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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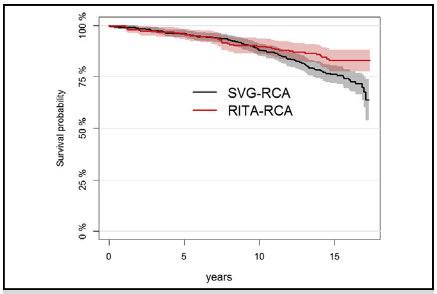
ABSTRACT

Objectives: Although the use of the right internal thoracic artery (RITA) as second arterial conduit to graft the left coronary system consistently has been shown to provide a survival benefit compared with the 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 SVG-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 SVG-RCA graft, respectively. Propensity score matching and time-segmented Cox regression were used to compare the 2 groups.

Results: Survival probability at 5, 10, and 15 years were 95.9% (95% confidence interval [CI], 93.4-98.4) versus 96.0% (95% CI, 94.3-97.8), 89.8% (95% CI, 85.9-93.7) versus 88.0% (95% CI, 85.0-91.0) and 82.9% (95% CI, 77.6-88.2) versus 76.3 (95% CI, 72.0-80.5) in the RITA-RCA and SVG-RCA group, respectively. Time-segmented Cox regression showed that during the first 9 years, the 2 strategies were associated with comparable risk of death (hazard ratio, 1.13; 95% confidence interval, 0.67-1.90; $P = .65$) but beyond 9 years, the RITA-RCA was associated with a significantly lower risk of death (hazard ratio, 0.43; 95% confidence interval, 0.22-0.84; $P = .01$).

Conclusions: Revascularization of the RCA system with the RITA was associated with superior late survival 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. (J Thorac Cardiovasc Surg 2017;154:1269-75)



Survival in the propensity score matched sample according to use of the RITA and SVG for revascularization of the RCA.

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 compared with saphenous vein grafting.

Perspective

The choice of conduit for the right coronary artery (RCA) system remains a controversial issue. The present long-term propensity score–based analysis showed that revascularization of the 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.

See Editorial Commentary page 1276.

The choice of conduit for coronary artery bypass graft (CABG) is debated widely by cardiac surgeons.[1] Although the use of the right internal thoracic artery (RITA) in addition to the left internal thoracic artery (LITA) to graft the left coronary system consistently has been shown to provide a survival benefit compared with saphenous vein graft

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Abbreviations and Acronyms

CABG	= coronary artery bypass graft
CI	= confidence interval
HR	= hazard ratio
LAD	= left anterior descending
LITA	= left internal thoracic artery
PS	= propensity score
RCA	= right coronary artery
RITA	= right internal thoracic artery
SVG	= saphenous vein

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(SVG),[2] the choice of conduit for the right coronary artery (RCA) system remains a controversial issue. To date, the only randomized controlled trial 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 that compared 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 comparisons between RITA versus SVG for grafting the RCA are limited by relatively short follow-up (~5 years).[7] 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 vs in situ grafts) were associated with similar survival rates.

PATIENTS 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 analyzed prospectively collected data from The National Institute for Cardiovascular Outcomes Research National Adult Cardiac Surgery Audit registry on June 1, 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. To summarize, duplicate records and nonadult 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 15,119 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: 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 (Video 1). In the present series, the RITA and SVG 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

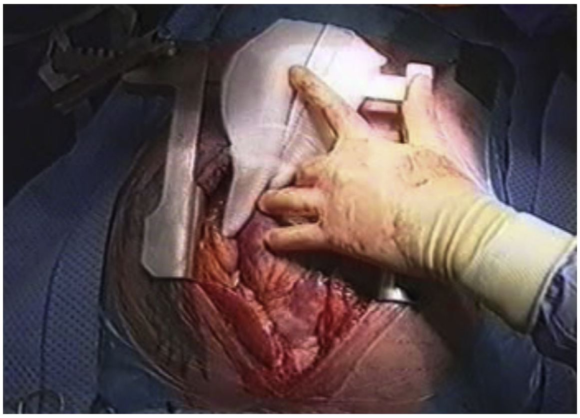
All-cause mortality during follow-up was the primary endpoint. This is considered the most robust and unbiased index in cardiovascular research because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments.[9] Information about postdischarge mortality 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 analyzed were re-exploration for bleeding, need for sternal wound reconstruction, postoperative cerebrovascular accident (defined as any confirmed neurologic deficit of abrupt onset that did not resolve within 24 hours), postoperative renal-replacement therapy, need for postoperative intra-aortic balloon pump, and in-hospital mortality.

Pretreatment Variables

The effect of RITA-RCA versus SVG-RCA on outcomes of interest was adjusted for the following pretreatment variables: age, sex, body mass index; Canadian Cardiovascular Society functional class III-IV; New York Heart Association grade III or IV; previous myocardial infarction within 30 days; previous percutaneous coronary intervention; diabetes mellitus on oral treatment or on insulin; chronic obstructive pulmonary disease; current smoking; serum creatinine ≥200 mmol/L, previous cerebrovascular accident; peripheral vascular disease; preoperative atrial fibrillation; left ventricular ejection fraction between 30% and 49%; left ventricular ejection fraction less than 30%; nonelective admission, cardiogenic shock; preoperative intra-aortic balloon pump; left main disease; concomitant circumflex artery disease grafted; total number of grafts; and off-pump CABG and eras of surgery.

Statistical Analysis

For baseline characteristics, variables are summarized as means ± standard deviation (SD) 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 pretreatment covariates as independent variables with treatment type (RITA-RCA vs SVG-RCA) as a binary dependent variable (https://cran.r-project.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 with the c-statistic and the Hosmer-Lemeshow goodness-of-fit (https://CRAN.R-project.org/package=ResourceSelection). Pairs of patients undergoing RITA-RCA



VIDEO 1. Multiple arterial grafting using the off-pump technique. Video available at: http://www.jtcvsonline.org/article/S0022-5223(17)31048-6/addons.

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 2 groups. The quality of the match was assessed by comparing selected pretreatment variables in PS-matched patients by use of the standardized mean difference, by which an absolute standardized difference of >10% is suggested to represent meaningful covariate imbalance.[11] Analytic methods for the estimation of the treatment effect in the matched sample were used. The 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 with 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 (Figure 1 and Figure E1). RITA was used as in situ in 198 (81%) and as free graft in 47 (19%). Baseline characteristics of the 2 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 left main disease 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 with those receiving RITA-RCA graft (standardized mean difference < 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 $P = .25$; Figure E2).

Short-Term Outcomes

Short-term outcomes are reported in Table 2. The 2 groups presented comparable incidence of postoperative complications rates. In-hospital mortality rate was comparable between RITA-RCA (0.4%) and SVG-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-SVG group, respectively. After PS matching, survival probability at 5, 10, and 15 years were 95.9% (95% confidence interval [CI], 93.4-98.4) versus 96.0% (95% CI, 94.3-97.8), 89.8% (95% CI, 85.9-93.7) versus 88.0% (95% CI, 85.0-91.0) and 82.9% (95% CI, 77.6-88.2) versus 76.3 (95% CI, 72.0-80.5) in the RITA-RCA and SVG-RCA group, respectively (Figure 2).

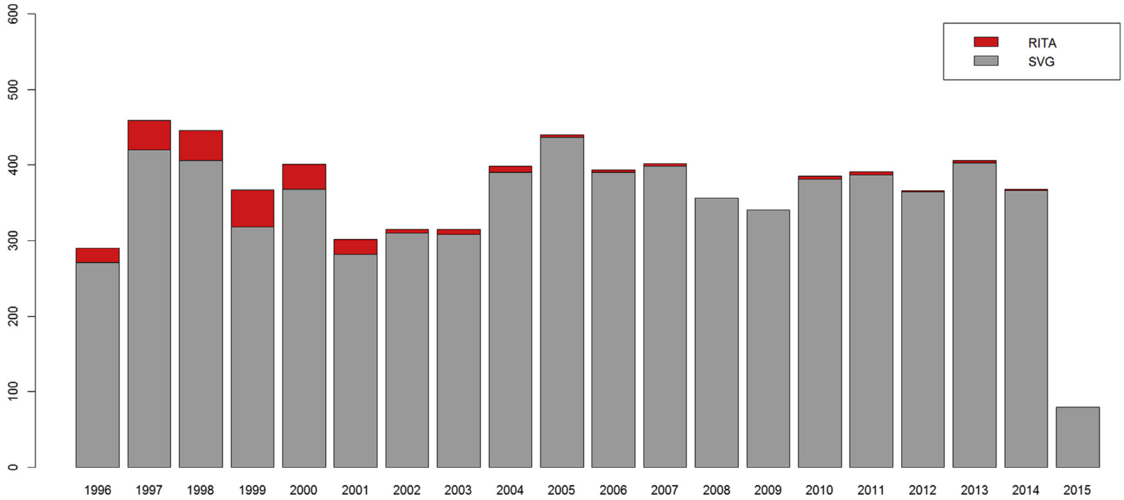


FIGURE 1. Use of the RITA and SVG for revascularization of the right coronary artery during the study period. *RITA*, Right internal thoracic artery; *SVG*, saphenous vein graft.

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)	<.001	1.547	57 (8)	.09	0.09
Female, n (%)	24 (9.8)	1307 (18.7)	.001	0.258	47 (9.6)	1.000	0.007
BMI, mean (SD)	27.59 (3.26)	27.79 (4.40)	.485	0.051	27.64 (4.06)	.873	0.013
CCS III-IV, n (%)	122 (49.8)	3409 (48.9)	.822	0.019	237 (48.4)	.774	0.029
NYHA III-IV, n (%)	55 (22.4)	2156 (30.9)	.006	0.192	116 (23.7)	.781	0.029
MI within 30 d, n (%)	13 (5.3)	1488 (21.3)	<.001	0.485	28 (5.7)	.955	0.018
PCI, n (%)	3 (1.2)	336 (4.8)	.014	0.211	6 (1.2)	1.000	<0.001
DM orally treated, n (%)	4 (1.6)	808 (11.6)	<.001	0.409	5 (1.0)	.722	0.054
DM on insulin, n (%)	7 (2.9)	572 (8.2)	.004	0.235	8 (1.6)	.406	0.083
Smoking, n (%)	50 (20.4)	849 (12.2)	<.001	0.225	96 (19.6)	.870	0.020
Creatinine, >200 mmol/L, n (%)	3 (1.2)	216 (3.1)	.136	0.129	7 (1.4)	1.000	0.018
COPD, n (%)	5 (2.0)	571 (8.2)	.001	0.282	12 (2.4)	.931	0.028
CVA, n (%)	3 (1.2)	290 (4.2)	.034	0.182	6 (1.2)	1.000	<0.001
PVD, n (%)	21 (8.6)	780 (11.2)	.241	0.087	35 (7.1)	.589	0.053
AF, n (%)	5 (2.0)	249 (3.6)	.272	0.093	10 (2.0)	1.000	<0.001
LVEF 30%-49%, n (%)	31 (12.7)	1705 (24.4)	<.001	0.307	68 (13.9)	.731	0.036
LVEF <30%, n (%)	2 (0.8)	387 (5.5)	.002	0.272	5 (1.0)	1.000	0.021
Shock, n (%)	0 (0.0)	36 (0.5)	.506	0.102	0 (0.0)	—	—
Preoperative IABP, n (%)	1 (0.4)	120 (1.7)	.187	0.128	1 (0.2)	1.000	0.037
Nonelective, n (%)	99 (40.4)	3433 (49.2)	.008	0.177	199 (40.6)	1.000	0.004
LMD, n (%)	18 (7.3)	1707 (24.5)	<.001	0.481	33 (6.7)	.878	0.024
Circumflex artery grafted, n (%)	104 (42.4)	5469 (78.4)	<.001	0.790	223 (45.5)	.479	0.062
Total n grafts, mean (SD)	2.73 (0.80)	3.07 (0.62)	<.001	0.469	2.79 (0.72)	.346	0.072
Off-pump, n (%)	60 (24.5)	3051 (43.7)	<.001	0.414	128 (26.1)	.698	0.038
Era of surgery, mean (SD)	2000 (4)	2005 (6)	<.001	1.140	2000 (4)	.367	0.072

RITA, Right internal thoracic artery; *RCA*, right coronary artery; *SVG*, saphenous vein graft; *SMD*, standardized mean difference; *SD*, standard deviation; *BMI*, body mass index; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *DM*, diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *PVD*, peripheral vascular disease; *AF*, atrial fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pump; *LMD*, left main disease.

Kaplan–Meier analysis showed that the 2 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 $P = .03$). Time-segmented Cox regression showed that during the first 9 years, the 2 strategies were associated with comparable risk of death (hazard ratio [HR], 1.13; 95% CI, 0.67-1.90; $P = .65$) 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; $P = .01$). When the RITA-RCA group was divided in free RITA-RCA graft (n = 47) and in situ RITA-RCA graft

TABLE 2. Operative outcomes

	RITA-RCA	SVG-RCA (unmatched)	*P*	2:1 Matched SVG-RCA	*P*
n	245	6978		490	
Mortality within 30 d, n (%)	1 (0.4)	103 (1.5)	.269	3 (0.6)	1.000
Re-exploration for bleeding, n (%)	9 (3.7)	215 (3.1)	.735	12 (2.4)	.481
Sternal wound reconstruction, n (%)	0 (0.0)	48 (0.7)	.367	0 (0.0)	–
Postoperative stroke, n (%)	0 (0.0)	114 (1.6)	.079	6 (1.2)	.192
Postoperative RRT, n (%)	3 (1.2)	173 (2.5)	.298	5 (1.0)	1.000

RITA, Right internal thoracic artery; *RCA*, right coronary artery; *SVG*, saphenous vein graft; *RRT*, renal-replacement therapy.

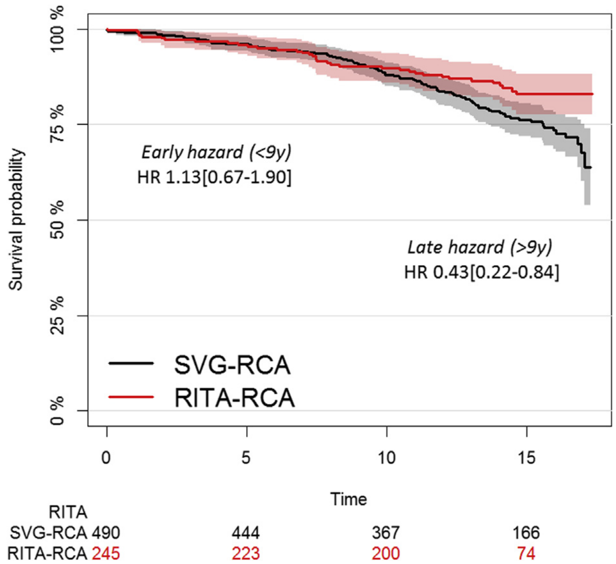


FIGURE 2. Survival in the propensity score matched sample according to use of the RITA or SVG for revascularization of the RCA. *HR*, Hazard ratio; *SVG*, saphenous vein graft; *RCA*, right coronary artery; *RITA*, right internal thoracic artery.

(n = 198), survival probability at 5, 10, and 15 years was 91.1% (95% CI, 82.9-99.4) versus 97.0 (95% CI, 94.6-99.4), 81.7 (95% CI, 70.3-93.2) versus 91.6% (95% CI, 87.7-95.6), and 71.1 (95% CI, 57.1-85.1) versus 85.5% (95% CI, 80.0-91.1), respectively. Patients receiving free RITA-RCA and in situ RITA-RCA were compared separately with 1:2 matched pairs of patients receiving SVG-RCA (Table E1 and Table E2). In situ RITA-RCA (HR, 0.60; 95% CI, 0.35-0.98; P = .04; Weight residual test P = .12; Figure 3, *right*) but not free RITA-RCA (HR, 1.03; 95% CI, 0.47-2.26; P = .94; residual weights test P = .58; Figure 3, *left*) was associated with better survival compared with SVG-RCA. Baseline characteristics and survival rates among in the unmatched SVG-RCA group are reported in Table E3 and Figure E3.

DISCUSSION

The main finding of the present analysis is that the use of the RITA to graft the right coronary artery system was associated with superior long-term survival compared with the SVG. Survival benefit was not 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 the free RITA graft configuration. However, the 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 center. 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 LAD 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.

Although the use of the RITA to graft the left coronary system has been reported consistently 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

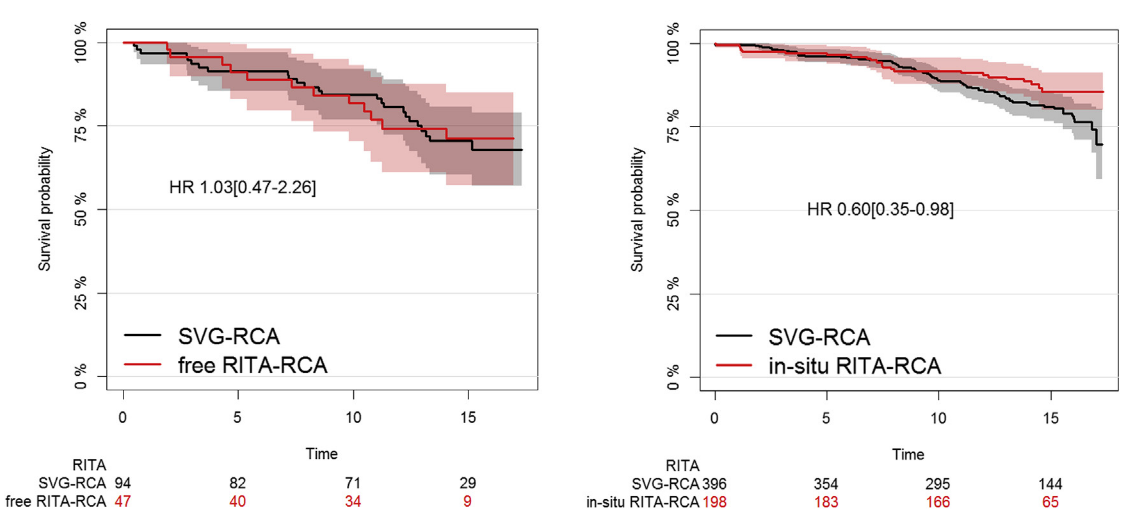


FIGURE 3. Survival after propensity score matching according to use of the RITA used as free (*left*) or in situ (*right*) graft versus SVG for revascularization of the RCA. *HR*, Hazard ratio; *SVG*, saphenous vein graft; *RCA*, right coronary artery; *RITA*, right internal thoracic artery.

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 an excellent patency rate.[16,17]

The variability of RITA-RCA graft patency rate according to the severity of the RCA stenosis might account partially for conflicting findings reported on survival benefit from the use of RITA instead of SVG. Schmidt and colleagues[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 ($P = .02$). In contrast, Kurlansky and colleagues[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 and colleagues[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 compared with SVG, 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 the rate of SVG failure 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 versus 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. In a previous report, Buxton and colleagues[8] 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. In contrast, large angiographic studies have confirmed excellent patency rates with free RITA graft.[13,19] Tatoulis and colleagues[13] found that in situ RITA ($n = 450$) and free RITA grafts ($n = 541$) had similar 10-year patency rates (89% vs 91%; $P = .44$). Interestingly, they found that for the posterior descending artery, in situ and free RITA grafts provided similar patency rates ($P = .67$) but for the main RCA, in situ RITA patency was associated with lower patency rate compared with free RITA (73.8% vs 93.1%; $P = .02$).

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 demonstrated consistently 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 used primarily in the first part of the series. Differences between the 2 groups can be caused by variation of patient risk profiles across different surgical eras. PS matching can adjust only for measurable and included variables, and we cannot exclude a selection bias based on nonmeasurable ‘‘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 noncardiac), 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 years) compared with SVG. Further evidence is 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.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: coronary artery bypass grafting, multiple arterial grafting, survival, propensity score matching

APPENDIX E1. R CODES FOR TIME-SEGMENTED COX REGRESSION

```
### 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+renal+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)
```

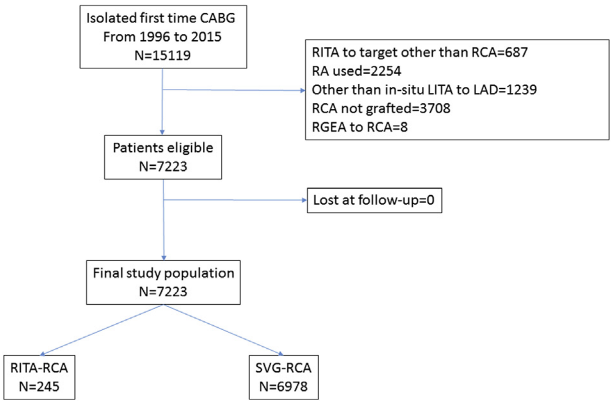

FIGURE E1. Flow chart for patient selection. *CABG*, Coronary artery bypass grafting; *RITA*, right internal thoracic artery; *RCA*, right coronary artery; *RA*, radial artery; *LITA*, left internal thoracic artery; *LAD*, left anterior descending; *RGEA*, right gastroepiploic artery; *SVG*, saphenous vein graft.

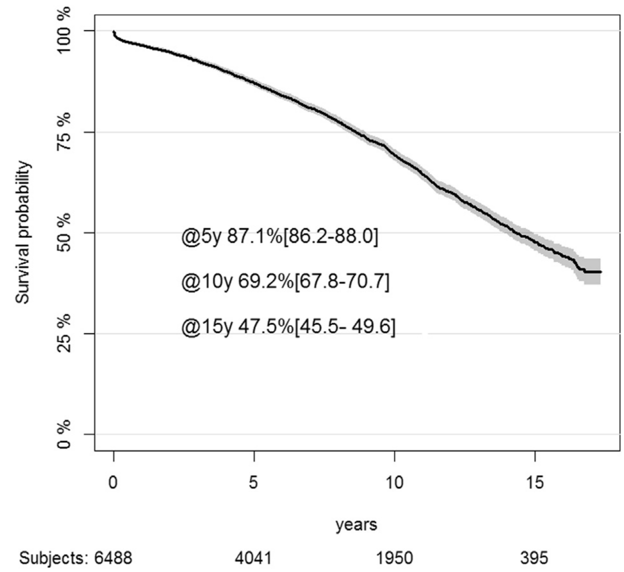

FIGURE E3. Survival rates in subjects receiving SVG to the RCA.

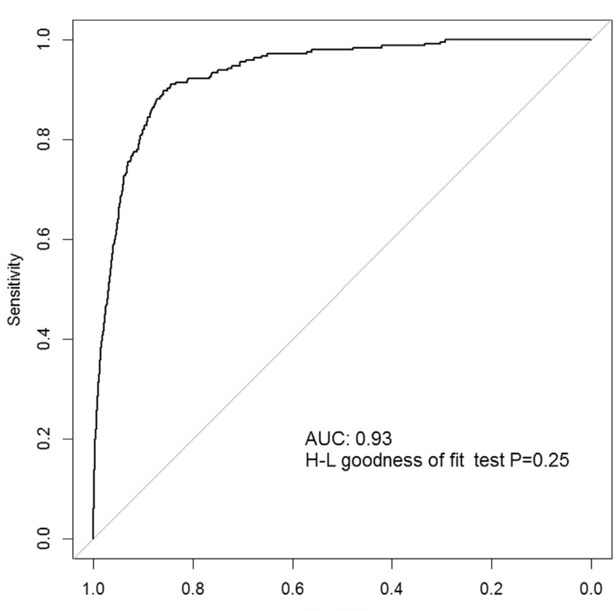

FIGURE E2. AUC (C statistics) for the propensity score model and relative H-L goodness of fit test. *AUC*, Area under the receiver operating characteristic curve; *H-L*, Hosmer and Lemeshow.

TABLE E1. Patients' characteristics distribution before and after matching in the in situ RITA-RCA and SVG-RCA groups

Characteristic	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)	<.001	1.597	56 (8)	.759	0.027
Female, n (%)	20 (10.1)	1307 (18.7)	.003	0.248	41 (10.4)	1.000	0.008
BMI, mean (SD)	27.71 (3.05)	27.79 (4.40)	.816	0.019	27.92 (4.41)	.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)	.007	0.210	93 (23.5)	.704	0.042
MI within 30 d, n (%)	9 (4.5)	1488 (21.3)	<.001	0.516	21 (5.3)	.842	0.035
PCI, n (%)	3 (1.5)	336 (4.8)	.047	0.189	8 (2.0)	.914	0.038
DM orally treated, n (%)	4 (2.0)	808 (11.6)	<.001	0.387	9 (2.3)	1.000	0.017
DM on insulin, n (%)	4 (2.0)	572 (8.2)	.003	0.283	12 (3.0)	.654	0.064
Smoking, n (%)	43 (21.7)	849 (12.2)	<.001	0.257	94 (23.7)	.654	0.048
Creatinine, >200 mmol/L, n (%)	1 (0.5)	216 (3.1)	.059	0.196	2 (0.5)	1.000	<0.001
COPD, n (%)	4 (2.0)	571 (8.2)	.003	0.283	8 (2.0)	1.000	<0.001
CVA, n (%)	1 (0.5)	290 (4.2)	.017	0.244	3 (0.8)	1.000	0.032
PVD, n (%)	14 (7.1)	780 (11.2)	.089	0.143	23 (5.8)	.674	0.051
AF, n (%)	3 (1.5)	249 (3.6)	.176	0.131	7 (1.8)	1.000	0.020
LVEF 30%-49%, n (%)	22 (11.1)	1705 (24.4)	<.001	0.354	50 (12.6)	.689	0.047
LVEF<30%, n (%)	2 (1.0)	387 (5.5)	.009	0.257	4 (1.0)	1.000	<0.001
Shock, n (%)	0 (0.0)	36 (0.5)	.615	0.102	0 (0.0)	—	—
Preoperative IABP, n (%)	1 (0.5)	120 (1.7)	.303	0.116	3 (0.8)	1.000	0.032
Nonelective, n (%)	81 (40.9)	3433 (49.2)	.026	0.167	167 (42.2)	.837	0.026
LMD, n (%)	16 (8.1)	1707 (24.5)	<.001	0.455	30 (7.6)	.957	0.019
Circumflex artery grafted, n (%)	86 (43.4)	5469 (78.4)	<.001	0.767	186 (47.0)	.467	0.071
Total n grafts, mean (SD)	2.73 (0.78)	3.07 (0.62)	<.001	0.487	2.80 (0.70)	.247	0.099
Off-pump, n (%)	42 (21.2)	3051 (43.7)	<.001	0.495	89 (22.5)	.807	0.031
Era of surgery, mean (SD)	2000 (4)	2005 (5)	<.001	1.163	2000 (5)	.133	0.09

RITA, Right internal thoracic artery; *RCA*, right coronary artery; *SVG*, saphenous vein graft; *SMD*, standardized mean difference; *SD*, standard deviation; *BMI*, body mass index; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *DM*, diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *PVD*, peripheral vascular disease; *AF*, atrial fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pump; *LMD*, left main disease.

TABLE E2. Patients' characteristics distribution before and after matching in the free RITA-RCA and SVG-RCA groups

Characteristic	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)	<.001	1.360	57 (8)	.531	0.09
Female, n (%)	4 (8.5)	1307 (18.7)	.109	0.301	5 (5.3)	.715	0.126
BMI, mean (SD)	27.06 (4.04)	27.79 (4.40)	.260	0.172	27.75 (3.83)	.322	0.176
CCS III-IV, n (%)	25 (53.2)	3409 (48.9)	.655	0.087	58 (61.7)	.432	0.173
NYHA III-IV, n (%)	12 (25.5)	2156 (30.9)	.525	0.119	23 (24.5)	1.000	0.025
MI within 30 d, n (%)	4 (8.5)	1488 (21.3)	.050	0.366	8 (8.5)	1.000	<0.001
PCI, n (%)	0 (0.0)	336 (4.8)	.231	0.318	0 (0.0)	—	—
DM orally treated, n (%)	0 (0.0)	808 (11.6)	.024	0.512	0 (0.0)	—	—
DM on insulin, n (%)	3 (6.4)	572 (8.2)	.853	0.070	5 (5.3)	1.000	0.045
Smoking, n (%)	7 (14.9)	849 (12.2)	.729	0.080	15 (16.0)	1.000	0.029
Creatinine, > 200 mmol/L, n (%)	2 (4.3)	216 (3.1)	.972	0.062	7 (7.4)	.715	0.136
COPD, n (%)	1 (2.1)	571 (8.2)	.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)	.567	0.111	16 (17.0)	.936	0.058
AF, n (%)	2 (4.3)	249 (3.6)	1.000	0.035	6 (6.4)	.898	0.095
LVEF 30%-49%, n (%)	9 (19.1)	1705 (24.4)	.503	0.128	16 (17.0)	.938	0.055
LVEF<30%, n (%)	0 (0.0)	387 (5.5)	.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)	.732	0.187	0 (0.0)	—	—
Nonelective, n (%)	18 (38.3)	3433 (49.2)	.179	0.221	35 (37.2)	1.000	0.022
LMD, n (%)	2 (4.3)	1707 (24.5)	.002	0.602	6 (6.4)	.898	0.095
Circumflex artery grafted, n (%)	18 (38.3)	5469 (78.4)	<.001	0.890	32 (34.0)	.756	0.089
Tot n grafts, mean (SD)	2.77 (0.89)	3.07 (0.62)	.001	0.397	2.85 (0.79)	.564	0.09
Off-pump, n (%)	18 (38.3)	3051 (43.7)	.549	0.110	36 (38.3)	1.000	<0.001
Era of surgery, mean (SD)	2000 (4)	2005 (5)	<.001	1.041	2000 (4)	.942	0.013

RITA, Right internal thoracic artery; *RCA*, right coronary artery; *SVG*, saphenous vein graft; *SMD*, standardized mean difference; *SD*, standard deviation; *BMI*, body mass index; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *DM*, diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *PVD*, peripheral vascular disease; *AF*, atrial fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pump; *LMD*, left main disease.

TABLE E3. Patients' characteristics distribution in unmatched subjects undergoing SVG-RCA

Characteristic	Unmatched SVG-RCA
n	6488
Age, mean (SD)	69 (8)
Female, n (%)	1260 (19.4)
BMI, mean (SD)	27.80 (4.43)
CCS III-IV, n (%)	3172 (48.9)
NYHA III-IV, n (%)	2040 (31.4)
MI within 30 d, n (%)	1460 (22.5)
PCI, n (%)	330 (5.1)
DM orally treated, n (%)	803 (12.4)
DM on insulin, n (%)	564 (8.7)
Smoking, n (%)	753 (11.6)
Creatinine, >200 mmol/L, n (%)	209 (3.2)
COPD, n (%)	559 (8.6)
CVA, n (%)	284 (4.4)
PVD, n (%)	745 (11.5)
AF, n (%)	239 (3.7)
LVEF 30%-49%, n (%)	1637 (25.2)
LVEF < 30%, n (%)	382 (5.9)
Shock, n (%)	36 (0.6)
Preop IABP, n (%)	119 (1.8)
Nonelective, n (%)	3234 (49.8)
LMD, n (%)	1674 (25.8)
Circumflex artery grafted, n (%)	5246 (80.9)
Tot n grafts, mean (SD)	3.09 (0.61)
Off-pump, n (%)	2923 (45.1)
Era of surgery, mean (SD)	2005 (5)

SVG, Saphenous vein graft; *RCA*, right coronary artery; *SD*, standard deviation; *BMI*, body mass index; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *DM*, diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *PVD*, peripheral vascular disease; *AF*, atrial fibrillation; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pump; *LMD*, left main disease.