Associations between Adding a Radial Artery Graft to Single and Bilateral Internal Thoracic Artery Grafts and Outcomes. Insights from the Arterial Revascularization Trial.

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Abstract

Background: Whether the use of the radial artery (RA) can improve clinical outcomes in coronary artery bypass graft (CABG) surgery remains unclear. The Arterial Revascularization Trial (ART) was designed to compare survival after bilateral internal thoracic artery (BITA) over single left internal thoracic artery (SITA). In the ART, a large proportion of patients (~20%) also received a RA graft instead of a saphenous vein graft (SVG). We aimed to investigate the associations between using the RA instead of SVG to supplement SITA or BITA grafts and outcomes by performing a post-hoc analysis of the ART.

Methods: Patients enrolled in the ART (n=3102) were classified based on conduits actually received (as treated). The analysis included 2737 patients who received a RA graft (RA group, n=632) or SVG only (SVG group, n=2105) in addition to SITA or BITA grafts. The primary endpoint was the composite of myocardial infarction, cardiovascular death and repeat revascularization at 5 years. Propensity score matching and stratified Cox regression were used to compare the two strategies.

Results: MI, cardiovascular death and repeat revascularization cumulative incidence was 2.3% (95%CI 1.1-3.4), 3.5% (95%CI 2.1-5.0) and 4.4% (95%CI 2.8-6.0) in the RA group and 3.4% (95%CI 2.0-4.8), 4.0% (95%CI 2.5-5.6) and 7.6% (95%CI 5.5- 9.7) in the SVG group respectively. The composite endpoint was significantly lower in the RA group (8.8%; 95%CI 6.5-11.0) when compared with the SVG group (13.6%; 95%CI 10.8-16.3) (P=0.005). This association was present when a RA graft was used to supplement both SITA and BITA grafts (interaction P=0.62)

Conclusions: This post-hoc ART analysis showed that an additional RA was associated with lower risk for mid-term major adverse cardiac events when used to supplement SITA or BITA grafts.

Clinical Perspective

What is new?

- The use of a radial artery graft (RA) has been associated with superior angiographic patency rates when compared with saphenous vein grafts (SVG), but the clinical impact of using the RA remains unclear.
- We found that the RA used to supplement either single or bilateral internal thoracic artery grafts instead of SVG only, was associated with a significantly lower risk for major adverse cardiac events with a significantly lower rate of reintervention and marginally lower risk for cardiovascular death and subsequent myocardial infarction.

What are the clinical implications?

- The RA graft is simple to perform as its caliber and handling properties are similar to vein grafts, and in view of its superior patency over SVGs, it is an ideal conduit to achieve multiple arterial grafting and may improve patient outcomes.

Introduction

Despite increasing interest in additional arterial conduits during coronary artery bypass graft (CABG) surgery [1], the search for the optimum additional arterial conduit to supplement the left internal thoracic artery continues. The radial artery (RA) has been shown to provide better patency rates than saphenous vein grafts (SVG) [2,3] but whether this translates into superior clinical outcomes remains unclear. A few randomized controlled trials investigating the effect of RA grafts on clinical outcomes were underpowered to detect differences in clinical outcomes [4-6]. On the other hand, observational studies that have focused only on survival have reported discordant results [7-16].

The Arterial Revascularization Trial (ART) was designed to compare survival after bilateral internal thoracic artery (BITA) versus single left internal thoracic artery (SITA). The interim mid-term results (5 years) demonstrated no difference between the groups [1]. A large proportion of the ART patients (~20%) received the RA as second conduit to supplement SITA graft or as third conduit to supplement BITA grafts, making the ART the largest series of RA grafting in the context of a randomized trial involving SITA or BITA.

We aimed to investigate the associations between the use of a RA graft when used to supplement either SITA or BITA grafts and clinical outcomes by performing a post-hoc analysis of the ART.

Methods

The present study is a post-hoc analysis of 5 year outcomes of the ART trial. This research adheres to the principles set forth in the Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html). In the ART, the use of the RA was based on surgeon's discretion. For the purpose of the present analysis, patients enrolled in the ART (n=3102) were classified based on conduits actually received (as treated principle). The present analyses compared the strategy using the RA with or without additional SVG (RA

group) versus SVG only (SVG group) to supplement single or bilateral internal thoracic artery grafts (SITA and BITA).

The following patients were excluded from the present analyses: neither SVG nor RA used (n=328); patients receiving SVG but neither SITA nor BITA graft (n=30); patients receiving a RA graft but neither SITA nor BITA used (n=7).

Trial design

The ART was approved by the institutional review board of all participating centers, and informed consent was obtained from each participant. The protocol for the ART has been published [17]. Briefly, the ART is a 2-arm, randomized multicenter trial conducted in 28 hospitals in 7 countries, with patients being randomized equally to SITA or BITA grafts. Eligible patients were those with multivessel coronary artery disease undergoing CABG, including urgent patients, with grafting recommended in case of target stenosis ≥75%. Only emergency patients (refractory myocardial ischemia/cardiogenic shock) and those requiring single grafts or redo CABG were excluded.

Follow-up

Questionnaires were sent to study participants by post at 6 months and every year after surgery. No clinic visits were planned apart from the routine clinical 6-week post-operative visit. Participants were sent stamped addressed envelopes to improve the return rates of postal questionnaires. Study co-ordinators contacted participants by telephone to alert them to the arrival of the questionnaire and to ask them about medications, adverse events and health services resource use.

Study outcomes

The primary outcome for this analysis was the composite of major adverse cardiac events (MACE) at 5 years including cardiovascular (CV) death, myocardial infarction (MI) and repeat

revascularization. The association between the use of a RA graft and MACE individual components and overall mortality were also investigated.

Hospital outcomes analyzed were: hospital mortality, return to the operating room, postoperative intra-aortic balloon pump (IABP), renal replacement therapy, sternal wound infection, MI, cerebrovascular accident (CVA), repeat revascularization and postoperative atrial fibrillation (POAF). Adverse events were adjudicated by a member(s) of the Clinical Event Review Committee blind to the surgical procedure.

Statistical Analysis

For baseline characteristics, variables are summarized as mean and SD for continuous variables and percentage for categorical variables. Multiple imputation (m=3) was used to address missing data. Rubin's method [18] was used to combine results from each of *m* imputed data sets (Amelia R package). Due to lack of randomization with regards to receiving RA, a propensity score (PS) was generated for each patient from a multivariable logistic regression model based on pre-treatment covariables as independent variables with RA versus SVG as a binary dependent variable [19]. Covariables included in the PS model were: age, female sex, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) at admission, creatinine, New York Heart Association functional class (NYHA), unstable angina (UA), treated hypertension, treated hyperlipidemia, diabetes mellitus (DM), smoking, chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), transient ischemic attack (TIA), cerebrovascular accident (CVA), myocardial infarction (MI), percutaneous coronary intervention (PCI), atrial fibrillation (AF), left ventricular ejection fraction (LVEF), dual antiplatelet therapy (DAPT), off-pump surgery, bilateral internal thoracic artery (BITA), left main stem disease (LMDS), left anterior descending artery (LAD) disease, circumflex artery (CX) disease, diagonal branch (DIA) disease and right coronary artery (RCA) disease. Pairs of patients were derived using greedy 1:1 matching with a caliper of width of 0.2 standard

deviation of the logit of the PS (nonrandom R package). The quality of the match was assessed by comparing selected pre-treatment variables in propensity score–matched patients using the standardized mean difference (SMD), for which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariable imbalance. McNemar's test and paired t test were used to assess the statistical significance of the risk difference in short term outcomes in the matched sample [19]. A Cox regression model, stratified on the matched pairs [19], was used to estimate the associations between treatment and the primary outcome and overall mortality. This approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets (survival R package). Competing risk analysis (prodlim and riskRegression R packages) was used to estimate the associations between treatment and the primary endpoint individual components. As sensitivity analysis, the associations between the use of a RA graft and outcomes was tested in a mixed effect Cox model to account for clustering effect due to individual surgeons and centers [20] (http://CRAN.R-project.org/package=coxme). The association between use of a RA graft and outomes was also adjusted for medication at discharge including aspirin, clopidogrel, beta-blockers, calcium channel antagonists (CCA), statins, and angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptors blockers (ARB). Finally, possible modifiers of associations tested using interaction analyses were: age $<$ and $\geq$ 70 years; female vs male sex; diabetes vs non diabetes; reduced vs preserved LVEF; SITA vs BITA graft; off- vs on-pump surgery.

All p-values were 2-sided, with $p<0.05$ were considered to indicate statistical significance. All statistical analysis was performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

Results

Study sample

The final population included 2737 patients who received a RA graft (RA group, n=632) or SVG only (SVG group, n=2105). Among those who received a RA graft, SITA graft was used in 359 patients (57%) and BITA grafts was used in 273 patients (43%). In the RA group, 397 (63%) patients underwent total arterial revascularization while the remaining 235 (37%) received at least 1 additional SVG. In the SVG group, 1330 patients had SITA graft (63%) and the remaining 775 (37%) had BITA grafts.

Grafts configuration and targets details

Graft configurations and targets characteristics in the RA and SVG groups are summarized in Table 1. Overall, the quality (including size and need for endarterectomy) of targets grafted using the RA was not superior to targets grafted using SVG in the SVG group. Supplementary Table 1 summarizes graft configuration and target details in subjects receiving a RA graft to supplement SITA and BITA grafts respectively. When the RA was used to supplement a SITA graft, it was preferentially used to graft the circumflex artery (65%) followed by the right coronary artery (22%). When the RA was used to supplement BITA grafts, it was preferentially used to graft the right coronary artery (64%) followed by the circumflex artery (25%).

RA usage variation across surgeons and centrers

The present post-hoc analysis included a total of 157 participating surgeons and 28 cardiac centrers. The use of the RA over SVG only significantly varied across surgeons (Supplementary Figure 1, information not available in 120 cases marked as #1) and across different centers (Supplementary Figure 2).

Propensity Score matching

Before matching, the RA and SVG groups showed significant differences in terms of preoperative nitrates administration, age, functional NYHA class, rate of BITA grafts usage, BMI, diabetes and preoperative LVEF. Patients receiving the RA were two years younger and

more likely to have insulin treated diabetes and decreased LVEF. After PS matching, the two groups were comparable for all pre-treatment characteristics (Table 2, Figure 1).

Hospital outcomes

Hospital outcomes are reported in Table 3. Mortality rates and postoperative complications were comparable between the two groups.

5 year-outcomes

Five-year outcomes are reported in Table 4. The rate of MACE was 8.8% (6.5-11.0) versus 13.6% (10.8-16.3) in the RA and SVG groups respectively. The use of a RA graft was associated with significantly lower risk for MACE (HR 0.60; 95%CI 0.41-0.85; P= 0.005). This result was mainly determined by a significantly lower risk for repeat revascularization in the RA group (4.4%; 95%CI 2.8-6.0) when compared with the SVG group (7.6%; 95%CI 5.5-9.7) (HR 0.59; 95%CI 0.36-0.95; P=0.03) (Figure 2). When compared with the SVG group, the RA group had a non-significant lower risk of MI (HR 0.68; 95%CI 0.34-1.38; P=0.30), CV death (HR 0.83; 95%CI 0.46-1.51; P=0.55) and overall death (HR 0.83; 95%CI 0.54-1.27; P= 0.39). The use of a RA graft remained associated with a lower incidence of MACE when the analysis also accounted for the clustering by individual surgeons (mixed effect HR 0.55; 95%CI 0.35-0.87; P=0.01) and hospital (mixed effect HR 0.59; 95%CI 0.41-0.86; P=0.005). When the analysis was restricted to patients requiring grafts only to the left coronary system, there was a larger but not significantly lower risk for the RA group (HR 0.25; 95%CI 0.05-1.17). We saw no associations with better outcomes using a RA graft without additional SVG (HR 0.71; 95%CI 0.46-1.10) when compared with the RA with additional SVG (HR 0.40; 95%CI 0.20-0.78).

Postoperative medications

Medications prescribed at discharge are reported in Supplementary Table 2. Patients receiving a RA graft were more likely to be discharged on CCA, although only 29% of them received

CCA. At 5-year follow-up, only 112 patients in the RA group were on CCA, of which 44 patients were initially discharged on CCA. Patients in the SVG group were more likely to be discharged on dual-antiplatelet therapy with clopidogrel. After adjustment for medications prescribed at discharge, the use of the RA remained associated with lower 5-year MACE rates (adjusted HR 0.59; 95%CI 0.39-0.91; P=0.01). Among patients receiving a RA graft, CCA prescribed at discharge was associated with a numerically lower incidence of MACE (5.2% vs 10.2%; P=0.2; Figure 3).

Modifiers of the Associations between RA Graft Use and Outcomes

None of possible modifiers of association investigated was found to influence the associations between RA graft use and MACE when compared with SVG only (Figure 4). Subgroup analysis showed that the association between the RA and lower risk of MACE was present for both SITA and BITA grafts (interaction P=0.62; Supplementary Table 3, Supplementary Figure 3 and Supplementary Figure 4).

Angiographic follow-up

Angiographic follow-up was performed only in symptomatic patients and therefore patency rates of different conduits could not be analyzed. For those who underwent repeat revascularization, clinical presentation and revascularization strategy adopted were not available in all cases. In the RA group, graft failure and native coronary disease progression were documented in 4 and 21 cases respectively among 27 cases of repeat revascularization. In the SVG group, graft failure and native coronary disease progression were documented in 54 and 90 cases respectively among 152 cases of repeat revascularization. All failed grafts were reported to be SVG. In the RA group, need for repeat CABG and repeat PCI was documented in 2 and 23 cases respectively. In the SVG group, need for repeat CABG and repeat PCI was documented in 6 and 113 cases respectively.

Discussion

The main finding of the present analysis is that a RA graft (with or without additional vein graft) used to supplement either SITA and BITA grafts instead of SVG only, was associated with ignificantly lower risk for major adverse cardiac events with a significantly lower rate of reintervention and marginally lower risk for CV death and subsequent MI, despite the fact that the quality of RA targets was not superior to SVG targets. On the other hand, use of a RA graft did not increase operative mortality or complications.

Although several randomized trials have shown that use of a RA graft is associated with superior 5 year patency rates when compared with SVGs [3,4], whether this translates into better clinical outcomes remains uncertain. In fact, randomized controlled trials conducted to date are limited by small sample sizes and the results are inconclusive. The Radial Artery Versus Saphenous Vein Patency Randomized (RSVP) Trial [4] compared 82 and 60 patients randomized to receive the SITA and RA grafts or SITA and SVGs. The only robust clinical outcome assessed was mortality. The 5-year survival rate was 94.4%, with no significant difference in survival between the 2 groups. In the Radial Artery Patency and Clinical Outcome (RAPCO) Study [5], patients aged 70 years or more were randomly assigned to receive either SITA and RA grafts (n=73) or SITA and SVGs grafts (n=80). At 5-year follow-up, cardiac event-free survival estimates were 0.84 (95% CI 0.64-0.99) for the RA subgroup and 0.89 (95% CI 0.72-0.99) for the SVG subgroup. Petrovic, et al. [6] randomized 200 patients to receive either SITA and RA grafts or SITA and SVGs. They found no difference in 8 year clinical outcomes. In a larger trial by Goldman, et al. [21], 757 patients were randomly assigned to receive either SITA and RA grafts (n=366) or SITA and SVGs grafts (n=367). There was no significant difference between the 2 groups at 1 year in terms of death, myocardial infarction, stroke, and repeat coronary revascularization. However, outcomes beyond 1 year are not available.

On the other hand, several retrospective studies that investigated the associations between the use of RA used as additional arterial conduit instead of SVG and outcomes reported discordant results for survival. Schwann, at al. [7] compared SITA+RA and SITA+SVG in two institutional US cohorts. Kaplan-Meier survival was significantly better for radial artery grafting ($P < 0.001$). Hayward, et al. [8] compared 1832 patients who received at least one RA graft in addition to SITA with 749 (29%) who received SITA and veins only from a multicenter database. At 7 years, survival rates between the RA and SVG groups were similar (RA: 75 ± 2.6% vs SVG: 74 ± 2.9%, $P = 0.65$). A few studies have investigated the associations between using RA grafts and survival in the context of BITA grafting with conflicting results. Di Mauro and colleagues [12] reported survival at 8 years of 91.9% ± 2.9% among 87 patients undergoing BITA+RA grafting and 95.6% ± 0.9% among patients undergoing BITA+SVG ($P = 0.12$). More recently, Grau and coworkers [13] published a series of 183 patients undergoing BITA+RA grafting. Long-term survival in the BITA+RA groups were comparable to those in the BITA+SVG groups ($P = .25$). Mohammadi and associates [14] have reported comparable long-term survival in 249 matched pairs of patients undergoing BITA+RA versus BITA+SVG ($P = 0.44$). Shi, et al. [15] compared 262 matched patient-pairs of BITA+RA and BITA+SVG. BITA+RA and at 15 years, BITA + RA patients experienced better risk-adjusted survival (72 ± 6.0% vs 82 ± 5.2%, $P = 0.02$). Finally, we have reported a longer term survival comparison in 275 matched patient-pairs of BITA+RA and BITA+SVG from a single institution [16], and the two groups showed comparable 15 year survival rates (log-rank $P = 0.54$).

The present post-hoc ART analyses support the hypothesis that an additional RA may reduce mid-term major adverse cardiac events when used to supplement either SITA or BITA grafts when compared with SVG only. The better clinical outcomes observed in patients receiving a RA graft can be attributed to its superior patency rate when compared with SVG [2,3,22]. Moreover, it has been shown that RA grafting has a strong protective effect against progression

of native coronary artery disease in previously grafted vessels that can translate into reduced incidence of adverse cardiac events [23].

An interim analysis of the ART [1] has shown that BITA grafts did not improve 5 year outcomes when compared with a SITA strategy. However, the primary endpoint of the ART is 10-year survival and those data will be needed to draw any conclusions on whether there is any potential benefit of BITA grafts over the longer term. Previous studies have supported the hypothesis that the beneficial effect from BITA on clinical outcomes may be delayed by as much as 7 to 10 years [24]. On the other hand, the RA graft is simple to perform as its caliber and handling properties are similar to vein grafts. The superior patency rate of the RA over SVGs at 5 years has been demonstrated by several randomized controlled trials [2] and the use of a RA graft has been reported to exhibit maximal benefit between 0.5 and 5 years [7].

Main limitations of the present analyses are the nonrandomized comparison and the low number of outcome events. Propensity score modeling included several variables, but we cannot exclude a residual selection bias based on a unmeasured or unmeasurable characteristics.

In conclusion, the present post-hoc analysis of the ART showed that the use of an additional RA graft to supplement both SITA and BITA grafts was associated with a lower risk for MACE at 5 years. Based on these results, it seems reasonable to consider the use of a RA graft a valid option for multiple arterial grafting.

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Figure Legend

Figure 1. Changes in standardized mean difference (SMD) between the radial artery (RA) and the saphenous vein graft (SVG) groups before and after propensity score matching (SMD: standardized mean difference; BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; NYHA: New York Heart Association; UA: unstable angina; COPD: Chronic obstructive pulmonary disease; PVD: peripheral vascular disease; TIA: transint ischemic attack; CVA: cerebrovascular accident; MI: myocardial infarction; PCI: percutaneous coronary intervention; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; DAPT: dual antiplatelet therapy; BITA bilateral internal thoracic artery; LMSD: left main stem disease; LAD: left anterior descending artery disease; CX: circumflex disease; DIA: diagonal branch disease; RCA: right coronary artery disease).

Figure 2. Cumulative incidence of myocardial infarction (MI), revascularization, cardiovascular (CV) death and the composite of major adverse cardiac event (MACE) in the Radial artery (RA) and Saphenous Vein Graft (SVG) group respectively after matching.

Figure 3. Cumulative incidence of the composite of major adverse cardiac event (MACE) in the Radial artery (RA) according to calcium channel antagonists (CCA) prescribed at discharge.

Figure 4. Subgroup analysis and interaction analysis on the effect of the radial artery (RA) over saphenous vein graft (SVG) on the composite of major adverse cardiac event (MACE)

Table 1. Conduits and relative targets details in the RA (top) and SVG (bottom) groups

	RA group (n=632)				
	LITA	other	RA	RITA	SVG
N conduits used	627	4	362	278	235
N of distal anastomosis	700	4	789	291	316
Sequential anastomosis	131 (18.7)	2 (50.0)	163 (20.7)	27 (9.3)	21 (6.6)
Proximal Anastomosis* n(%)					
Aorta	34 (16.3)	1 (25.0)	574 (73.4)	20 (16.8)	304 (97.1)
Other conduit	175 (83.7)	3 (75.0)	208 (26.6)	99 (83.2)	9 (2.9)
Target n (%)					
CX	130 (18.6)	2 (50.0)	394 (49.9)	123 (42.3)	75 (23.7)
DIA	75 (10.7)	0 (0.0)	75 (9.5)	21 (7.2)	57 (18.0)
LAD	493 (70.4)	0 (0.0)	24 (3.0)	133 (45.7)	2 (0.6)
RCA	2 (0.3)	2 (50.0)	296 (37.5)	14 (4.8)	182 (57.6)
Vessel_diameter (mean (sd))	1.79 (0.35)	1.75 (0.20)	1.73 (0.38)	1.79 (0.37)	1.70 (0.33)
Vessel quality n (%)					
Good	287 (41.5)	2 (50.0)	296 (37.9)	102 (35.5)	141 (45.8)
Satisfactory	327 (47.3)	1 (25.0)	419 (53.6)	144 (50.2)	135 (43.8)
Poor	78 (11.3)	1 (25.0)	66 (8.5)	41 (14.3)	32 (10.4)
Endarterectomy n (%)	1 (0.1)	0 (0.0)	10 (1.3)	4 (1.4)	2 (0.6)
	SVG group (n=2105)				
	LITA	other	RA	RITA	SVG
N conduits used	2079	0	0	801	2015
N of distal anastomosis	2221	0	0	825	3877
Sequential anastomosis	182 (8.2)	-	-	43 (5.2)	271 (7.0)
Proximal Anastomosis* n(%)		-	-		
Aorta	48 (16.7)	-	-	66 (22.2)	3713 (96.2)
Other conduit	237 (82.3)	-	-	229 (77.1)	145 (3.8)
Target n (%)					
CX	356 (16.0)			377 (45.7)	1673 (43.2)
DIA	176 (7.9)	-	-	53 (6.4)	480 (12.4)
LAD	1687 (76.0)	-	-	378 (45.8)	71 (1.8)
RCA	2 (0.1)	-	-	17 (2.1)	1653 (42.6)
Vessel_diameter (mean (sd))	1.86 (0.46)	-	-	1.87 (0.44)	1.83 (0.51)
Vessel quality					
Good	1048 (48.1)	-	-	397 (49.2)	1816 (47.7)
Satisfactory	813 (37.3)	-	-	295 (36.6)	1555 (40.9)
Poor	317 (14.6)	-	-	115 (14.3)	433 (11.4)
Endarterectomy (%)	10 (0.5)	-	-	3 (0.4)	32 (0.8)

* for LITA and RITA, numbers refer to non in-situ configuration

LITA: left internal thoracic artery; RA: radial artery; RITA: right internal thoracic artery; SVG: saphenous vein graft; CX: circumflex; LAD: left anterior descending artery; DIA; diagonal branch; RCA: right coronary artery

Table 2. Baseline characteristics in the RA and unmatched and matched SVG group respectively with relative P value and standardized mean difference.

	RA group	SVG group (unmatched)	P	SMD	SVG group (matched)	P	SMD
N	632	2105			632		
Age (mean (sd))	62.30 (9.08)	64.01 (8.88)	<0.001	0.190	62.64 (8.96)	0.51	0.037
Female, n(%)	80 (12.7)	288 (13.7)	0.55	0.030	80 (12.7)	1.000	<0.001
BMI (mean (sd))	28.63 (4.01)	28.13 (3.97)	0.006	0.124	28.85 (4.24)	0.32	0.056
SBP (mean (sd))	132.49 (18.85)	131.56 (17.82)	0.26	0.050	132.14 (18.22)	0.74	0.019
DBP (mean (sd))	74.98 (11.37)	74.98 (10.91)	0.99	0.001	74.30 (10.95)	0.28	0.061
Creatinine mmol/L (mean (sd))	96.00 (20.97)	97.23 (21.87)	0.21	0.057	96.43 (21.20)	0.72	0.020
NYHA III/IV , n(%)	106 (16.8)	478 (22.7)	0.002	0.150	102 (16.1)	0.82	0.017
Unstable Angina , n(%)	41 (6.5)	166 (7.9)	0.28	0.054	48 (7.6)	0.51	0.043
Treated Hypertension , n(%)	471 (74.5)	1653 (78.5)	0.04	0.095	471 (74.5)	1.00	<0.001
Treated Hyperlipidemia , n(%)	588 (93.0)	1981 (94.1)	0.37	0.044	590 (93.4)	0.91	0.013
Diabetes, n(%)			0.07	0.099		0.97	0.014
No history of diabetes	465 (73.6)	1614 (76.7)			461 (72.9)		
Insulin treated diabetes	46 (7.3)	106 (5.0)			47 (7.4)		
Non insulin treated diabetes	121 (19.1)	385 (18.3)			124 (19.6)		
Smoking, n(%)			0.47	0.056		0.91	0.025
Current smoking	94 (14.9)	290 (13.8)			89 (14.1)		
Ex-smoker	345 (54.6)	1207 (57.3)			351 (55.5)		
Never smoked	193 (30.5)	608 (28.9)			192 (30.4)		
COPD , n(%)	11 (1.7)	60 (2.9)	0.16	0.074	12 (1.9)	1.00	0.012
Asthma, n(%)	30 (4.7)	88 (4.2)	0.61	0.027	28 (4.4)	0.89	0.015
PVD, n(%)	45 (7.1)	148 (7.0)	1.00	0.003	51 (8.1)	0.60	0.036
TIA, n(%)	19 (3.0)	85 (4.0)	0.28	0.056	13 (2.1)	0.37	0.060
CVA, n(%)	15 (2.4)	67 (3.2)	0.36	0.049	12 (1.9)	0.70	0.033
MI, n(%)	260 (41.1)	891 (42.3)	0.63	0.024	269 (42.6)	0.65	0.029
PCI, n(%)	86 (13.6)	332 (15.8)	0.21	0.061	91 (14.4)	0.75	0.023

AF pre, n(%)	8 (1.3)	32 (1.5)	0.78	0.022	11 (1.7)	0.64	0.039
LVEF pre, n(%)			0.09	0.100		0.88	0.028
≥50%	454 (71.8)	1602 (76.1)			446 (70.6)		
31-49%	163 (25.8)	456 (21.7)			170 (26.9)		
≤30%	15 (2.4)	47 (2.2)			16 (2.5)		
DAPT pre, n(%)	135 (21.4)	484 (23.0)	0.42	0.039	152 (24.1)	0.28	0.064
Antiplatelet within 3 days , n(%)	96 (15.2)	350 (16.6)	0.43	0.039	91 (14.4)	0.75	0.022
Nitrates pre , n(%)	249 (39.4)	1079 (51.3)	<0.001	0.240	255 (40.3)	0.77	0.019
OFF-PUMP , n(%)	239 (37.8)	842 (40.0)	0.35	0.045	247 (39.1)	0.69	0.026
BITA , n(%)	273 (43.2)	775 (36.8)	0.004	0.130	272 (43.0)	1.00	0.003
LMSD, n(%)	142 (22.5)	410 (19.5)	0.11	0.074	134 (21.2)	0.63	0.031
LAD, n(%)	625 (98.9)	2073 (98.5)	0.56	0.036	625 (98.9)	1.00	<0.001
CX , n(%)	581 (91.9)	1952 (92.7)	0.56	0.030	576 (91.1)	0.69	0.028
DIA, n(%)	221 (35.0)	691 (32.8)	0.34	0.045	228 (36.1)	0.72	0.023
RCA , n(%)	469 (74.2)	1598 (75.9)	0.41	0.039	473 (74.8)	0.85	0.015
N grafts (%)			0.84	0.053		0.82	0.070
2	69 (10.9)	246 (11.7)			78 (12.3)		
3	332 (52.5)	1119 (53.2)			314 (49.7)		
4	191 (30.2)	630 (29.9)			201 (31.8)		
5	38 (6.0)	104 (4.9)			36 (5.7)		
6	2 (0.3)	6 (0.3)			3 (0.5)		

RA: radial artery; SVG: saphenous vein graft; SMD: standardized mean difference; BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; NYHA: New York Heart Association; UA: unstable angina; COPD: Chronic obstructive pulmonary disease; PVD: peripheral vascular disease; TIA: transint ischemic attack; CVA: cerebrovascular accident; MI: myocardial infarction; PCI: percutaneous coronary intervention; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; DAPT: dual antiplatelet therapy; BITA bilateral internal thoracic artery; LMSD: left main stem disease; LAD: left anterior descending artery; CX: circumflex; DIA: diagonal; RCA: right coronary artery.

Table 3. Hospital outcomes

	RA group	SVG group (unmatched)	P*	SVG group (matched)	P‡
N	632	2105		632	
Death, n(%)	9 (1.4)	20 (1.0)	0.42	5 (0.8)	0.42
Return to operating room, n(%)	27 (4.3)	72 (3.4)	0.38	19 (3.0)	0.29
IABP post, n(%)	21 (3.3)	91 (4.3)	0.32	29 (4.6)	0.31
Renal replacement therapy, n(%)	45 (7.1)	100 (4.8)	0.03	36 (5.7)	0.36
Sternal wound infection, n(%)	25 (4.0)	67 (3.2)	0.41	19 (3.0)	0.44
MI, n(%)	6 (0.9)	40 (1.9)	0.15	15 (2.4)	0.08
CVA, n(%)	5 (0.8)	31 (1.5)	0.26	5 (0.8)	1.00
Repeat Revascularization, n(%)	2 (0.3)	13 (0.6)	0.55	5 (0.8)	0.45
POAF, n(%)	152 (24.1)	524 (24.9)	0.71	165 (26.1)	0.44

*chi squared test (binary outcomes) and paired t-test (continuous outcomes)

‡ McNemar's test (binary outcomes) and paired t-test (continuous outcomes)

RA: Radial artery; SVG: saphenous vein graft; IABP: intra-aortic balloon pump; MI: myocardial infarction; CVA: cerebral vascular accident; POAF: postoperative atrial fibrillation.

Table 4. Five-year outcomes rates (95% confidence interval, CI)

	RA group	SVG group (unmatched)	P*	SVG group (matched)	P‡
n	632	2105		632	
MI	14 (2.3%[1.1-3.4])	78(3.7%[2.9-4.6])	0.07	21(3.4%[2.0-4.8])	0.30
Repeat revascularization	27(4.4%[2.8-6.0])	152(7.3%[6.2-8.5])	0.008	47(7.6%[5.5- 9.7)	0.033
CV death	22(3.5%[2.1-5.0])	73(3.5%[2.7-4.3])	0.99	25(4.0%[2.5-5.6])	0.55
Overall death	45 (7.3%(5.2-9.3])	189(9.2%[7.9-10.4])	0.15	51(8.3%[6.1-10.5])	0.39
CV death/MI/repeat revascularization	53(8.8%[6.5--11.0])	261 (12.9%[11.4-14.3])	0.005	82(13.6%[10.8-16.3])	0.005

* unadjusted Cox model

‡ Cox model stratified for matched pairs

RA: radial artery; SVG: saphenous vein graft; CV: cardiovascular; MI: myocardial infarction