative major adverse cardiac and cerebrovascular events was significantly lower in the BITA±SVG group (1.4% versus 7.6%, $P<0.001$). Overall survival (hazard ratio 0.23; 95% confidence interval 0.066–0.81; $P=0.022$) and major adverse cardiac and cerebrovascular events–free survival (hazard ratio 0.18; 95% confidence interval 0.08–0.42; $P<0.001$) were significantly better in the BITA±SVG group compared to the LITA+RA±SVG group.

Conclusions**—**The results of our study provide strong evidence for the superiority of a RITA graft compared to RA as a second conduit in MAR. **(*Circulation*. 2011;124:1321-1329.)**

Key Words: revascularization ■ radial artery ■ internal thoracic artery

There is conclusive evidence that the use of a left internal thoracic artery (LITA) in coronary artery bypass grafting (CABG) surgery reduces morbidity and mortality compared with saphenous vein grafts (SVG) only.[1] Therefore, as arterial grafts are thought to provide better long term patency than SVG, it has become an implication for the routine use of more arterial grafts in the face of ever-improving stent technologies.

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Currently, multiple arterial revascularization (MAR) is performed in <13% of CABG procedures; the radial artery (RA) is most commonly used as a second conduit of choice.[2] However, outcome studies investigating the RA as a bypass conduit show conflicting results. A retrospective angiographic study by Khot et al demonstrated a significantly lower patency rate for RA compared with internal thoracic arteries (ITA) or even SVG.[3] Recently, Goldman et al showed in a prospective randomized clinical trial that RA was not superior to SVG relative to 1-year patency.[4] On the other hand, other studies have reported improved long-term survival and patency rates for patients receiving RA as a second arterial graft compared with patients receiving concomitant SVG grafts only.[5–7] In contrast to the diverging results for the RA, several observational CABG studies using the right internal thoracic artery (RITA) as a second arterial graft have shown not only superior survival but also a 60%-lower need for a further redo CABG procedure within 20 years after CABG procedure.[8–10]

Still, 1 unanswered major clinical question remains, namely, which arterial conduit used as a second graft will provide the best result relative to long-term cardiac morbidity and mortality. So far, only 2 outcome studies have addressed the short- and intermediate-term results of patients receiving either a concomitant RITA or a RA as a second conduit analyzed by a direct comparison.[11,12] Borger et al concluded a safe use of 2

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From the Departments of Cardiac Surgery (E.R., N.F., A.S., O.C., R.S., M.G.), Cardiology (H.A.), and Medical Statistics, Informatics and Health Economics (H.U.), Innsbruck Medical University, Innsbruck, Austria.

Correspondence to Elfriede Ruttmann, MD, Department of Cardiac Surgery, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria. E-mail elfriede.ruttmann@i-med.ac.at

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arterial grafts but could not show an advantage for either a RITA or RA graft.[11] Caputo et al did not find a survival benefit at 18 months after MAR.[12] However, in both studies, analyses were done in subgroups of patients who were not comparable in terms of relevant comorbidities and age.

As the only currently ongoing prospective study that investigates the benefit of a second ITA graft compared with SVG (the Arterial Revascularization trial, or ART), the main question of which second arterial conduit is best for CABG surgery will remains unanswered for the foreseeable future. Therefore, as the principle invesigators conclude, a prospective randomized clinical trial is very much needed.[13,14,15]

Therefore, the aim of our propensity score–matched analysis was to evaluate the perioperative and long-term outcome of patients undergoing MAR, comparing the performance of the RA and RITA graft. In the perioperative and postoperative periods, both major cardiac and cerebrovascular events (MACCE) and MACCE-free survival were obtained to investigate the best second arterial conduit for CABG surgery.

Methods

Patients

This study analyzes all patients who underwent CABG between August 2001 and August 2010 at the Innsbruck Medical University and who received MAR with a LITA graft and either a RITA or RA bypass as a second arterial conduit. Inclusion criteria for this study were first, nonemergent isolated coronary CABG for multivessel coronary artery disease performed by a median sternotomy access. Patients suffering a prior myocardial infarction within 1 week before the CABG procedure were excluded. Additionally, patients receiving a bilateral internal thoracic artery (BITA) together with a concomitant RA (n=89 patients) and patients receiving a totally endoscopic CABG procedure assisted by the Da Vinci telemanipulation device for multivessel disease (either 2-vessel disease or as a hybrid procedure with concomitant percutaneous coronary intervention [PCI]) were excluded from the study (n=45 patients).

A total of 1001 consecutive patients undergoing MAR fulfilled the inclusion criteria of our observational study. A total of 277 patients (27.7%) received a BITA with or without concomitant SVG (BITA±SVG group). A total of 724 patients (72.3%) received LITA together with at ≥1 RA with or without concomitant SVG grafts (LITA+RA±SVG group).

Surgical Technique

Sixteen different surgeons with at least 6 years of surgical experience performed both CABG procedures. There were no significant differences between the treatment groups relative to surgical experience. Surgical technique and grafting strategy did not change over the last 10 years, with the exception of the switch to skeletonization of ITA grafts in 2006. All surgeons aimed to perform an in situ RITA through the transverse sinus to graft the circumflex territories. If the RITA was too short, 2 different strategies were performed, but the choice was left to the preference of the surgeon, namely grafting the RITA to the left anterior descending artery and the RITA to circumflex territory or creation of a T-graft LITA+RITA to bypass the left coronary system. Since the introduction of skeletonization, the success rate for using in situ RITA through the transverse sinus increased tremendously because we are now able to obtain significantly longer grafts. All RA were harvested using open surgical technique, and these patients received nitrates or diltiazem for at least 3 to 6 months after CABG surgery to avoid vasospasm. Complete revascularization was attempted in all cases.

Study End Points and Cardiac Event Assessment

The primary end point of the study was long-term overall survival and MACCE-free survival. All MACCE were defined as combined end point including (1) myocardial infarction, (2) stroke, (3) cardiac-related death, and (4) repeated revascularization (either by PCI or CABG procedure). Perioperative myocardial infarction was defined according to the Joint Eureopean Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation Task Force for the Redefinition of Myocardial Infarction.[16] Perioperative neurological events were defined as postoperative new-onset neurological deficit lasting >72 hours after the appearance of symptoms.

Patient data were prospectively collected in full accordance with the standards of the Quality Control Working Group of the Austrian Society of Cardiothoracic Surgery. The data acquisition included a telephone interview by a trained study nurse a month after patient discharge to obtain 30-day mortality and morbidity. Long-term follow-up was performed by telephone interviews with patients and referring cardiologists to evaluate the freedom from angina, myocardial infarction, death from all causes, and cardiac-related deaths. Additionally, coronary angiography reports in patients who underwent repeated cardiac catheterization were obtained and evaluated. Late death was obtained from routine anniversary follow-up supplemented with the Social Security Death Index (Statistics Austria database). Permission for this study was obtained by the local institutional review board.

Propensity Score Matching and Statistical Analysis

Propensity score matching was used to reduce the impact of treatment selection in comparing RA and RITA as the second conduit for MAR. Preoperative characteristics of patients in these study groups were summarized as mean±SD, median, or prevalence (in percentage), as appropriate. Student t test for independent sample or Mann-Whitney U test for continuous variables and χ^2 test for categorical variables were applied to examine differences between the BITA±SVG and LITA+RA±SVG groups. Variables revealing a P value <0.2 in this analysis were entered into a logistic regression analysis with the use of RA versus RITA as the dependent variable. This was performed to generate a propensity score for each patient representing the probability to receive either a RITA or a RA as described by Blackstone[17] and Austin.[18]

The resulting propensity score was used to create a matched pair patient subsample. Five-digit matching without replacement was applied to form the matched sample.

For each BITA±SVG patient, 1 LITA+RA±SVG patient was randomly selected in a 1:1 manner in case of an agreement of the propensity score (2 digits behind comma). The balance of measured variables between the study groups in the matched sample was assessed using paired t test or Wilcoxon test for continuous measures and the McNemar test for categorical measures.

Kaplan-Meier analysis, together with log-rank testing, was used to evaluate the postoperative survival and MACCE-free survival in the full unmatched patient population. Finally, a Cox proportional hazards regression model stratified on matched pairs was used to estimate the treatment effect and its statistical significance relative to cumulative survival and MACCE-free survival between BITA±SVG and LITA+RA±SVG groups.

Results

Patient Characteristics in the Full Unmatched Patient Population

Median follow-up of all patients was 57.7 months (range 3–112 months). Median follow-up of the BITA±SVG group was 32.7 months (3–111 months) and 67.3 months (3–112 months) in the LITA+RA±SVG group (P<0.001). Table 1 displays preoperative characteristics of the full unmatched study population. Patients undergoing MAR receiving BITA grafts were significantly younger than patients receiving a RA as concomitant second arterial conduit but showed a significantly higher rate of chronic pulmonary obstructive disease (both P<0.001). Mean creatinine levels (P=0.003) and dialysis before surgery

Table 1. Preoperative Characteristics of Patients Undergoing Multiple Arterial Revascularization (Full Unmatched Patient Population)

	BITA±SVG (n=277)	LITA+RA±SVG (n=724)	P
Male	249 (89.9)	624 (86.2)	0.12
Age	56.6±9.6	59.9±7.9	<0.001
Age groups			
<50 y	73 (26.4)	83 (11.5)	
50 to 55 y	50 (18.1)	90 (12.4)	
55 to 60 y	62 (22.4)	159 (22.0)	
60 to 65 y	37 (13.3)	216 (29.8)	
65 to 70 y	30 (10.8)	118 (16.3)	
70+ y	25 (9.0)	58 (8.0)	<0.001
BMI, kg/m^2	27.4±3.4	27.7±4.0	0.24
Obesity (BMI ≥30 kg/m^2)	63 (22.7)	174 (24.0)	0.67
Smoker (active or previous)	113 (40.8)	292 (40.3)	0.89
Diabetes mellitus	59 (21.3)	174 (24.0)	0.36
Insuline-dependent diabetes mellitus	14 (5.1)	37 (5.1)	0.97
COPD	92 (33.2)	143 (19.8)	≤0.001
COPD classification (Gold)			
Mild	55 (19.9)	113 (15.6)	
Moderate	33 (11.9)	27 (3.7)	
Severe	4 (1.4)	3 (0.4)	<0.001
Renal function			
Normal (creatinine <1.17 mg/dL)	220 (79.4)	585 (80.8)	
Slightly elevated (creatinine 1.17–<2 mg/dL)	49 (17.7)	130 (18.0)	
Elevated (creatinine ≥2 mg/dL)	8 (2.9)	9 (1.2)	0.20
Preoperative creatinine, mg/dL	1.17±0.27	1.01±0.39	0.003
Preoperative dialysis	6 (2.2)	3 (0.4)	0.009
Peripheral arterial disease	30 (10.8)	83 (11.5)	0.77
Cerebrovascular disease	12 (4.3)	40 (5.5)	0.45
Previous cerebrovascular event	5 (1.8)	20 (2.8)	0.39
Previous PCI	54 (19.5)	109 (15.1)	0.89
No. of diseased coronary vessels			
2-Vessel disease	86 (31.0)	246 (33.9)	
3-Vessel disease	191 (69)	478 (66.1)	0.70
Impaired left ventricular function (LVEF <48)	56 (20.2)	173 (23.9)	0.22
Ejection fraction, inches	54.9±10.8	51.2±12.3	<0.001
Isolated left main stenosis (≥70)	27 (9.7)	75 (10.4)	0.76
Logistic EuroSCORE	2.3±2.6	2.8±2.3	0.002

Values are expressed as means±SD, median (range) or n (%), BITA indicates bilateral internal thoracic arteries; SVG, saphenous vein graft; LITA, left internal thoracic artery; RA, radial artery; BMI, body mass index; COPD, chronic pulmonary obstructive disease; PCI, percutaneous coronary intervention; and LVEF, left ventricular ejection fraction.

Table 2. Intra- and Perioperative Characteristics and Outcome (Full Unmatched Patient Population)

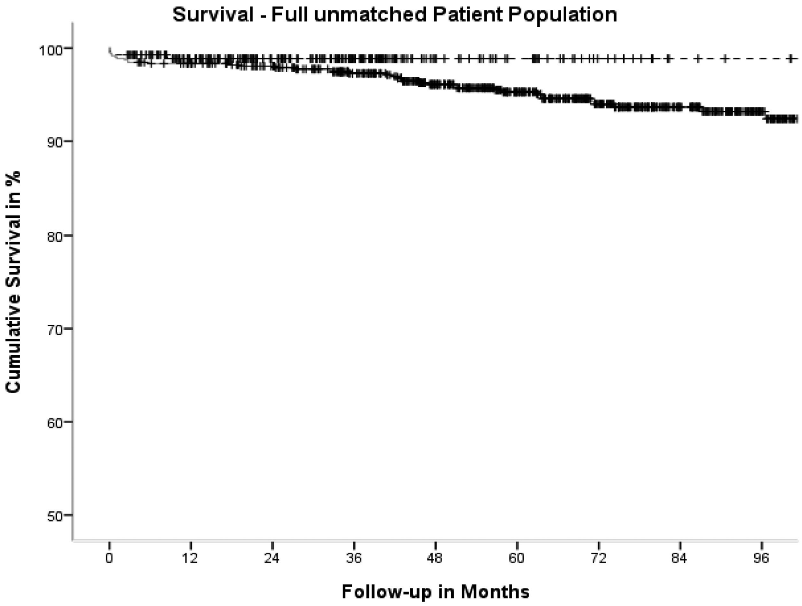
	BITA±SVG (n=277)	LITA+RA±SVG (n=724)	P
Coronary anastomoses	3.2±0.87	3.1±0.86	0.88
Central (aortic) bypass anastomoses	1.1±0.75	2.2±0.84	<0.001
No central (aortic) anastomosis	64 (23)	1 (0.14)	<0.001
Pedicle preparation of ITA grafts	90 (32.5)	640 (88.4)	<0.001
Configuration of RITA			
In situ through transverse sinus	162 (58.5)		
Free graft	51 (18.4)		
In situ to LAD	56 (20.2)		
In situ to RCA	8 (2.9)		
Configuration of RA			
Circumflex territories		682 (94.2)	
Right coronary artery		42 (5.8)	
2 Arterial grafts to left coronary artery system	269 (97.1)	682 (94.2)	0.07
Perfusion time, min	126±42.4	112.5±39.5	<0.001
Aortic cross-clamp time, min	77.7±30.2	62.3±25.2	<0.001
Single aortic cross-clamping	15 (5.4)	32 (4.4)	0.82
Need for IABP	3 (1.1)	21 (2.9)	0.11
Rethoracotomy due to bleeding/tamponade	11 (4.0)	41 (5.7)	0.28
Median ICU time, h	20 (11–804)	21 (12–936)	0.001
Median ventilation time, h	8 (0–369)	9 (0–600)	0.23
MACCE (patient related)	4 (1.4)	41 (5.7)	0.004
Perioperative myocardial infarction	1 (0.4)	23 (3.2)	0.009
Perioperative stroke	1 (0.4)	18 (2.5)	0.027
Cardiac-related death	2 (0.7)	7 (1.0)	0.70
Sternal dehiscence	9 (3.2)	30 (4.1)	0.51
Median follow-up, mos	32.7 (3–111)	67.3 (3–112)	<0.001

Values are expressed as mean±SD, median (range) or n (%). BITA indicates bilateral internal thoracic arteries; SVG, saphenous vein graft; ITA, internal thoracic artery; RITA, right internal thoracic artery; LAD, left anterior descending artery; RCA, right coronary artery; RA, radial artery; IABP, intra-aortic ballon pump; ICU, intensive care unit; and MACCE, major cardiac and cerebrovascular events.

(P=0.009) were more frequent in this patient group (P=0.009). In addition, mean ejection fraction was higher in the BITA±SVG group (P<0.001). However, the prevalence of patients with impaired left ventricular function was not significantly different between patient groups (P=0.22). Other cardiovascular risk factors such as diabetes mellitus, peripheral artery disease, or cerebrovascular morbidities did not differ significantly between treatment groups.

Outcome in the Full Unmatched Patient Population

Table 2 displays the intra- and postoperative outcome data of the full unmatched patient population. Mean number of



BITA±SVG	228	168	117	68	54	36	27	25
LITA+RA±SVG	700	668	608	527	426	315	217	119

Figure 1. Survival after MAR in the full unmatched patient population: BITA±SVG (dashed line) versus LITA+RA±SVG (solid line); log-rank: P=0.054. BITA indicates bilateral internal thoracic arteries; SVG, saphenous vein grafts; LITA, left internal thoracic artery; and RA, radial artery.

bypass grafts was 3.2±0.87 in the BITA±SVG group and 3.1±0.86 grafts in the LITA+RA±SVG group (P=0.88). The mean number of central (aortic) anastomoses was significantly higher in the LITA+RA±SVG group (1.1±0.75 versus 2.2±0.84 grafts, P<0.001). In the BITA±SVG group, 64 patients (23.1%) did not receive any central aortic anastomosis; 162 RITA grafts (58.5%) were used as in situ grafts through the transverse sinus. Right interior transverse artery conduits used as free grafts were anastomosed as T-graft into the LITA bypass. In the BITA±SVG group, a higher number of patients received a skeletonized ITA harvesting than in the LITA+RA±SVG group (67.5% versus 47.3%, P<0.001). Single aortic cross-clamping was performed in 5.4% and 4.4% in patients with heavily calcified aorta, respectively (P=0.82). The mean perfusion time and aortic cross-clamp time was significantly longer in the BITA±SVG group (both P<0.001). Intensive care unit stay was significantly shorter in the BITA±SVG group, mean postoperative ventilation time was not different within both treatment groups (P=0.23). An intra-aortic balloon pump (IABP) was implanted in 3 patients of the BITA±SVG group (1.1%) and in 21 patients (2.9%) of the LITA+RA±SVG group (P=0.11). Rethoracotomy because of bleeding was necessary in 4% of the BITA±SVG and in 5.7% of the LITA+RA±SVG group (P=0.28).

Perioperative MACCE occurred in 4 patients of the BITA±SVG group (1.4%) and in 41 patients (5.7%) of the LITA+RA±SVG group (P=0.004). Perioperative myocardial infarction occurred in 1 patient (0.4%) of the BITA±SVG group and in 23 patients (3.2%) of the LITA+RA±SVG group (P=0.009). Among these 23 patients suffering perioperative myocardial infarction, 8 patients (34.7%) had to undergo emergency CABG reoperation because of acute RA graft failure during the initial hospital stay. A new-onset neurological event was diagnosed in 1 patient (0.4%) of the BITA±SVG group and in 18 patients (2.5%) of the LITA+RA±SVG group (P=0.027). Perioperative death occurred in 2 patients (0.7%) of the BITA±SVG patients and in 7 patients (1.0%) undergoing LITA+RA±SVG grafting (P=0.70). Postoperatively, sternal dehiscence with a need for surgical intervention was not significantly different between treatment groups (3.2% versus 4.1%, P=0.51).

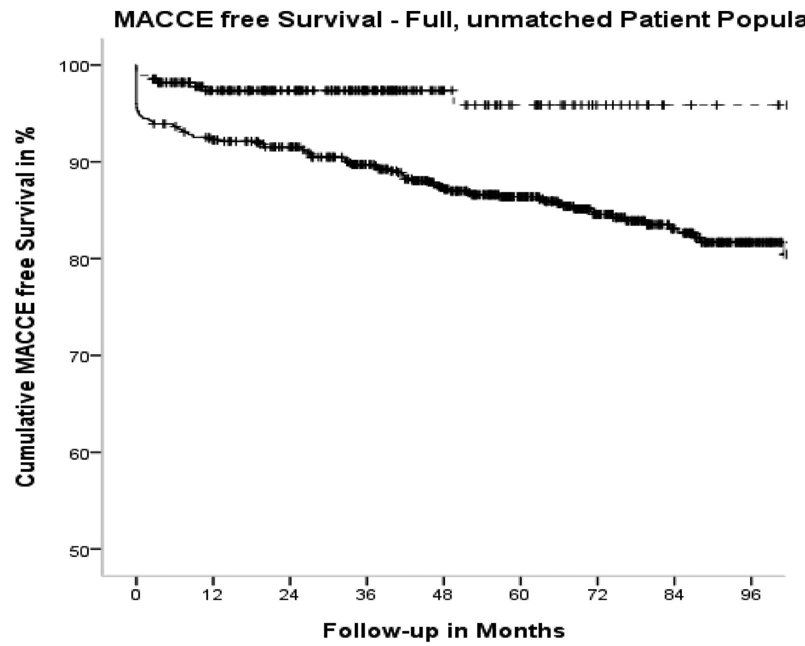
Figure 1 displays the postoperative patient survival in the full unmatched patient population. Postoperative survival at 1, 3, and 5 years was 98.9% each in the BITA±SVG group and 96.8%, 96.3%, and 93.0% in the LITA+RA±SVG group (log-rank: P=0.054). Figure 2 shows the MACCE-free survival at 1,3, and 5 year, which was 97.4%, 97.4%, and 95.9% in the BITA±SVG group and 92.3%, 89.7%, and 86.4% in the LITA+RA±SVG group (log-rank: P<0.001).

Patient Characteristics in the Propensity Score–Matched Patient Population

Table 3 displays the patient characteristics of the propensity score–matched population. Because the patients were comparable for chronic obstructive pulmonary disease (COPD) prevalence and impaired renal function, more patients in the BITA±SVG groups had moderate or severe COPD and still higher mean preoperative creatinine levels.

Outcome in the Propensity-Matched Patient Population

Table 4 shows the perioperative outcome of the propensity score–matched patient population. Perioperative MACCE occurred in 4 patients (1.4%) of the BITA±SVG group and in 21 patients (7.6%) of the LITA+RA±SVG group (P<0.001). The perioperative myocardial infarction rate was 0.4% in the BITA±SVG group and 3.6% in the LITA+RA±SVG group (both P=0.01). Perioperative



BITA±SVG	224	165	111	67	52	34	25	23
LITA+RA±SVG	659	624	559	479	389	284	191	99

Figure 2. Major adverse cardiac and cerebrovascular events–free survival after MAR in the full unmatched patient population. BITA±SVG (dashed line) versus LITA+RA±SVG (solid line); log-rank: $P<0.001$. MACCE indicates major adverse cardiac and cerebrovascular events; BITA, bilateral internal thoracic arteries; SVG, saphenous vein grafts; LITA, left internal thoracic artery; and RA, radial artery.

cardiac-related death was not significantly different between treatment groups (0.7% versus 1.8%, $P=0.45$).

A total of 118 repeated cardiac catheterization procedures among 107 patients were performed (10.7% of all patients) after a median follow-up of 32.9 months (0–101 months) after CABG procedure. During follow up, 19 patients in the BITA±SVG group (6.9%) and 88 patients (12.2%) in the LITA+RA±SVG group underwent repeated cardiac catheterization. In the BITA±SVG group, a total of 4 (1.4%) required repeated revascularization (1 CABG reoperation, 3 by PCI intervention). In the LITA+RA±SVG group, 66 patients (9.1%) had pathological angiographies. In 53 patients (7.3%), disease or occlusion of ≥1 bypass conduit was diagnosed, and 40 patients received (35 by PCI, 5 by CABG reoperation) repeated revascularization during long-term follow-up. Repeated cardiac catheterization was performed in 6.9% of the BITA±SVG group and in 37 patients (13.3%) of the LITA+RA±SVG group ($P=0.012$). Repeated revascularization was necessary in 4 patients (1.4%) in the BITA+SVG group and in 28 patients (10.1%) in the LITA+RA±SVG group ($P<0.001$).

A total of 313 anastomoses (132 ITA, 95 RA, and 86 SVG) were angiographically investigated. Classification of graft patency was defined according to the published definition of Khot et al.[3] Occlusion or diseased grafts were diagnosed in 13/132 (10.2%) of ITA anastomoses and in 18/86 (20.9%) anastomoses of SVG ($P=0.02$). The worst patency rate was diagnosed for RA grafts with an occlusion/disease rate of 36/95 (37.9%) and was significantly lower than for ITA grafts ($P<0.001$) or even SVG ($P=0.014$).

Figures 3 and 4 present the long-term outcome of the propensity score–matched patient population. Postoperative survival at 1, 3, and 5 years after CABG was 98.9% each in patients receiving BITA±SVG grafting compared with 96.8%, 96.3%, and 93.0% in the LITA+RA±SVG group (hazard ratio 0.23; 95% confidence interval 0.07–0.81, $P=0.022$). Major cardiac and cerebrovascular events–free survival was 97.4%, 97.4%, and 95.9% in the BITA+SVG group compared with 89.6%, 86.2%, and 82.2% in patients receiving LITA+RA±SVG (hazard ratio 0.18; 95% confidence interval 0.08–0.42; $P<0.001$).

Discussion

The results of our study among 1001 patients provide strong evidence for the superiority of a RITA graft compared with RA as a second conduit for MAR and indicate that the RA is not an equal alternative conduit to RITA relative to both survival and cardiac-related morbidity. The propensity score–matched approach showed significant advantages of the RITA procedure not only for the perioperative, but also for the long-term outcome.

The short-term benefit of RITA grafting was demonstrated not only by a lower myocardial infarction rate, but also by a significantly reduced incidence of neurological events. The occurrence of a perioperative myocardial infarction is likely to be attributed to the known susceptibility of RA to vasospasm.[19,20] The lower incidence of stroke almost certainly reflects less aortic manipulation when a second ITA graft is used. BITA patients received significantly fewer central aortic anastomoses (23% of BITA patients did not receive central aortic anastomoses at all), eliminating the need for partial aortic clamping and second exposure to an embolic event. Aortic manipulation is a substantial risk for stroke, especially in younger CABG patients who present with premature vulnerable soft plaques of the aorta. Plaques with soft lipid cores are difficult to localize for the surgeon and are therefore at greater risk for rupture.[21,22]

The main reason for the long-term benefit of BITA grafting lies in the anatomic structure of the ITAs that are less susceptible to atherosclerosis than RA. The lower capacity of

Table 3. Preoperative Characteristics of Patients Undergoing Arterial Revascularization (Propensity Score–Matched Patient Population)

	BITA±SVG (n=277)	LITA+RA±SVG (n=277)	*P*
Male	249 (89.9)	249 (89.9)	1.0
Age	56.6±9.6	57.8±9.0	0.14
Age groups			
<50 y	73 (26.4)	73 (26.4)	
50 to 55 y	50 (18.1)	50 (18.1)	
55 to 60 y	62 (22.4)	62 (22.4)	
60 to 65 y	37 (13.4)	37 (13.4)	
65 to 70 y	30 (10.8)	30 (10.8)	
>70 y	25 (9.0)	25 (9.0)	1.0
BMI, kg/m^2	27.4±3.4	27.7±4.0	0.24
Obesity (BMI ≥30 kg/m^2)	63 (22.7)	65 (23.5)	0.25
Smoker (active or previous)	113 (40.8)	125 (45.1)	0.31
Diabetes mellitus	59 (21.3)	62 (22.4)	0.45
Insuline-dependent diabetes mellitus	14 (5.1)	15 (5.4)	0.84
COPD	92 (33.2)	92 (33.2)	1.0
COPD classification (Gold)			
Mild	55 (59.8)	62 (67.4)	
Moderate	33 (35.9)	27 (29.3)	
Severe	4 (4.3)	3 (3.3)	0.03
Renal function			
Normal (creatinine <1.17 mg/dL)	220 (79.4)	225 (81.2)	
Slightly elevated (1.17 to <2 mg/dL)	49 (17.7)	47 (17.0)	
Elevated (creatinine ≥2 mg/dL)	8 (2.9)	5 (1.8)	0.59
Preoperative creatinine, mg/dL	1.17±0.27	1.03±0.50	0.03
Preoperative dialysis	6 (2.2)	2 (0.7)	0.22
Peripheral arterial disease	30 (10.8)	26 (9.4)	0.67
Cerebrovascular disease	12 (4.3)	13 (4.7)	0.57
Previous cerebrovascular event	5 (1.8)	4 (1.5)	0.38
Previous PCI	54 (19.5)	48 (17.3)	0.91
Impaired left ventricular function (LVEF <48)	56 (20.2)	54 (19.5)	0.91
Ejection fraction, %	54.9±10.8	52.9±12.1	0.06
Isolated left main stenosis (≥70)	27 (9.7)	23 (8.3)	0.55
Logistic EuroSCORE	2.3±2.6	2.4±2.5	0.21

Values are expressed as means±SD, median (range), or n (%). BITA indicates bilateral internal thoracic arteries; SVG, saphenous vein graft; LITA, left internal thoracic artery; RA, radial artery; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; and LVEF, left ventricular ejection fraction.

Table 4. Intra- and Perioperative Characteristics and Outcome (Propensity Score–Matched Patient Population)

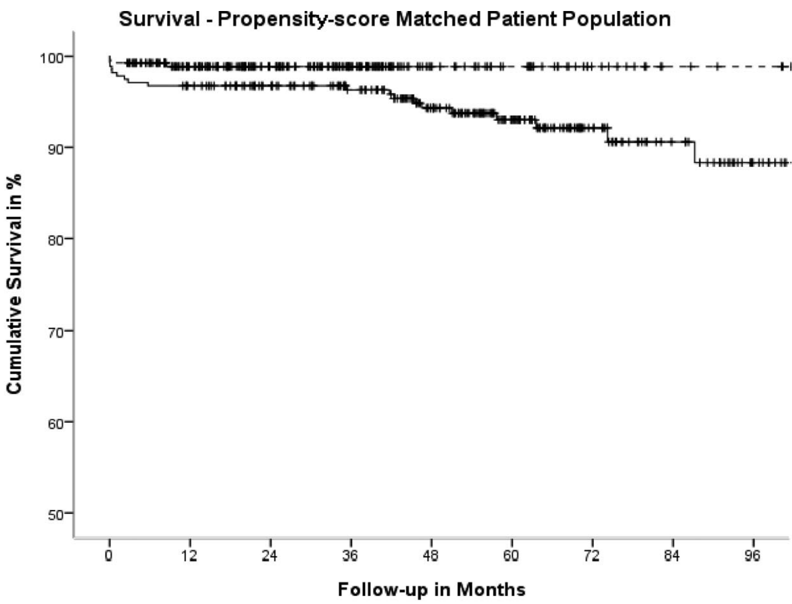
	BITA±SVG (n=277)	LITA+RA±SVG (n=277)	*P*
Coronary anastomoses	3.2±0.87	3.2±0.90	0.14
Aortic bypass anastomoses	1.1±0.75	2.3±0.88	<0.001
Pedicle preparation of ITA grafts	90 (32.5)	146 (52.7)	<0.001
2 Arterial grafts to left coronary artery system	269 (97.1)	266 (95.7)	0.37
Perfusion time, min	126±42.4	118.2±39.0	0.03
Aortic cross-clamp time, min	77.7±30.2	65.1±25.3	<0.001
Need for IABP	3 (1.1)	10 (3.6)	0.09
Rethoracotomy due to bleeding/tamponade	11 (4.0)	18 (6.5)	0.25
Median ICU time, h	20 (11–804)	21 (12–936)	0.09
Ventilation time, h	8 (0–369)	9 (0–600)	0.006
MACCE (patient related)	4 (1.4)	21 (7.6)	<0.001
Perioperative myocardial infarction	1 (0.4)	10 (3.6)	0.01
Perioperative stroke	1 (0.4)	10 (3.6)	0.01
Cardiac-related death	2 (0.7)	5 (1.8)	0.45
Sternal dehiscence	9 (3.2)	10 (3.6)	1.0

Values are expressed as means±SD, median (range), or n (%). BITA indicates bilateral internal thoracic arteries; SVG, saphenous vein graft; LITA, left internal thoracic artery; RA, radial artery; ITA, internal thoracic artery; IABP, intra-aortic balloon pump; ICU, intensive care unit; and MACCE, major adverse coronary and cerebrovascular events.

NO release contributes to the susceptibility of RA to atherosclerosis, and is therefore responsible for the inferior long-term graft patency.[19,20] Late graft degeneration is rare in ITA grafts, and becomes more evident with longer patient follow-up.[1] In our study, the RITA was preferentially used as an in situ graft in 82% of patients and was predominantly routed through the transverse sinus. An angiographic study by Ura et al[23] has found a similar high patency rate of LITA and RITA grafts at 6 years after CABG when the RITA was routed through the transverse sinus. The application of this technique may further contribute to long-term benefit in the BITA group.

Additionally, concerns about the long-term patency of RA that support our findings have previously been raised by Khot and Goldman.[3,4] Even the preferential use of RA compared with SVG is still a matter of debate, and there is still disagreement about the relative merits of RA.[3–7] In one of the largest studies comparing RA and SVG, Desai et al found a significantly higher patency of RA at 1 year. However, Desai et al classified RA conduits with diffuse narrowing or string sign as patent and of little or no clinical consequence even despite inadequate blood flow.[24] This opinion, however, has been critically discussed by international experts.[25,26]

Worldwide, the RA is more frequently used than a RITA graft, mainly because of the increased risk for sternal wound complications.[2] Because deep sternal wound infection has been advocated to be an indicator for quality of care, favoring short-time results at the expense of inferior long-term outcome, most cardiac surgeons try to avoid BITA harvesting in case of availability of alternative graft material. In our study, however, sternal dehiscence was similar in both treatment groups and may be attributed to the greater likelihood that BITA patients would receive skeletonized rather than pedicled ITA grafts, thus lowering additional chest wall trauma



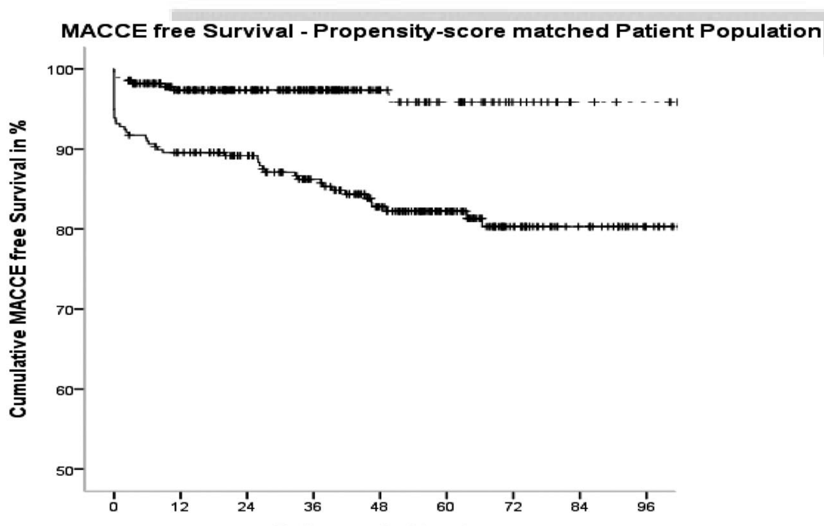
BITA±SVG	228	168	117	68	54	36	27	25
LITA+RA±SVG	265	242	214	174	120	68	43	22

Figure 3. Survival after MAR in the propensity score–matched patient population. BITA±SVG (dashed line) versus LITA+RA±SVG (solid line; hazard ratio 0.23; 95% confidence interval 0.066–0.81; P=0.022). BITA indicates bilateral internal thoracic arteries; SVG, saphenous vein grafts; LITA, left internal thoracic artery; and RA, radial artery.

and ischemia. This benefit of skeletonization of BITA has been previously reported by Saso et al.[27] Their meta-analysis of 12 studies concluded a <50% risk for sternal wound complications for skeletonized ITA grafts. Another randomized, double-blind, within-patient comparison has shown reduced postoperative pain and increased sternal perfusion after skeletonized preparation of the ITA, further supporting our results.[28]

Previous studies involving BITA mainly compared RITA versus SVG rather than RITA versus RA grafts. Studies versus SVG did all show clear advantages relative to survival and occurrence of MACCE in favor of BITA.[8–10,29] Two previous studies on MAR comparing RITA with RA, however, could not find a benefit of BITA grafting.[11,12] In both studies, patients were not comparable in terms of baseline characteristics and revascularization strategy. In these studies, patients receiving a BITA graft were not as likely to receive the second arterial graft to the left coronary system than patients receiving a RA. In our study, however, the revascularization strategy was very similar between both treatment groups, targeting the circumflex territory with the second arterial conduit in >95% of patients. It is, however, still undecided whether the location of the second ITA influences outcome of CABG.[30,31]

Even though this is by far the largest study comparing BITA and RA, there are several limitations to mention. Although the propensity score–matching algorithm produced rather comparable groups, the study was not randomized, and we cannot rule out additional effects of missing covariates. The longer follow-up of patients in the LITA+RA±SVG



BITA±SVG	224	165	111	67	52	34	25	23
LITA+RA±SVG	244	221	188	152	107	59	36	17

Figure 4. Major adverse cardiac and cerebrovascular events–free survival after MAR in the propensity score–matched patient population. BITA±SVG (dashed line) versus LITA+RA±SVG (solid line); hazard ratio 0.18; 95% confidence interval 0.08–0.42; P<0.001). MACCE indicates major adverse cardiac and cerebrovascular events; BITA, bilateral internal thoracic arteries; SVG, saphenous vein grafts; LITA, left internal thoracic artery; and RA, radial artery.

group compared with BITA±SVG is a further limitation for the interpretation of the findings. However, even despite shorter follow-up, there is a clear difference between early and long-term outcome supporting a benefit of BITA grafting. Survival and MACCE-free survival in the RA group of our study were very similar to the results of recently published outcome studies.

Summary

The vast majority of symptomatic patients with graft failure will preferentially undergo PCI first rather than CABG reoperation. Additionally, a substantial proportion of patients will undergo repeated cardiac reintervention unrelated to previous surgical revascularization. Because current PCI studies reach better results for left main interventions compared with noncontemporary CABG surgery, further improvement of CABG surgery by MAR with the preferential use of a BITA is warranted for all CABG patients in the future.[32] Based on the results of our study, a second ITA graft provides improved results relative to overall and MACCE-free survival compared with an additional RA; therefore, the second ITA graft ought to be used more frequently for CABG surgery in the future. We conclude that the use of RITA, but not the RA, may extend the benefits of MAR to a larger population undergoing CABG surgery, producing better long-term results even though the initial operation is longer and technically more demanding.

Disclosures

None.

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CLINICAL PERSPECTIVE

Studies of coronary artery bypass grafting have implied that arterial grafts are superior to saphenous venous grafts (SVG). At this time, only the benefit of the single internal thoracic artery (ITA) has been proven by randomized trials. Moreover, observational studies on bilateral ITA use have shown similar results, namely a benefit of a second ITA over SVG. Long-term results, however, are awaited from the Arterial Revascularization Trial (ART). Sternal wound complications have prevented more common bilateral ITA use, and surgeons have been trying to find grafts that act more like ITA and less like SVG. Worldwide, the radial artery (RA) is used more commonly, but results from several studies are conflicting. Studies comparing the outcome of either concomitant RA or second ITA in addition to left ITA are missing. This propensity score–matched study was performed to investigate the outcome of RA compared with second ITA as concomitant arterial graft among 1001 consecutive coronary artery bypass grafting patients. In the study, the use of RA was associated with a significantly higher perioperative major adverse cardiac and cerebrovascular events rate ($P<0.001$) and, additionally, an SVG-like progressive graft failure. Sternal dehiscence rate was similar among both groups (3.2% versus 3.6%, $P=1.0$) and was attributed to the higher rate of skeletonized ITA grafts among patients receiving bilateral ITA. Overall survival (hazard ratio 0.23; $P=0.022$) and major adverse cardiac and cerebrovascular events–free survival (hazard ratio 0.18; $P<0.001$) were significantly improved in patients receiving second ITA. Our study provides strong evidence for the superiority of a second ITA graft compared with RA, indicating that the RA is not an equivalent alternative to a right ITA.