



Original research

Right internal mammary artery versus radial artery as second arterial conduit in coronary artery bypass grafting: A case-control study of 1526 patients



Shahzad G. Raja^{*}, Umberto Benedetto, Anand Jothidasan, Raju Krishnam Jujjavarapu, Uchenna Franklin Ukwu, Fabio De Robertis, Toufan Bahrami, Jullien A. Gaer, Mohamed Amrani, on behalf of the Harefield Cardiac Outcomes Research Group

Department of Cardiac Surgery, Harefield Hospital, London, United Kingdom

HIGHLIGHTS

- Arterial grafts improve long-term outcomes in coronary artery bypass grafting (CABG).
- Radial artery (RA) is preferred over right internal mammary artery (RIMA) for CABG.
- RIMA is underutilised due to perceived operative risk and sternal wound issues.
- This largest clinical study to date validates short-term safety of RIMA.
- This study also confirms superiority of RIMA over RA in the long-term.

ARTICLE INFO

Article history:

Received 15 June 2014

Received in revised form

4 August 2014

Accepted 9 August 2014

Available online 19 August 2014

Keywords:

Coronary artery bypass grafting

Multiple arterial grafting

Radial artery

Internal mammary artery

Propensity score analysis

ABSTRACT

Objective: Additional arterial grafts such as the right internal mammary artery (RIMA) or the radial artery (RA) have been proposed to improve long term outcomes in coronary artery bypass grafting (CABG). RA is largely preferred over RIMA as it is less technically demanding and there is a perception that bilateral IMA usage increases the risk of sternal wound complications. However, there is a paucity of direct comparison of the two conduits to guide surgeons to choose the best second arterial conduit for CABG. **Methods:** A propensity score adjusted analysis of patients undergoing multiple arterial grafting with RIMA ($n = 747$) and RA ($n = 779$) during the study period (2001–2013) was conducted to investigate the impact of the two strategies on early and late outcomes. **Results:** RIMA did not increase the incidence of postoperative complications including deep sternal wound infection ($P = 0.8$). Compared to the RIMA, the RA was associated with an increased risk for late mortality (Hazard Ratio [HR] 1.9; 95% confidence interval (CI) 1.2–3.1; $P = 0.008$) and repeat revascularization (HR 1.5; 95% CI 1.0–2.2; $P = 0.044$). A trend towards an extra risk for late mortality from RA over RIMA was observed among diabetic (HR 3.3; 95% CI 1.1–9.7) and obese patients (HR 2.1; 95% CI 0.8–5.46). **Conclusions:** RIMA as a second conduit did not increase the operative risk including sternal wound complications and improved long term outcomes including overall survival when compared to RA. This advantage was stronger among diabetic and obese patients. These findings strongly support RIMA as the first choice second arterial conduit in CABG. Further randomized studies with angiographic control and long-term follow-up are needed to address this issue.

© 2014 IJS Publishing Group Limited. Published by Elsevier Ltd. All rights reserved.

Coronary artery bypass grafting (CABG) is a well-established therapy for patients with multivessel coronary disease, with excellent short- and long-term outcomes [1]. This is best

illustrated by studies comparing percutaneous coronary interventions with surgical revascularization, where CABG continues to offer enhanced freedom from re-intervention and improved event-free survival [2,3]. However, the success of CABG, the gold standard for the treatment of multivessel coronary artery disease, is limited by poor long-term vein-graft patency [1,4,5]. By contrast, the left internal mammary artery (LIMA) has been

^{*} Corresponding author.

E-mail addresses: drshahzad@hotmail.com, drsgraja@gmail.com (S.G. Raja).

demonstrated to have superior graft patency rate and has provided excellent clinical results [6,7] suggesting that the use of multiple arterial conduits for CABG may be beneficial for long-term results [1,8–10].

Despite increasing recognition that multiple arterial conduits improve long-term outcomes following CABG, the quest for the second best arterial conduit to supplement LIMA continues [11]. Over the past decade, right internal mammary artery (RIMA) and radial artery (RA) have emerged as the most likely contenders for this slot. The use of RIMA as a second arterial graft has been shown to improve long-term survival as well as provide superior freedom from re-intervention when compared with single-LIMA strategy [12,13]. Bilateral IMA use is, however, still limited because of the increased operative time, the potentially increased morbidity rate, and the technical complexity of the operation [14]. On the other hand, RA due to being larger and easier to work with than the RIMA; easier to harvest; and not associated with sternal wound infection (SWI) [15,16] is largely preferred over RIMA. Despite, these aforementioned merits and demerits of RIMA and RA there is a paucity of direct comparison of the two conduits to guide surgeons to choose the best second arterial conduit for CABG.

The present study was undertaken to investigate the impact of RIMA or RA as the second conduit on early and late outcomes following multiple arterial grafting.

1. Methods

1.1. Study population

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local ethical committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analysed prospectively collected data from the institutional surgical database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) from April 2001 to May 2013. The PATS database captures detailed information on a wide range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients undergoing CABG in our institution. The data is collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain & Ireland database criteria. The database is maintained by a team of full-time clinical information analysts, who are responsible for continuous prospective data collection as part of a continuous audit process. Data collection is validated regularly.

Patients included in the final analysis met the following criteria: a) first time isolated CABG; b) ≥ 2 grafts received; c) surgical strategies included single LIMA for the left anterior descending (LAD) artery and the radial artery for non LAD targets with or without additional saphenous vein grafts (RA group) or the use of the bilateral internal mammary arteries with or without additional saphenous vein grafts (RIMA group).

1.2. Operative technique

Grafting strategy, choice of conduits and harvesting technique was influenced by surgeon's preference in accordance with the universally recognized indications and contraindications. All interventions were performed via a midline sternotomy. Left and right IMA were harvested with minimal trauma as pedicled or skeletonised grafts and treated with papaverine solution prior to use. Great saphenous vein was harvested using open technique or vein stripper prior to 2007 and endoscopically from then onwards. RA was harvested from the non-dominant arm and

treated with a flushing solution that consisted of verapamil hydrochloride 5 mg, nitroglycerin 2.5 mg, 20 mL of blood, and 2000 U of heparin.

Conventional CABG on CPB was performed at 34 °C. CPB was instituted with single two-stage right atrial cannulation and an ascending aorta perfusion cannula. Standard bypass management included membrane oxygenators, arterial line filters, and non-pulsatile flow of 2.4 l/min/m², with a mean arterial pressure greater than 50 mm Hg. The myocardium was protected by using intermittent antegrade cold blood cardioplegia (4:1 blood to crystalloid ratio). Anticoagulation was achieved using 300 U/kg of heparin. If required, heparin was supplemented to maintain the activated clotting time above 480 s and was reversed by protamine at the end of the procedure.

For off-pump CABG the heart was stabilised using a suction-irrigation tissue stabilisation system. A deep pericardial retraction suture helped position the heart for grafting. Anticoagulation was achieved with 150 U/kg of heparin. If required, heparin was supplemented to maintain the activated clotting time above 250 s and was reversed by protamine at the end of the procedure. Blood pressure was continually optimised during the procedure, and the mean arterial pressure was maintained above 50 mm Hg by repositioning the heart and by intravenous fluids or selective use of vasoconstrictors, or both.

1.3. Postoperative management

All patients received intravenous nitroglycerin (0.1–8 $\mu\text{g kg}^{-1} \text{min}^{-1}$) infusions for the first 24 h unless hypotensive (systolic blood pressure < 90 mm Hg). Choice of inotropic agents was dictated by the haemodynamic data. Other routine medications included daily aspirin and resumption of cholesterol-lowering agents and β -blockers unless contraindicated. All diabetic patients were commenced on an insulin infusion immediately after surgery to maintain normoglycaemia. Dose of insulin infusion was adjusted according to the patients' blood glucose level in accordance with an institutional protocol. Insulin infusion was stopped once regular oral hypoglycaemics and subcutaneous insulin therapy was commenced. Calcium channel blockers were not prescribed in the postoperative period for patients with RA grafts due to lack of evidence for their efficacy.

1.4. Pre-treatment variables and study end-point

The effect of the RA over the RIMA was adjusted for the following 24 pre-treatment variables: age, female gender, prior NYHA functional class III–IV, history of congestive heart failure (HxCHF), prior myocardial infarction (MI) prior percutaneous coronary intervention (PCI), diabetes mellitus (DM), hypertension, hypercholesterolaemia, current smoking, chronic obstructive pulmonary disease (COPD), cerebrovascular accident (CVA), peripheral vascular disease (PVD), history of atrial fibrillation (AF), left main stem (LMS) disease, left ventricular ejection fraction (LVEF) less than 50%, renal impairment defined as a serum creatinine more than 200 $\mu\text{mol/l}$, body mass index ≥ 30 , non-elective indication, preoperative use of intra-aortic balloon pump (IABP), surgery performed by resident, number of grafts, incomplete revascularization and the use of cardiopulmonary bypass.

The short-term outcomes investigated were: the incidence of superficial and deep sternal wound infection (SWI) as defined by the Centers for Disease Control and Prevention [17], postoperative CVA, need for renal replacement therapy (RRT), reintubation for acute respiratory failure, re-exploration for bleeding, postoperative atrial fibrillation (POAF) and operative mortality (within 30 days).

Long-term outcomes investigated was all-cause late mortality which represents the most robust and unbiased index because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments [18]. In addition we investigated the need for repeat revascularization including PCI and/or redo CABG.

Information about death from any cause is regularly obtained from the General Register Office approximately 1 week after the event and data on repeat revascularization from national surgical and interventional database.

1.5. Statistical analysis

The authors adhered to STROBE guidelines [19] for reporting observational studies. For baseline characteristics, variables are summarized as mean for continuous variables and proportion for categorical variables.

Multiple imputation using bootstrapping-based expectation-maximization algorithm was used to address missing data. To control for measured potential confounders in the data set, a propensity score (PS) was generated for each patient from a multi-variable logistic regression model based on 24 pre-treatment covariates as independent variables with treatment type (RA versus RIMA) as a binary dependent variables. The resulting propensity score represented the probability that a patient received RA over RIMA as second arterial conduit. Pairs of patients receiving BIMA and SIMA with RA were derived using greedy 1:1 matching with a caliper of width of 0.20 Standard Deviation of the logit of the PS. The quality of the match was assessed by comparing selected pre-treatment variables in propensity score-matched patient using the standardized mean difference (SMD), by which an absolute standardized difference of greater than 20% is suggested to represent meaningful covariate imbalance. Analytic methods for the estimation of the treatment effect in the matched sample included McNemar's to compare proportions. Kaplan–Meier survival curves between treated and untreated subjects in the matched sample were compared using a test described by Klein and Moeschberger. **R version 2.15.2** (<http://www.R-project.org>), **Amelia package** (<http://www.jstatsoft.org/v45/i07/>), **MatchIt package** (<http://www.jstatsoft.org/v42/i08/>), **survival package** (<http://CRAN.R-project.org/package=survival>) and **survplot package** (<http://CRAN.R-project.org/package=survplot>) were used for statistical analysis.

2. Results

The study population consisted of 1526 patients undergoing CABG receiving RA ($n = 779$, 51%) or RIMA ($n = 747$, 49%) as second arterial conduit. In the RIMA group, the RIMA was used as in-situ graft to the LAD in 453 cases. For these cases, the LIMA was used as in-situ graft to the circumflex territory. A total of 165 patients had the RIMA grafted as in-situ conduit to the circumflex territory through the transverse sinus. The RIMA was used as Y graft to the circumflex territory in 90 cases and to the right coronary artery in 39 cases. In the RA group, LAD was grafted with in-situ LIMA in all cases.

The RA was used to graft the right coronary artery territory in 283 cases, non-LAD targets in the LAD territory in 38 cases and the circumflex territory in the remaining cases. The RA was used as a Y graft to the circumflex territory in 96 cases and to the right coronary artery in 23 cases.

The index of completeness of revascularisation, defined as the total number of distal grafts constructed divided by the number of the affected coronary vessels reported on the preoperative

coronary angiogram, was similar for the two groups (RIMA = 1.16 ± 0.22 versus RA = 1.14 ± 0.27 ; $P = 0.76$).

2.1. Missing data

Fraction missing ranged from 0% (age) to 2.1% (HxCHF). Pattern of missingness in the data were 36 and rows after listwise deletion were 1361. Rows after imputation were 1526 and the imputation models showed normal expectation-maximization convergence.

2.2. PS matching

Table 1 summarizes for each pre-treatment variable, the unmatched and matched means for the treatment group and control group with relative SMD. Before matching, 6 out of 24 pre-treatment covariates showed SMD equal or higher than 0.20. Specifically, patients receiving RA were older, more likely to have diabetes and a body mass index equal or higher than 30. Patients receiving RA were more likely operated on by a trainee. On the other hand, patients receiving RIMA were more likely to have a previous PCI and non-elective indication. PS matching created a total of 510 matching sets. After matching, all covariates were well balanced among the 2 groups being SMD less than 20% for all pre-treatment variables. PS distribution among RIMA and RA groups was significantly different before matching (0.58 versus 0.41) but comparable in the matched sample (0.52 versus 0.49, **Fig. 1**).

2.3. Short-term outcomes

Fig. 2 shows the rate of postoperative complications and operative mortality (within 30 days) in the matched sample. The rate of deep SWI was comparable in the RA and RIMA groups (13 versus 14; $P = 0.8$). With regard to other postoperative complications the two groups did not differ for need for re-exploration for bleeding which was required in 24 and 24 patients ($P = 0.88$), re-intubation which occurred in 12 and 14 patients ($P = 0.84$), postoperative RRT which was required in 20 and 16 patients ($P = 0.61$), the incidence of postoperative CVA which was observed in 6 and 4 patients ($P = 0.75$) and POAF which was observed in 115 and 94 patients ($P = 0.16$) in the RA and RIMA groups respectively. Operative mortality rate was 12 and 5 among patients receiving RIMA and RA respectively ($P = 0.84$).

2.4. Long-term outcomes

In the matched sample the mean follow-up time was 8.0 years [interquartile range: 3.0–10.3, max 12.2]. A total of 62 deaths in the RA group and 23 deaths in RIMA group were recorded. Survival probability was $94.5\% \pm 1.0$ versus 97.8 ± 0.6 at 1 year, 91.7 ± 1.2 versus 94.4 ± 1.2 at 5 years and 87.8 ± 1.4 versus 93.4 ± 1.5 at 10 years in the RA and the RIMA groups respectively (**Fig. 3**). Compared to the RIMA, the RA was associated with an increased risk for late mortality (Hazard Ratio [HR] 1.9; 95% confidence interval (CI) 1.2–3.1; $P = 0.008$).

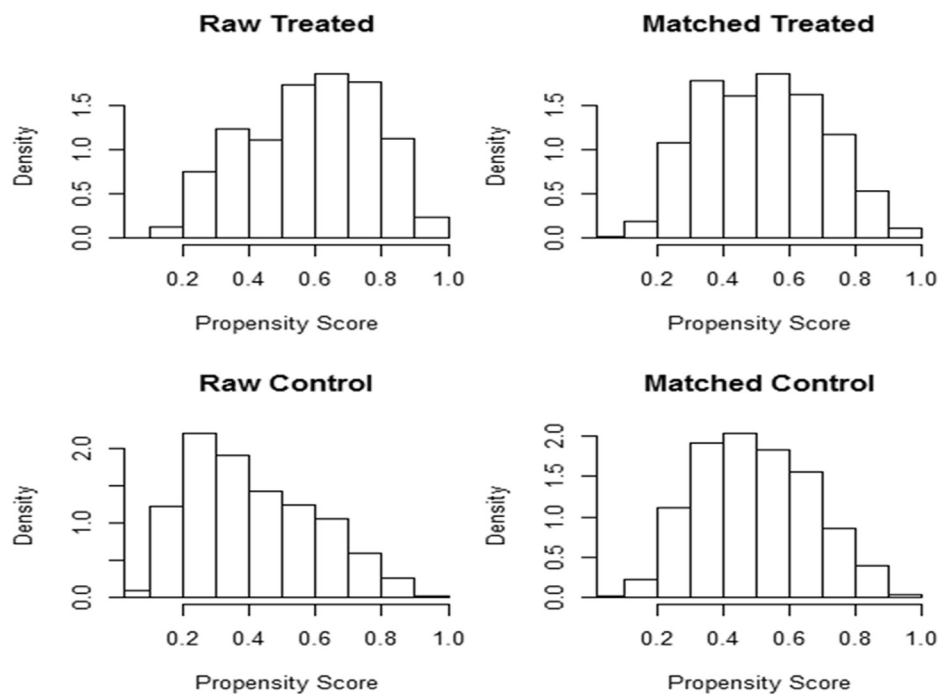
A total of 86 and 39 patients required repeat revascularization in the RA and RIMA groups respectively. In the RA group, 44 patients required repeat intervention due to RA graft failure, 32 due to saphenous vein graft failure, 8 due to progression of disease in the native coronary arteries, and 2 due to LIMA graft failure. On the other hand, in the RIMA group, repeat revascularization was undertaken to address RIMA failure in 4 patients, LIMA failure in 2 patients, progression of disease in native coronary arteries in 13 patients and 20 cases of saphenous vein graft failure. Repeat revascularization free survival probability was $93.7\% \pm 1.0$ versus 95.9 ± 0.9 at 1 year, 89.3 ± 1.3 versus 91.6 ± 1.4 at 5 years and

Table 1

Patients' characteristics in the unmatched and matched samples.

| | Unmatched RA N = 779 | Unmatched RIMA N = 747 | SMD | Matched RA N = 510 | Matched RIMA N = 510 | SMD |
|-----------------------|----------------------|------------------------|-------|--------------------|----------------------|-------|
| PS distance | 0.58 | 0.41 | 0.93 | 0.52 | 0.49 | 0.15 |
| Age | 62.37 | 60.22 | 0.25 | 62.02 | 61.49 | 0.06 |
| Female | 0.16 | 0.11 | 0.14 | 0.15 | 0.12 | 0.10 |
| NYHA III–IV | 0.25 | 0.20 | 0.13 | 0.23 | 0.20 | 0.06 |
| HxCHF | 0.04 | 0.04 | −0.01 | 0.04 | 0.04 | 0.03 |
| Prior MI | 0.40 | 0.40 | −0.02 | 0.40 | 0.39 | 0.01 |
| Prior PCI | 0.10 | 0.18 | −0.25 | 0.12 | 0.12 | −0.01 |
| Hypercholesterolaemia | 0.86 | 0.86 | 0.02 | 0.85 | 0.85 | 0.00 |
| Hypertension | 0.70 | 0.73 | −0.05 | 0.72 | 0.70 | 0.03 |
| Current smoking | 0.12 | 0.12 | 0.00 | 0.12 | 0.12 | −0.01 |
| COPD | 0.07 | 0.08 | −0.03 | 0.07 | 0.07 | 0.00 |
| CVA | 0.06 | 0.03 | 0.14 | 0.04 | 0.04 | 0.01 |
| PVD | 0.07 | 0.06 | 0.02 | 0.06 | 0.06 | 0.02 |
| HxAF | 0.02 | 0.02 | 0.00 | 0.03 | 0.02 | 0.03 |
| LMS disease | 0.26 | 0.33 | −0.16 | 0.28 | 0.31 | −0.05 |
| LVEF less than 0.50 | 0.18 | 0.13 | 0.12 | 0.17 | 0.15 | 0.05 |
| Non elective | 0.17 | 0.29 | −0.32 | 0.21 | 0.22 | −0.04 |
| Renal impairment | 0.01 | 0.02 | −0.10 | 0.01 | 0.01 | 0.00 |
| Diabetes mellitus | 0.31 | 0.16 | 0.32 | 0.25 | 0.21 | 0.09 |
| BMI ≥ 30 | 0.35 | 0.23 | 0.24 | 0.30 | 0.28 | 0.02 |
| Preoperative IABP | 0.01 | 0.02 | −0.12 | 0.01 | 0.01 | 0.00 |
| Trainee as operator | 0.54 | 0.29 | 0.50 | 0.44 | 0.41 | 0.06 |
| Number of grafts | 2.76 | 2.88 | −0.17 | 2.78 | 2.79 | −0.02 |
| IR | 0.19 | 0.12 | 0.17 | 0.18 | 0.15 | 0.08 |
| CPB | 0.34 | 0.28 | 0.11 | 0.32 | 0.33 | −0.03 |

HxCHF: history of congestive heart failure; MI: myocardial infarction; PCI: percutaneous coronary intervention; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; HxAF: history of atrial fibrillation; LMS: left main stem; LVEF: left ventricular ejection fraction; BMI: body mass index; IABP: intra-aortic balloon pump; IR: incomplete revascularization; CPB: cardiopulmonary bypass.

**Fig. 1.** Propensity score (PS) distribution before and after matching in the RA (treated) and RIMA (control) groups.

82.7 ± 1.7 versus 87.8 ± 1.5 at 10 years in the RA and the RIMA groups respectively (Fig. 4). Compared to the RIMA, the RA was associated with an increased risk for repeat revascularization (HR 1.5; 95% CI 1.0–2.2; $P = 0.044$).

Subgroup analysis showed a trend towards an extra risk from RA over RIMA among diabetic and obese patients. Among 227 diabetics (RA = 124, RIMA = 103), RA was associated with an

increased risk for late mortality (HR 3.3; 95% CI 1.1–9.7) and need for repeat revascularization (HR 3.1; 95% CI 1.2–8.2).

Among 299 obese patients (RA = 155, RIMA = 144), RA was associated with an increased risk for late mortality (HR 2.1; 95% CI 0.8–5.46) and need for repeat revascularization (HR 1.58; 95% CI 0.78–3.2).

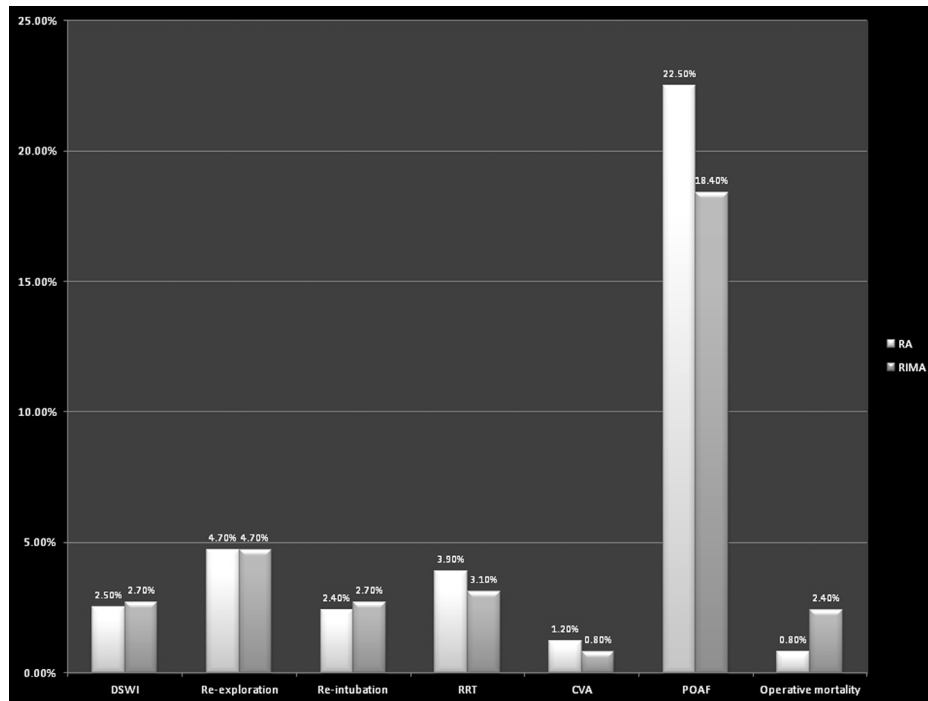


Fig. 2. Incidence of postoperative complications in the RA and RIMA groups. CVA: cerebrovascular accident; DSWI: deep sternal wound infection; POAF: postoperative atrial fibrillation; RA: radial artery; RIMA: right internal mammary artery; RRT: renal replacement therapy.

3. Discussion

The main finding of the present propensity matched study is that the use of the RIMA as additional arterial graft instead of the RA resulted in comparable operative outcomes, including the incidence of deep SWI and better long term outcomes including improved survival and reduced need for repeat revascularization. An extra benefit from the use of the RIMA over the RA was observed among high risk patients such as diabetics and obese patients.

Given the limitations of saphenous vein grafting, multiple arterial grafting using the RIMA or the RA as additional arterial conduits is the increasingly recognized and recommended optimal treatment of multivessel coronary artery disease [20,21]. However, the choice between the RA and the RIMA as the preferred second best arterial graft remains a matter of controversy [22].

There are few previous studies comparing the RA versus the RIMA in patients undergoing CABG and discordant results have been reported. Caputo et al. [23] compared patients who received both a LIMA graft and either a RIMA ($n = 336$) or a RA graft ($n = 325$). Using Cox regression model, they showed a strong protective effect of RA over RIMA against all causes of death at 18 months follow-up (hazard ratio, 0.25; 95% CI, 0.12–0.51; $P < 0.0001$). However, it must be highlighted that the fraction of patients receiving arterial grafts (LIMA and RIMA/RA) to both LAD and circumflex arteries was significantly lower in the RIMA group (47% versus 61.8%, $P = 0.001$) and this aspect might have affected the outcomes in the RIMA group. Calafiore et al. [24] compared 139 patients receiving the RA to graft lateral wall targets versus 149 patients receiving the RIMA. They found comparable operative outcomes for the two strategies. After a mean of 35 ± 28 months, the patency rate was comparable in the RA and RIMA group (99% in the RA group versus 100% in group B, $P = 0.560$). Ruttman et al. [25] reported short- and long-term results for 277 patients receiving a RIMA and 724 patients receiving a RA in addition to a left internal thoracic artery. In a propensity matched analysis, they

found that the incidence of perioperative major adverse cardiac and cerebrovascular events was significantly lower in patients receiving the RIMA (1.4% versus 7.6%, $P < 0.001$). After a mean follow-up time of 57 months overall survival (HR 0.23; 95% CI 0.066–0.81; $P < 0.022$) and major adverse cardiac and cerebrovascular events-free survival (HR 0.18; 95% CI 0.08–0.42; $P < 0.001$) were significantly better in patients receiving the RIMA as second arterial conduit. Hayward et al. [26] reported similar 5-year survival and patency in a prospective randomized controlled trial (RCT)—the Radial Artery Patency and Clinical Outcomes trial—in patients younger than 70 years, comparing the RA (198 patients) with the free RIMA (196 patients) to bypass the next best coronary artery (which was the circumflex coronary artery in 54% of the RA group and 61% in the RIMA group). At mean follow up of 5.5 years, estimates of patency showed trend to difference between RA and RIMA ($P = 0.28$).

Recently, Navia et al. [27] reported on 1447 patients who received the RIMA graft and 253 patients who received the RA graft. Among 149 pairs of propensity matched patients, hospital mortality was 4.03% in the RIMA group and 3.36% in the RA group respectively ($P = 0.5$). Perioperative major complication rate was 10.7% in the RIMA group and 9.40% in the RA group ($P = 0.5$). The incidence of reintervention or readmission (HR, 0.40; 95% CI, 0.18–0.88; $P = 0.02$) and combined end points including survival (HR, 0.54; 95% CI, 0.32–0.92; $P = 0.02$) were significantly better in patients who received the RIMA. On the other hand, Tranbaugh et al. [28] compared a total of 528 propensity matched pairs who received either a RA or a free RIMA to bypass the circumflex coronary artery. Hospital and 30-day mortality was 0.6% for the RA and 1.7% for the RIMA patients, which was not statistically different ($P = 0.082$). RA and RIMA patients had similar long-term 10-year survival being 85% for RA and 80% for RIMA patients, ($P = 0.060$). Interestingly they found a non significant trend towards a better patency rate among RIMA grafts ($P = 0.1$). Overall patency for the

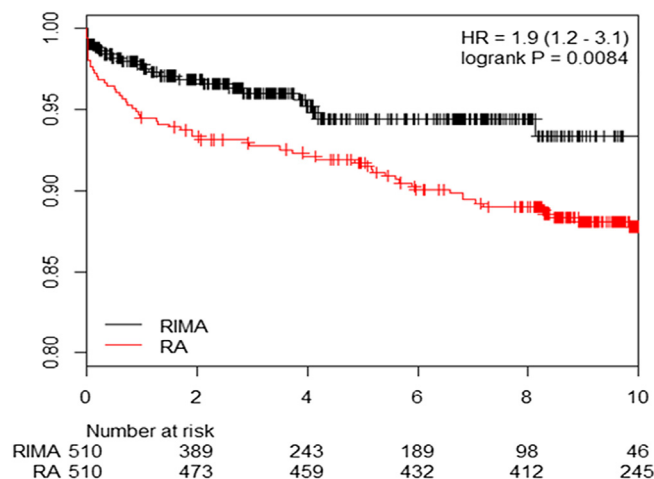


Fig. 3. Kaplan–Meier analysis for overall survival in the matched sample.

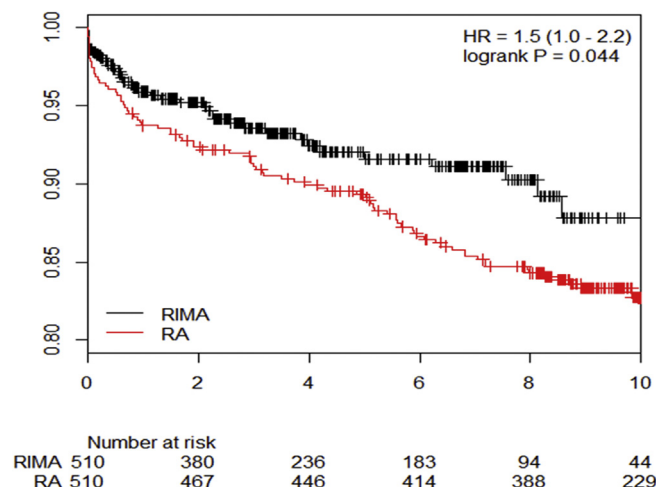


Fig. 4. Kaplan–Meier analysis for repeat revascularisation free survival in the matched sample.

RA was 83.9% (276 of 329 anastomoses) and, for the RIMA, patency was 87.4% (160 of 183 anastomoses).

The present study represents one of the largest series comparing outcomes in patients undergoing multiple arterial grafting using either the RIMA or the RA grafts. We found that the use of the RIMA did not increase the incidence of postoperative complications including deep SWI as reported by others [27]. On the other hand, the use of the RIMA was associated with an improved long term survival and reduced need for repeat revascularization. The survival benefit was enhanced in high risk patients such as diabetics and obese.

The present findings support the superiority of the RIMA graft over the RA graft as second arterial conduit. The main reason for the long-term benefit of RIMA grafting has been attributed to its reduced susceptibility to atherosclerosis than RA [29]. The lower capacity of nitric oxide release contributes to the susceptibility of the RA to atherosclerosis and might therefore be responsible for the inferior long-term graft patency [29]. Moreover, it can be speculated that the vulnerability of the RA to atherosclerosis may be enhanced in high risk patients such as diabetics or obese, thus partially explaining the extra benefit from the RIMA observed in such subgroups.

A recently published network meta-analysis comparing angiographic patency of arterial conduits to identify the second best arterial conduit reported that the RIMA was associated with a non-significant trend towards a decreased risk of functional and complete graft occlusion when compared with the RA, and right gastroepiploic artery, thus achieving the highest probability to be the best conduit (75%) in a rank probability analysis. Furthermore, the RIMA was associated with a non-significant 27% absolute risk reduction for late (≥ 4 years) functional graft occlusion when compared with the RA [30]. The findings of this network meta-analysis could also be used to partially explain the findings of our study.

Despite the well-recognized advantages of bilateral IMA grafting, adoption rates of bilateral IMA usage are fairly low. In the USA, bilateral IMA usage is only around 4% and in Europe 12% [20]. One of the principle reasons for these low adoption rates is the common perception that bilateral IMA usage is associated with an increased rate of sternal dehiscence and wound infection [14]. Skeletonization of the IMAs is a strategy claimed to lower the risk of DSWI in patients undergoing bilateral IMA grafting [31]. In comparison with the pedicle technique, the skeletonization technique preserves the collateral circulation to the sternum and the drainage of internal

mammary veins. Thus, skeletonized bilateral IMA is confirmed to carry a lower risk of sternal infection than pedicled bilateral IMA [32]. However, in our experience the technique of IMA harvesting did not impact the rate of SWI. For the 510 propensity matched patients undergoing bilateral IMA grafting, 211 had skeletonized while 299 had pedicled bilateral IMA. The rates of DSWI for the two techniques of IMA harvesting were similar (6/211 and 8/299; $P = 0.78$). We attribute these similar DSWI rates to an institutional policy of strict perioperative glycaemic control, adherence to meticulous closure technique and postoperative surgical wound management [33].

The principal limitation of the present analysis is the inability to address hidden biases due to unobserved or unrecorded differences between treated and control patients before treatment. As a consequence our results could reflect the effects of unknown or unmeasured confounders. Also, there were many staff surgeons operating at our institution during the time frame of the present study, and surgeon performance may be an unexplained factor that accounts for the observed results. Lastly, our analysis would have been substantially enhanced if long-term graft patency comparisons were available. However, due to costs and reluctance of patients to undergo invasive as well as non-invasive investigations, routine follow-up coronary angiography was not performed. The need for coronary angiography was dictated by the occurrence of angina, instability, or electrocardiogram changes in the perioperative or late follow-up period. It is however, worth mentioning that initially when RIMA and RA grafting were adopted in our institution early postoperative angiography to check the quality of the grafts and anastomoses was undertaken [34,35].

In conclusion, RIMA as a second conduit did not increase the operative risk including sternal wound complications and improved long-term outcomes including overall survival when compared to RA. This advantage was stronger among diabetic and obese patients. These findings strongly support RIMA as the first choice second arterial conduit in CABG. Further randomized studies with angiographic control and long-term follow-up are needed to address this issue.

Disclosures

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Ethical approval

Ethical approval waived due to retrospective nature of the study.

Financial support

No financial support or funding received for this study.

Author contribution

SR study design, writing.
UB data analysis, writing.
AJ, RKJ, UFU data collection.
FDR, TB study design & final approval.
JAG article draft & final approval.
MA final approval.

Conflict of interest

The authors disclose no conflict of interest.

References

- [1] S.G. Raja, Composite arterial grafting, *Expert Rev. Cardiovasc. Ther.* 4 (2006) 523–533.
- [2] S.G. Raja, Drug-eluting stents and the future of coronary artery bypass surgery: facts and fiction, *Ann. Thorac. Surg.* 81 (2006) 1162–1171.
- [3] F.W. Mohr, M.C. Morice, A.P. Kappetein, T.E. Feldman, E. Stähle, A. Colombo, et al., Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial, *Lancet* 381 (2013) 629–638.
- [4] G.M. FitzGibbon, A.J. Leach, W.J. Keon, J.R. Burton, H.P. Kafka, Coronary bypass graft fate. Angiographic study of 1,179 vein grafts early, one year, and five years after operation, *J. Thorac. Cardiovasc. Surg.* 91 (1986) 773–778.
- [5] S.G. Raja, Z. Haider, M. Ahmad, H. Zaman, Saphenous vein grafts: to use or not to use? *Heart Lung Circ.* 13 (2004) 403–409.
- [6] B.W. Lytle, F.D. Loop, D.M. Cosgrove, N.B. Ratliff, K. Easley, P.C. Taylor, Long-term (5 to 12 years) serial studies of internal mammary artery and saphenous vein coronary bypass grafts, *J. Thorac. Cardiovasc. Surg.* 89 (1985) 248–258.
- [7] F.D. Loop, B.W. Lytle, D.M. Cosgrove, R.W. Stewart, M. Goormastic, G.W. Williams, et al., Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events, *N. Engl. J. Med.* 314 (1986) 1–6.
- [8] R. Kelly, K.J. Buth, J.F. Légaré, Bilateral internal thoracic artery grafting is superior to other forms of multiple arterial grafting in providing survival benefit after coronary bypass surgery, *J. Thorac. Cardiovasc. Surg.* 144 (2012) 1408–1415.
- [9] L.M. Stevens, M. Carrier, L.P. Perrault, Y. Hébert, R. Cartier, D. Bouchard, et al., Single versus bilateral internal thoracic artery grafts with concomitant saphenous vein grafts for multivessel coronary artery bypass grafting: effects on mortality and event-free survival, *J. Thorac. Cardiovasc. Surg.* 127 (2004) 1408–1415.
- [10] C. Locker, H.V. Schaff, J.A. Dearani, L.D. Joyce, S.J. Park, H.M. Burkhardt, et al., Multiple arterial grafts improve late survival of patients undergoing coronary artery bypass graft surgery: analysis of 8622 patients with multivessel disease, *Circulation* 126 (2012) 1023–1030.
- [11] S.O. Bello, E.W. Peng, P.K. Sarkar, Conduits for coronary artery bypass surgery: the quest for second best, *J. Cardiovasc. Med. Hagerst.* 12 (2011) 411–421.
- [12] B.W. Lytle, E.H. Blackstone, F.D. Loop, P.L. Houghtaling, J.H. Arnold, R. Akhrass, et al., Two internal thoracic artery grafts are better than one, *J. Thorac. Cardiovasc. Surg.* 117 (1999) 855–872.
- [13] A.J. Weiss, S. Zhao, D.H. Tian, D.P. Taggart, T.D. Yan, A meta-analysis comparing bilateral internal mammary artery with left internal mammary artery for coronary artery bypass grafting, *Ann. Cardiothorac. Surg.* 2 (2013) 390–400.
- [14] S.G. Raja, U. Benedetto, M. Husain, R. Soliman, F. De Robertis, M. Amrani, on behalf of the Harefield Cardiac Outcomes Research Group, Does grafting of the left anterior descending artery with the in situ right internal thoracic artery have an impact on late outcomes in the context of bilateral internal thoracic artery usage?, *J. Thorac. Cardiovasc. Surg.* (2014 Jan 2), pii:S0022-5223(13)01491-8. <http://dx.doi.org/10.1016/j.jtcvs.2013.11.045> (Epub ahead of print).
- [15] S.G. Raja, Radial artery as the second choice conduit: some unsolved problems, *Circulation* 110 (2004) e62–3.
- [16] U. Benedetto, M. Codispoti, Age cutoff for the loss of survival benefit from use of radial artery in coronary artery bypass grafting, *J. Thorac. Cardiovasc. Surg.* 146 (2013) 1078–1084.
- [17] J.S. Garner, W.R. Jarvis, T.G. Emori, T.C. Horan, J.M. Hughes, CDC definitions for nosocomial infections, *Am. J. Infect. Control* 16 (1988) 128–140.
- [18] M.S. Cohen, E.H. Blackstone, J.B. Young, E.J. Topol, Cause of death in clinical research: time for a reassessment? *J. Am. Coll. Cardiol.* 34 (1999) 618–620.
- [19] E. von Elm, D.G. Altman, M. Egger, S.J. Pocock, P.C. Gøtzsche, J.P. Vandenbroucke, for the STROBE Initiative, The Strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies, *Int. J. Surg.* 12 (12) (2014) 1495–1499.
- [20] J. Tatoulis, B.F. Buxton, J.A. Fuller, The right internal thoracic artery: is it underutilized? *Curr. Opin. Cardiol.* 26 (2011) 528–535.
- [21] R.F. Tranbaugh, K.R. Dimitrova, P. Friedmann, C.M. Geller, L.J. Harris, P. Stelzer, B.M. Cohen, W. Ko, H. DeCastro, D. Lucido, D.M. Hoffman, Coronary artery bypass grafting using the radial artery: clinical outcomes, patency, and need for reintervention, *Circulation* 126 (11 Suppl. 1) (2012) S170–S175.
- [22] J. Tatoulis, Total arterial coronary revascularization-patient selection, stenoses, conduits, targets, *Ann. Cardiothorac. Surg.* 2 (2013) 499–506.
- [23] M. Caputo, B. Reeves, G. Marchetto, B. Mahesh, K. Lim, G.D. Angelini, Radial versus right internal thoracic artery as a second arterial conduit for coronary surgery: early and midterm outcomes, *J. Thorac. Cardiovasc. Surg.* 126 (2003) 39–47.
- [24] A.M. Calafiore, M. Di Mauro, S. D'Alessandro, G. Teodori, G. Vitolla, M. Contini, A.L. Iacò, G. Spira, Revascularization of the lateral wall: long-term angiographic and clinical results of radial artery versus right internal thoracic artery grafting, *J. Thorac. Cardiovasc. Surg.* 123 (2002) 225–231.
- [25] E. Ruttman, N. Fischler, A. Sakic, O. Chevtchik, H. Alber, R. Schistek, et al., Second internal thoracic artery versus radial artery in coronary artery bypass grafting: a long-term, propensity score-matched follow-up study, *Circulation* 124 (2011) 1321–1329.
- [26] P.A. Hayward, D.L. Hare, I. Gordon, G. Matalanis, B.F. Buxton, Which arterial conduit? Radial artery versus free right internal thoracic artery: six-year clinical results of a randomized controlled trial, *Ann. Thorac. Surg.* 84 (2007) 493–497.
- [27] D. Navia, M. Vrancic, F. Piccinini, M. Camporotondo, J. Thierier, C. Gil, et al., Is the second internal thoracic artery better than the radial artery in total arterial off-pump coronary artery bypass grafting? A propensity score-matched follow-up study, *J. Thorac. Cardiovasc. Surg.* 147 (2014) 632–638.
- [28] R.F. Tranbaugh, K.R. Dimitrova, D.J. Lucido, D.M. Hoffman, G.R. Dincheva, C.M. Geller, et al., The second best arterial graft: a propensity analysis of the radial artery versus the free right internal thoracic artery to bypass the circumflex coronary artery, *J. Thorac. Cardiovasc. Surg.* 147 (2014) 133–142.
- [29] G.W. He, Z.G. Liu, Comparison of nitric oxide release and endothelium-derived hyperpolarizing factor-mediated hyperpolarization between human radial and internal mammary arteries, *Circulation* 104 (12 Suppl. 1) (2001) I344–I349.
- [30] U. Benedetto, S.G. Raja, A. Albanese, M. Amrani, G. Biondi-Zoccai, G. Frati, Searching for the second best graft for coronary artery bypass surgery: a network meta-analysis of randomized controlled trials, *Eur. J. Cardiothorac. Surg.* (2014 Mar 30), <http://dx.doi.org/10.1093/ejcts/ezu111> (Epub ahead of print).
- [31] E.B. Savage, J.D. Grab, S.M. O'Brien, A. Ali, E.J. Okum, R.A. Perez-Tamayo, et al., Use of both internal thoracic arteries in diabetic patients increases deep sternal wound infection, *Ann. Thorac. Surg.* 83 (2007) 1002–1006.
- [32] R. De Paulis, S. de Notaris, S. Scaffa, S. Nardella, J. Zeitani, C. Del Giudice, et al., The effect of bilateral internal thoracic artery harvesting on superficial and deep sternal infection: the role of skeletonization, *J. Thorac. Cardiovasc. Surg.* 129 (2005) 536–543.
- [33] S.G. Raja, K. Salhiyyah, M.U. Rafiq, M. Navaratnarajah, D. Chudasama, C.P. Walker, et al., In-hospital outcomes of pedicled bilateral internal mammary artery use in diabetic and nondiabetic patients undergoing off-pump coronary artery bypass grafting: single-surgeon, single-center experience, *Heart Surg. Forum* 16 (2013) E1–E7.
- [34] S. Al-Ruzzeh, S. George, M. Bustami, K. Nakamura, C. Ilsley, M. Amrani, Early clinical and angiographic outcome of the pedicled right internal thoracic artery graft to the left anterior descending artery, *Ann. Thorac. Surg.* 73 (2002) 1431–1435.
- [35] A.C. Anyanwu, I. Saeed, M. Bustami, C. Ilsley, M.H. Yacoub, M. Amrani, Does routine use of the radial artery increase complexity or morbidity of coronary bypass surgery? *Ann. Thorac. Surg.* 71 (2001) 555–559.