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**Is the right internal thoracic artery superior to saphenous vein for grafting the right coronary artery? A propensity score based analysis**

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**Abbreviation list**

BMI: body mass index

CABG: coronary artery bypass graft

COPD: chronic obstructive pulmonary disease

CVA: cerebrovascular accident

DM: diabetes mellitus

IABP: intraaortic balloon pump

LAD: left anterior descending

LMD: left main disease

LITA: left internal thoracic artery

LVEF: left ventricular ejection fraction

OPCAB; off-pump coronary artery bypass

PSM: propensity score matching

PVD: peripheral vascular disease

RCA: right coronary artery

RITA: right internal thoracic artery (RITA)

RRT renal replacement therapy

SMD: standardized mean difference

sCr: serum creatinine

SV: saphenous vein

SWR: sternal wound reconstruction

**Central message:** In a low risk population, Revascularization of the right coronary artery system with the right internal thoracic artery was associated with superior late survival when compared with saphenous vein grafting

**Perspective statement:** The choice of conduit for the right coronary artery system remains a controversial issue. The present long-term propensity score based analysis showed that revascularization of the right coronary artery (RCA) system with the right internal thoracic artery (RITA) is associated with superior late survival when compared with saphenous vein grafting in a low risk population. However, the beneficial impact on survival from the use of the RITA was delayed by as much as 9 to 10 years. This supports the view that, the use of RITA to graft the RCA should be encouraged especially in patients with long life expectancy.

**Abstract**

**Objectives:** While the use of the right internal thoracic artery (RITA) as second arterial conduit to graft the left coronary system has been consistently shown to provide a survival benefit when compared to saphenous vein graft (SVG), the choice of conduit for the right coronary artery (RCA) system remains controversial. We compared long term (>15 years) survival in patients who underwent RITA-RCA versus SV-RCA grafting at a single institution.

**Methods:** The study population consisted of 7223 patients undergoing coronary artery bypass graft surgery. Of them 245 (3.4%) and 6978 (96.6%) received RITA-RCA and SV-RCA graft respectively. Propensity score (PS) matching and time-segmented Cox regression were used to compare the two groups.

**Results:** Survival probability at 5,10 and 15 years were 95.9%[93.4-98.4] versus 96.0%[94.3-97.8], 89.8%[85.9-93.7] versus 88.0%[85.0-91.0] and 82.9%[77.6-88.2] versus 76.3[72.0-80.5] in the RITA-RCA and SVG-RCA group respectively (Figure 2). Time segmented Cox regression showed that during the first 9 years, the two strategy were associated with comparable risk of death (HR 1.13;95%CI 0.67-1.90; P=0.65) but beyond 9 years, the RITA-RCA was associated with a significantly lower risk of death (HR 0.43;95%CI 0.22-0.84; P=0.01).

**Conclusions:** Revascularization of the RCA system with the RITA was associated with superior late survival when compared with SVG. This supports the view that, the use of RITA to graft the RCA should be encouraged especially in patients with long life expectancy.

The choice of conduit for coronary artery bypass graft (CABG) is widely debated by cardiac surgeons [1]. While the use of the right internal thoracic artery (RITA) in addition to the left internal thoracic artery (LITA) to graft the left coronary system has been consistently shown to provide a survival benefit when compared to saphenous vein graft (SVG) [2], the choice of conduit for the right coronary artery (RCA) system remains a controversial issue. To date, the only randomized controlled trial (RCT) designed to compare long term survival after CABG with bilateral versus single internal thoracic artery grafting (ART trial) included only patients receiving the arterial conduit on the left coronary system [3]. Observational studies comparing RITA-RCA versus SVG-RCA have shown conflicting results. Some reports have suggested that the RITA grafting improves long-term survival over LITA plus SVGs, and propose that the RITA should be used to bypass the circumflex artery rather than the RCA [4]. Others documented equivalent long-term results with the use of the RITA, whether applied to the left or RCA system [5,6]. Current comparison between RITA vs SVG for grafting the RCA are limited by relatively short follow-up (~5 years). In the present study, we aimed to get further insights into the role of RITA graft for revascularization of the RCA by comparing long term (>15 years) survival in patients who underwent RITA-RCA versus SVG-RCA strategy at a single institution. We also aimed to investigate whether different RITA-RCA configurations (free versus in-situ grafts) were associated with similar survival rates.

**Methods and Methods**

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local audit committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analysed prospectively collected data from The National Institute for Cardiovascular Outcomes Research National Adult Cardiac Surgery Audit registry on 1 June 2015 for all isolated first time CABG procedures performed at the Bristol Heart Institute (Bristol, United Kingdom) from 1996 to April 2015. Reproducible cleaning

algorithms were applied to the database and regularly updated as required. Briefly, duplicate records and non-adult cardiac surgery entries were removed; transcriptional discrepancies were harmonized; and clinical conflicts and extreme values were corrected or removed. The data were returned regularly to the local units for validation. Further details and definition of variables are available at http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets. Among 15119 isolated first time CABG cases performed during the study period, we selected subjects who met the following criteria: multivessel coronary artery disease including left main and/or left anterior descending (LAD) coronary disease; requiring at least 2 grafts; CABG performed by using the following strategies: left internal thoracic artery (LITA) used to graft the LAD territory and RITA graft the RCA with or without additional SVG (RITA-RCA group) or LITA to LAD graft with SVG to RCA with or without additional SVG for non-RCA target (SVG-RCA group). Exclusion criteria were: 1) RITA graft to target other than RCA; 2) radial artery used; 3) LITA to target other than LAD; 4) RCA not grafted; right gastroepiploic artery used. In the present series, the RITA and SV graft were used to graft the RCA in case of target stenosis ≥75% [8]. SVGs were used proximally connected to the ascending aorta in all cases. The internal thoracic artery was harvested as a pedicle in all cases. LITA was used as *in situ* graft that remained proximally connected to its respective subclavian artery and distally connected to the LAD. The RITA was used as both *in situ* graft or as a free graft proximally connected to ascending aorta.

*Study Endpoints*

All-cause mortality during follow-up was the primary endpoint. This is considered the most robust and unbiased index in cardiovascular research because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments [9]. Information about post-discharge mortality tracking was available for all patients (100%) and was obtained by linking the institutional database with the National General Register Office. Other short-term

outcomes analysed were: re-exploration for bleeding, need for sternal wound reconstruction, postoperative cerebrovascular accident (CVA) (defined as any confirmed neurologic deficit of abrupt onset that did not resolve within 24 hours), postoperative renal replacement therapy (RRT), need for postoperative intra-aortic balloon pump (IABP) and in hospital mortality.

*Pre-treatment variables*

The effect of RITA-RCA vs SV-RCA on outcomes of interest was adjusted for the following pre-treatment variables: age, gender, body mass index (BMI); Canadian Cardiovascular Society functional class III-IV; New York Heart Association grade III or IV; previous myocardial infarction (MI) within 30 days; previous percutaneous coronary intervention (PCI); diabetes mellitus (DM) on oral treatment or on insulin; chronic obstructive pulmonary disease (COPD); current smoking; serum creatinine ≥200 mmol/l, previous CVA; peripheral vascular disease (PVD); preoperative atrial fibrillation (AF); left ventricular ejection fraction (LVEF) between 30% and 49%; LVEF less than 30%; non elective admission, cardiogenic shock; preoperative IABP; left main disease (LMD); concomitant circumflex artery disease grafted; total number of grafts; off-pump coronary artery bypass and eras of surgery.

*Statistical Analysis*

For baseline characteristics, variables are summarized as means ± standard deviation for continuous variables and frequencies and proportions for categorical variables. Multiple imputation was used to address missing data (http://www.jstatsoft.org/v45/i07/). To control for measured potential confounders in the data set, a propensity score (PS) was generated for each patient from a multivariable logistic regression model that was based on pre-treatment covariates as independent variables with treatment type (RITA-RCA vs SVG-RCA) as a binary dependent variable (http://CRAN.Rproject.org/package=nonrandom) [10]. The resulting PS represented the probability of a patient having RITA to RCA graft. PS model discrimination power and fit were tested using c-statistic and the Hosmer-Lemeshow goodness-of-fit

(https://CRAN.R-project.org/package=ResourceSelection). Pairs of patients undergoing RITA-RCA and SVG-RCA grafting were derived with greedy 1:2 matching with a caliper of width of 0.2 SD of the logit of the PS. A matching ratio ≥3 resulted in significantly imbalance between the two groups. The quality of the match was assessed by comparing selected pre-treatment variables in PS-matched patients by using the standardized mean difference, by which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance [11]. Analytic methods for the estimation of the treatment effect in the matched sample were used. McNemar test was used to compare short term outcomes in the matched sample [10]. Kaplan–Meier analyses was used to calculate survival rates. Conditional Cox regression model stratified for matched pairs was used to estimate the treatment effect on survival [10]. Residual weights were used to test the proportional hazard assumption and in case of violation, time segmented Cox regression before and after the curves diverged was used (http://CRAN.R-project.org/package=survival) [12]. All statistical analysis were performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

**Results**

The final study population consisted of 7223 patients. Of them 245 (3.4%) and 6978 (96.6%) received RITA-RCA and SVG-RCA graft respectively (Supplementary Figure 1 and Figure 1). RITA was used as *in situ* in 198 (81%) and as free graft in 47 (19%). Baseline characteristics of the two groups before and after PS matching are reported in Table 1. Patients receiving RITA-RCA were significantly younger, less likely to be female and presented a lower burden of comorbidities. Patients receiving SVG-RCA were more likely to have LMD and circumflex artery disease and undergo off-pump surgery. Finally RITA-RCA was more likely performed during the first study period. PS matching selected 490 patients receiving SVG-RCA graft who comparable to those receiving RITA-RCA graft. (SMD<10%). The PS model presented a very

good discriminatory power (C-statistics 0.93) to predict the treatment status with no evidence of poor fit (Hosmer and Lemeshow goodness of fit test P=0.25; Supplementary Figure 2).

*Short term outcomes*

Short term outcomes are reported in Table 2. The two groups presented comparable incidence of postoperative complications rates. In-hospital mortality rate was comparable between RITA-RCA (0.4%) and SV-RCA graft (0.6%).

*Survival*

After a mean follow-up time of 8±5 years (max 17 years) there were 36 and 1948 deaths in the RITA-RCA and RITA-SV group respectively. After PS matching, survival probability at 5,10 and 15 years were 95.9%[93.4-98.4] versus 96.0%[94.3-97.8], 89.8%[85.9-93.7] versus 88.0%[85.0-91.0] and 82.9%[77.6-88.2] versus 76.3[72.0-80.5] in the RITA-RCA and SVG-RCA group respectively (Figure 2). Kaplan Meier analysis showed that the two survival curves were superimposed up to ~9 years. At ~9 years, the survival curves crossed and, between 10 and 15 years, the RITA-RCA group demonstrated superior survival (residual weights test P=0.03). Time segmented Cox regression showed that during the first 9 years, the two strategy were associated with comparable risk of death (HR 1.13;95%CI 0.67-1.90; P=0.65) but beyond 9 years, the RITA-RCA was associated with a significantly lower risk of death (HR 0.43;95%CI 0.22-0.84; P=0.01). When the RITA-RCA group was divided in free RITA-RCA graft (n=47) and *in situ* RITA-RCA graft (n=198) survival probability at 5, 10 and 15 years were 91.1 %[82.9-99.4] versus 97.0[94.6-99.4], 81.7[70.3-93.2] versus 91.6%[87.7-95.6] and 71.1[57.1-85.1] versus 85.5%[80.0-91.1] respectively. Patients receiving free RITA-RCA and in-situ RITA-RCA were separately compared to 1:2 matched pairs of patients receiving SV-RCA (Supplementary Table 1 and Supplementary Table 2). In situ RITA-RCA (HR 0.60; 95%CI 0.35-0.98; P=0.04; Weight residual test P=0.12; Figure 3 right) but not free RITA-RCA

(HR 1.03; 95%CI 0.47-2.26; P=0.94; residual weights test P=0.58; Figure 3 left) was associated with better survival when compared to SVG-RCA.

**Discussion**

The main findings of the present analysis is that when the use of the RITA to graft the right coronary artery system was associated with superior long term survival compared to the SVG. Survival benefit was no apparent during the first 9 years but became evident afterwards. Our subgroup analysis suggested that this benefit might be more relevant with in-situ instead of free RITA graft configuration. However, free RITA graft subgroup was particularly small to draw any definitive conclusion. RITA graft was not associated with increased postoperative complications or hospital mortality.

In the present cohort, the use of RITA for the RCA system was relatively low and it was mainly used during the first part of the study period and never gained popularity in our centre. This observation might be partially explained by a larger body of evidence supporting a survival benefit from RITA when used to graft the left coronary artery system. In fact in the present cohort, in the majority of cases, the RITA was used to graft the left anterior descending artery (n=273) and the circumflex artery (n=414). Another possible explanation for preferring the RITA for the left coronary system is the increased technical complexity in particular when the RITA is used as in-situ graft to the posterior descending artery which can potentially result in graft kinking and stretching.

While the use of the RITA to graft the left coronary system has been consistently reported to be associated to excellent patency rate [13] and improved outcomes [14], the role of the RITA for revascularization of the RCA remains controversial [15]. Angiographic follow-up studies have demonstrated a hierarchy of RITA patency; best for the LAD, then the circumflex, and lowest to the RCA [8]. Although, a similar hierarchy of patency has been also observed for SVG, it has been shown that the patency of the RITA is significantly affected by the stenosis

of the recipient RCA [13], most likely as a result of competitive flow or poorer runoff [16]. However, when the RITA is used to bypass high grade proximal stenosis [17] it has been shown to achieve excellent patency rate [16,17]. The variability of RITA-RCA graft patency rate according to the severity of the RCA stenosis might partially account for conflicting findings reported on survival benefit from the use of RITA instead of SVG. Schmidt et al. [4] observed long-term survival of 93% when the RITA was used to bypass left-sided coronary arteries but only 70% when grafted to the RCA system after a mean follow-up of 9.2 years ($P$=0.02). In contrast, Kurlansky et al. [5] found similar survival after a mean follow-up of 12 years. In their series, *in situ* grafting was used in the majority of cases (approximately 98% of arteries grafted) and when the RITA was used to graft the RCA, efforts were made to graft severely stenosed vessels and distal branches rather than the main RCA. In this context, also, Sabik at al. [6] were able to document equivalent long-term results with the use of the RITA, whether applied to the left or RCA system, and this was attributed to careful patient selection. Two important factors were: (1) RCA stenosis of 70% to 90% with viable myocardium in its distribution; and (2) freedom from distal stenosis. In the present cohort, the RITA was used only in case of native vessel stenosis >75% and this can partially explain the observed survival benefit from the use of RITA over SVG.

In the present long term survival analysis, we found that when compared to SV, the use of RITA for revascularization of the RCA system was associated with improved late survival. The beneficial impact on survival from the use of the RITA was delayed by as much as 9 to 10 years but persisted beyond that period. The present findings seem to be supported by recently published interim analysis of the ART trial which did not show any mid-term benefit from the RITA grafted to the left coronary system [3]. A possible explanation for these findings is that SVG failure rate increases significantly after 5 years and a longer follow-up is needed to demonstrate a survival benefit from the use of RITA regardless the coronary artery

system treated. The present study population included relatively young subjects with low burden of comorbidities and anticipated prolonged life expectancy and therefore the use of the RITA may be less appreciated in older patients with coexistent morbidities and limited life expectancy.

We attempted to compare *in situ* vs free RITA graft configuration for the RCA and we found some evidence towards better results with in-situ configuration. However, very few subjects received free RITA graft and the present subgroup analysis was largely underpowered to detect significant difference in late survival in this group. Despite concerns that direct ascending aorta RITA inflow may lead to vascular wall "reactivity" have been raised, this aspect remains controversial with conflicting findings reported . Calafiore and colleagues [18] initially reported that the patency rate of the free right ITA proximally anastomosed to the aorta was inferior to that anastomosed to the left ITA. They suggested that the reason for this poor graft patency rate was because of a mismatch between the aorta and the conduit wall and a difference in the flow pattern [18]. A previous report from Buxton and colleagues, who concluded that proximal attachment to the aorta compared with *in situ* RITA grafts resulted in a 2-fold increase in the risk of graft failure [8]. On the other hand, large angiographic studies have confirmed excellent patency rates with free RITA graft [13,19]. Tatoulis et al [13], found that in-situ RITA (n=450), and free RITA grafts (n=541) had similar ten-year patencies (89% vs 91%; P=0.44). Interestingly, they found that for the posterior descending artery, in situ and free RITA grafts provided similar patency rates (P=0.67) but for the main RCA, in situ RITA patency was associated with lower patency rate compared to free RITA (73.8% versus 93.1%; P=0.02).

Finally, we found that the RITA-RCA graft can be performed without increasing the risk of postoperative complications including sternal wound reconstruction. Bilateral internal thoracic arteries harvesting has been consistently demonstrated to be associated with increased sternal wound complications especially when these conduits are harvested as pedicle [20]. For the he

present analysis, only information regarding sternal wound reconstruction were available and we cannot exclude that the use of the RITA was associated with increased incidence of sternal wound infection not requiring sternal rewiring.

The present analysis has intrinsic limitations. The RITA-RCA bypass was used very infrequently in general, and was primarily used in the first part of the series. Differences between the two groups can be caused by variation of patients risk profile across different surgical eras. PS matching can adjust only for measurable and included variables and we cannot exclude a selection bias based on non-measurable "eye-ball" variables (with the RITA reserved to healthier and better patients). No follow-up data were available to compare the groups with respect to the cause of death (cardiac vs non-cardiac), need for repeated revascularization, and graft patency. Therefore, we can only speculate that the mechanism beyond the superior long-term survival observed in our RITA group is related to the better patency rate of the RITA over the SVG. Finally the analysis for the free RITA-RCA cohort was underpowered to detect significant difference between groups.

In conclusion, in a selected low risk group of patients, revascularization of the RCA system with the RITA was associated with superior late survival (beyond 9 year) when compared with SVG. Further evidence are needed to clarify the best configuration for RITA-RCA graft. This supports the view that, the use of RITA to graft the RCA should be encouraged especially in patients with long life expectancy.

**Figures Legends**

Central Picture: Survival in the propensity score matched sample according to use of the right internal thoracic artery (RITA) used as *in situ* or free graft or saphenous vein (SV) for revascularization of the right coronary artery.

Figure 1: Use of the right internal thoracic artery (RITA) or saphenous vein graft (SVG) for revascularization of the right coronary artery during the study period.

Figure 2. Survival in the propensity score matched sample according to use of the right internal thoracic artery (RITA) or saphenous vein graft (SVG) for revascularization of the right coronary artery (RCA).

Figure 3. Survival after propensity score matching according to use of the right internal thoracic artery (RITA) used as free (left) or *in situ* (right) graft versus saphenous vein graft (SVG) for revascularization of the right coronary artery (RCA).

Supplementary Figure 1. Flow chart for patient selection (CABG: Coronary artery bypass grafting; RITA: right internal thoracic artery; RA: radial artery; LITA: left internal thoracic artery; RCA: right coronary artery; RGEA: right gastroepiploic artery)

Supplementary Figure 2: Area under the ROC curve (C statistics) for the propensity score model and relative Hosmer and Lemeshow goodness of fit test

Table 1. Patients' characteristics distribution before and after matching in the RITA-RCA and SVG-RCA groups

| | RITA-RCA | SVG-RCA (unmatched) | P | SMD | 2:1 Matched SVG-RCA | P | SMD |
|---|---|---|---|---|---|---|---|
| n | 245 | 6978 | | | 490 | | |
| Age (mean (sd)) | 56 (8) | 68 (8) | <0.001 | 1.547 | 57 (8) | 0.09 | 0.09 |
| Female n(%) | 24 ( 9.8) | 1307 (18.7) | 0.001 | 0.258 | 47 ( 9.6) | 1.000 | 0.007 |
| BMI (mean (sd)) | 27.59 (3.26) | 27.79 (4.40) | 0.485 | 0.051 | 27.64 (4.06) | 0.873 | 0.013 |
| CCS III-IV n(%) | 122 (49.8) | 3409 (48.9) | 0.822 | 0.019 | 237 (48.4) | 0.774 | 0.029 |
| NYHA III-IV n(%) | 55 (22.4) | 2156 (30.9) | 0.006 | 0.192 | 116 (23.7) | 0.781 | 0.029 |
| MI within 30 days n(%) | 13 ( 5.3) | 1488 (21.3) | <0.001 | 0.485 | 28 ( 5.7) | 0.955 | 0.018 |
| PCI n(%) | 3 ( 1.2) | 336 ( 4.8) | 0.014 | 0.211 | 6 ( 1.2) | 1.000 | <0.001 |
| DM orally treated n(%) | 4 ( 1.6) | 808 (11.6) | <0.001 | 0.409 | 5 ( 1.0) | 0.722 | 0.054 |
| DM on insulin n(%) | 7 ( 2.9) | 572 ( 8.2) | 0.004 | 0.235 | 8 ( 1.6) | 0.406 | 0.083 |
| Smoking n(%) | 50 (20.4) | 849 (12.2) | <0.001 | 0.225 | 96 (19.6) | 0.870 | 0.020 |
| Creatinine>200mmol/l n(%) | 3 ( 1.2) | 216 ( 3.1) | 0.136 | 0.129 | 7 ( 1.4) | 1.000 | 0.018 |
| COPD n(%) | 5 ( 2.0) | 571 ( 8.2) | 0.001 | 0.282 | 12 ( 2.4) | 0.931 | 0.028 |
| CVA n(%) | 3 ( 1.2) | 290 ( 4.2) | 0.034 | 0.182 | 6 ( 1.2) | 1.000 | <0.001 |
| PVD n(%) | 21 ( 8.6) | 780 (11.2) | 0.241 | 0.087 | 35 ( 7.1) | 0.589 | 0.053 |
| AF n(%) | 5 ( 2.0) | 249 ( 3.6) | 0.272 | 0.093 | 10 ( 2.0) | 1.000 | <0.001 |
| LVEF 30-49% n(%) | 31 (12.7) | 1705 (24.4) | <0.001 | 0.307 | 68 (13.9) | 0.731 | 0.036 |
| LVEF<30% n(%) | 2 ( 0.8) | 387 ( 5.5) | 0.002 | 0.272 | 5 ( 1.0) | 1.000 | 0.021 |
| Shock n(%) | 0 ( 0.0) | 36 ( 0.5) | 0.506 | 0.102 | 0 ( 0.0) | - | - |
| Preop IABP n(%) | 1 ( 0.4) | 120 ( 1.7) | 0.187 | 0.128 | 1 ( 0.2) | 1.000 | 0.037 |
| Non-elective n(%) | 99 (40.4) | 3433 (49.2) | 0.008 | 0.177 | 199 (40.6) | 1.000 | 0.004 |
| LMD n(%) | 18 ( 7.3) | 1707 (24.5) | <0.001 | 0.481 | 33 ( 6.7) | 0.878 | 0.024 |
| Circumflex artery grafted n(%) | 104 (42.4) | 5469 (78.4) | <0.001 | 0.790 | 223 (45.5) | 0.479 | 0.062 |
| Tot n grafts (mean (sd)) | 2.73 (0.80) | 3.07 (0.62) | <0.001 | 0.469 | 2.79 (0.72) | 0.346 | 0.072 |
| Off-pump n(%) | 60 (24.5) | 3051 (43.7) | <0.001 | 0.414 | 128 (26.1) | 0.698 | 0.038 |
| Era of surgery (mean (sd)) | 2000 (4) | 2005 (6) | <0.001 | 1.140 | 2000 (4) | 0.367 | 0.072 |

RITA: right internal thoracic artery; SVG: saphenous vein graft; SMD: standardized mean difference; BMI: body mass index; CCS: Canadian Cardiovascular Society; NYHA: New York American Heart; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA:

cerebrovascular accident; PVD: peripheral vascular disease; AF: Atrial Fibrillation; LVEF: left ventricular ejection fraction; IABP: intraaortic balloon pump; LMD: left main disease

Table 2. Operative outcomes

| | RITA-RCA | SVG-RCA (unmatched) | P | 2:1 Matched SVG-RCA | P |
|---|---|---|---|---|---|
| n | 245 | 6978 | | 490 | |
| Mortality within 30 days n(%) | 1 (0.4) | 103 (1.5) | 0.269 | 3 (0.6) | 1.000 |
| Re-exploration for bleeding n(%) | 9 (3.7) | 215 (3.1) | 0.735 | 12 (2.4) | 0.481 |
| Sternal wound reconstruction n(%) | 0 (0.0) | 48 (0.7) | 0.367 | 0 (0.0) | - |
| Postoperative stroke n(%) | 0 (0.0) | 114 (1.6) | 0.079 | 6 (1.2) | 0.192 |
| Postoperative Dialysis n(%) | 3 (1.2) | 173 (2.5) | 0.298 | 5 (1.0) | 1.000 |

RITA: right internal thoracic artery; SVG: saphenous vein graft

Supplementary Table 1. Patients' characteristics distribution before and after matching in the in-situ RITA-RCA and SVG-RCA groups

| | In-situ RITA-RCA | SVG-RCA (unmatched) | P | SMD | 2:1 Matched SVG-RCA | P | SMD |
|---|---|---|---|---|---|---|---|
| n | 198 | 6978 | | | 396 | | |
| Age (mean (sd)) | 56 (7) | 68 (8) | <0.001 | 1.597 | 56 (8) | 0.759 | 0.027 |
| Female n(%) | 20 (10.1) | 1307 (18.7) | 0.003 | 0.248 | 41 (10.4) | 1.000 | 0.008 |
| BMI (mean (sd)) | 27.71 (3.05) | 27.79 (4.40) | 0.816 | 0.019 | 27.92 (4.41) | 0.545 | 0.056 |
| CCS III-IV n(%) | 97 (49.0) | 3409 (48.9) | 1.000 | 0.003 | 194 (49.0) | 1.000 | <0.001 |
| NYHA III-IV n(%) | 43 (21.7) | 2156 (30.9) | 0.007 | 0.210 | 93 (23.5) | 0.704 | 0.042 |
| MI within 30 days n(%) | 9 ( 4.5) | 1488 (21.3) | <0.001 | 0.516 | 21 ( 5.3) | 0.842 | 0.035 |
| PCI n(%) | 3 ( 1.5) | 336 ( 4.8) | 0.047 | 0.189 | 8 ( 2.0) | 0.914 | 0.038 |
| DM orally treated n(%) | 4 ( 2.0) | 808 (11.6) | <0.001 | 0.387 | 9 ( 2.3) | 1.000 | 0.017 |
| DM on insulin n(%) | 4 ( 2.0) | 572 ( 8.2) | 0.003 | 0.283 | 12 ( 3.0) | 0.654 | 0.064 |
| Smoking n(%) | 43 (21.7) | 849 (12.2) | <0.001 | 0.257 | 94 (23.7) | 0.654 | 0.048 |
| Creatinine>200mmol/l n(%) | 1 ( 0.5) | 216 ( 3.1) | 0.059 | 0.196 | 2 ( 0.5) | 1.000 | <0.001 |
| COPD n(%) | 4 ( 2.0) | 571 ( 8.2) | 0.003 | 0.283 | 8 ( 2.0) | 1.000 | <0.001 |
| CVA n(%) | 1 ( 0.5) | 290 ( 4.2) | 0.017 | 0.244 | 3 ( 0.8) | 1.000 | 0.032 |
| PVD n(%) | 14 ( 7.1) | 780 (11.2) | 0.089 | 0.143 | 23 ( 5.8) | 0.674 | 0.051 |
| AF n(%) | 3 ( 1.5) | 249 ( 3.6) | 0.176 | 0.131 | 7 ( 1.8) | 1.000 | 0.020 |
| LVEF 30-49% n(%) | 22 (11.1) | 1705 (24.4) | <0.001 | 0.354 | 50 (12.6) | 0.689 | 0.047 |
| LVEF<30% n(%) | 2 ( 1.0) | 387 ( 5.5) | 0.009 | 0.257 | 4 ( 1.0) | 1.000 | <0.001 |
| Shock n(%) | 0 ( 0.0) | 36 ( 0.5) | 0.615 | 0.102 | 0 ( 0.0) | - | - |
| Preop IABP n(%) | 1 ( 0.5) | 120 ( 1.7) | 0.303 | 0.116 | 3 ( 0.8) | 1.000 | 0.032 |
| Non-elective n(%) | 81 (40.9) | 3433 (49.2) | 0.026 | 0.167 | 167 (42.2) | 0.837 | 0.026 |
| LMD n(%) | 16 ( 8.1) | 1707 (24.5) | <0.001 | 0.455 | 30 ( 7.6) | 0.957 | 0.019 |
| Circumflex artery grafted n(%) | 86 (43.4) | 5469 (78.4) | <0.001 | 0.767 | 186 (47.0) | 0.467 | 0.071 |
| Tot n grafts (mean (sd)) | 2.73 (0.78) | 3.07 (0.62) | <0.001 | 0.487 | 2.80 (0.70) | 0.247 | 0.099 |
| Off-pump n(%) | 42 (21.2) | 3051 (43.7) | <0.001 | 0.495 | 89 (22.5) | 0.807 | 0.031 |
| Era of surgery (mean (sd)) | 2000 (4) | 2005 (5) | <0.001 | 1.163 | 2000 (5) | 0.133 | 0.09 |

RITA: right internal thoracic artery; SVG: saphenous vein graft; SMD: standardized mean difference; BMI: body mass index; CCS: Canadian Cardiovascular Society; NYHA: New York American Heart; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA:

12 cerebrovascular accident; PVD: peripheral vascular disease; AF: Atrial Fibrillation; LVEF: left ventricular ejection fraction; IABP: intraaortic
13 balloon pump; LMD: left main disease

Supplementary Table 2. Patients' characteristics distribution before and after matching in the free RITA-RCA and SVG-RCA groups

| | Free RITA-RCA | SVG-RCA (unmatched) | P | SMD | 2:1 Matched SVG-RCA | P | SMD |
|---|---|---|---|---|---|---|---|
| n | 47 | 6978 | | | 94 | | |
| Age (mean (sd)) | 56 (9) | 68 (8) | <0.001 | 1.360 | 57 (8) | 0.531 | 0.09 |
| Female n(%) | 4 ( 8.5) | 1307 (18.7) | 0.109 | 0.301 | 5 ( 5.3) | 0.715 | 0.126 |
| BMI (mean (sd)) | 27.06 (4.04) | 27.79 (4.40) | 0.260 | 0.172 | 27.75 (3.83) | 0.322 | 0.176 |
| CCS III-IV n(%) | 25 (53.2) | 3409 (48.9) | 0.655 | 0.087 | 58 (61.7) | 0.432 | 0.173 |
| NYHA III-IV n(%) | 12 (25.5) | 2156 (30.9) | 0.525 | 0.119 | 23 (24.5) | 1.000 | 0.025 |
| MI within 30 days n(%) | 4 ( 8.5) | 1488 (21.3) | 0.050 | 0.366 | 8 ( 8.5) | 1.000 | <0.001 |
| PCI n(%) | 0 ( 0.0) | 336 ( 4.8) | 0.231 | 0.318 | 0 ( 0.0) | - | - |
| DM orally treated n(%) | 0 ( 0.0) | 808 (11.6) | 0.024 | 0.512 | 0 ( 0.0) | - | - |
| DM on insulin n(%) | 3 ( 6.4) | 572 ( 8.2) | 0.853 | 0.070 | 5 ( 5.3) | 1.000 | 0.045 |
| Smoking n(%) | 7 (14.9) | 849 (12.2) | 0.729 | 0.080 | 15 (16.0) | 1.000 | 0.029 |
| Creatinine>200mmol/l n(%) | 2 ( 4.3) | 216 ( 3.1) | 0.972 | 0.062 | 7 ( 7.4) | 0.715 | 0.136 |
| COPD n(%) | 1 ( 2.1) | 571 ( 8.2) | 0.213 | 0.276 | 2 ( 2.1) | 1.000 | <0.001 |
| CVA n(%) | 2 ( 4.3) | 290 ( 4.2) | 1.000 | 0.005 | 3 ( 3.2) | 1.000 | 0.056 |
| PVD n(%) | 7 (14.9) | 780 (11.2) | 0.567 | 0.111 | 16 (17.0) | 0.936 | 0.058 |
| AF n(%) | 2 ( 4.3) | 249 ( 3.6) | 1.000 | 0.035 | 6 ( 6.4) | 0.898 | 0.095 |
| LVEF 30-49% n(%) | 9 (19.1) | 1705 (24.4) | 0.503 | 0.128 | 16 (17.0) | 0.938 | 0.055 |
| LVEF<30% n(%) | 0 ( 0.0) | 387 ( 5.5) | 0.180 | 0.343 | 0 ( 0.0) | - | - |
| Shock n(%) | 0 ( 0.0) | 36 ( 0.5) | 1.000 | 0.102 | 0 ( 0.0) | - | - |
| Preop IABP n(%) | 0 ( 0.0) | 120 ( 1.7) | 0.732 | 0.187 | 0 ( 0.0) | - | - |
| Non-elective n(%) | 18 (38.3) | 3433 (49.2) | 0.179 | 0.221 | 35 (37.2) | 1.000 | 0.022 |
| LMD n(%) | 2 ( 4.3) | 1707 (24.5) | 0.002 | 0.602 | 6 ( 6.4) | 0.898 | 0.095 |
| Circumflex artery grafted n(%) | 18 (38.3) | 5469 (78.4) | <0.001 | 0.890 | 32 (34.0) | 0.756 | 0.089 |
| Tot n grafts (mean (sd)) | 2.77 (0.89) | 3.07 (0.62) | 0.001 | 0.397 | 2.85 (0.79) | 0.564 | 0.09 |
| Off-pump n(%) | 18 (38.3) | 3051 (43.7) | 0.549 | 0.110 | 36 (38.3) | 1.000 | <0.001 |
| Era of surgery (mean (sd)) | 2000 (4) | 2005 (5) | <0.001 | 1.041 | 2000 (4) | 0.942 | 0.013 |

RITA: right internal thoracic artery; SVG: saphenous vein graft; SMD: standardized mean difference; BMI: body mass index; CCS: Canadian Cardiovascular Society; NYHA: New York American Heart; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA:

cerebrovascular accident; PVD: peripheral vascular disease; AF: Atrial Fibrillation; LVEF: left ventricular ejection fraction; IABP: intraaortic balloon pump; LMD: left main disease

Appendix A: R codes for

```
### packages used for analysis ###
require (survival)
require (nonrandom)
require (prodlim)
###PS model###
ps=pscore(RITA~Age+Female+BMI+CCS+NYHA+MI30d+PCI+DMO+DMI+smoking+ren
al+COPD+CVA+PVD+AF+LV5030+Lvless30+shock+preopIABP+non_elective+LMD+CX
+NGrafts+OPCAB+YOP, rdata)
###PS matching 1:2####
psm=ps.match(ps, ratio=2)
###new dataset with matched pairs only and
m.data=psm$data.matched
### Proportional Hazard check####
Cox.zph(coxph(Surv(time, death==1)~RITA+strata(match.index), m.data))
### Survival curves plot ###
plot(prodlim(Hist(time/365.25, death==1)~RITA, m.data), legend.legend=c('SVG-
RCA','RITA-RCA'), at.risk.at=c(0,5,10,15))
##time segmented analysis @ 9 years ###
#1# time and event variables censored @ 9 years ###
m.data$M9y=m.data$death
m.data$M9y[m.data$death==1&m.data$time>365.25*9]=0
m.data$time9y=m.data$time
m.data$time9y[m.data$time>365.25*9]=365.25*9
###Cox early hazard phase (<9years) ###
coxph(Surv(time9y, M9y==1)~RITA+strata(match.index), m.data)
###Cox late hazard phase(≥9 years) ###
coxph(Surv(time, death)~RITA+strata(match.index), m.data, subset=time≥365.25*9)
```

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