Right internal thoracic artery or radial artery? A propensity-matched comparison on the second-best arterial conduit

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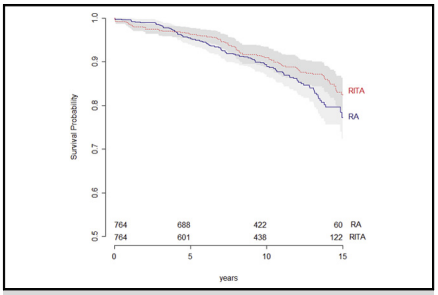
ABSTRACT

Objectives: We conducted propensity score matching to determine whether the use of the right internal thoracic artery (RITA) confers a survival advantage when compared with the radial artery (RA) as second arterial conduit in coronary artery bypass grafting.

Methods: The study population included a highly selected low-risk group of patients who received the RITA (n = 764) or the RA (n = 1990) as second arterial conduit. We obtained 764 matched pairs that were comparable for all pretreatment variables. A time-segmented Cox regression model that stratified on the matched pairs was used to investigate the effect of treatment on late mortality.

Results: After a mean follow-up of 10.2 ± 4.5 years (maximum 17.3 years), survival probabilities at 5, 10, and 15 years were 96.4% ± 0.7% versus 95.4% ± 0.7%, 91.0% ± 1.1% versus 89.1% ± 1.2%, and 82.4% ± 1.9% versus 77.2% ± 2.5% in the RITA and RA groups, respectively. During the first 4 years, RITA and RA were comparable in terms of mortality (hazard ratio [HR], 1.00; 95% confidence interval [CI], 0.56-1.78; $P = .98$). However, after 4 years RITA was associated with a significant reduction in late mortality (HR, 0.67; 95% CI, 0.48-0.95; $P = .02$). RITA was superior to RA when the experimental conduit was used to graft the left coronary system (HR, 0.69; 95% CI, 0.47-0.99; $P = .04$) but not the right coronary system (HR, 0.98; 95% CI, 0.59-1.62; $P = .93$).

Conclusions: In a highly selected low-risk group of patients, the use of the RITA as second arterial conduit instead of the RA was associated with better survival when used to graft the left but not the right coronary artery. (J Thorac Cardiovasc Surg 2017;153:79-88)



Kaplan-Meier survival curve probabilities in the right internal thoracic artery (RITA) and the radial artery (RA) groups in the propensity-score-matched population.

Central Message

In a highly selected low-risk group of patients, the use of the RITA as second arterial conduit instead of the RA was associated with better survival when used to graft the left but not the right coronary artery.

Perspective

The choice of the right internal thoracic artery (RITA) or radial artery (RA) as the second conduit in patients undergoing CABG remains controversial. In a highly selected low-risk group of patients, the use of the RITA as second arterial conduit instead of the RA was associated with better survival when used to graft the left but not the right coronary artery.

See Editorial Commentary page 89.

Despite increasing recognition that multiple arterial conduits improve long-term outcomes after coronary artery bypass grafting (CABG),[1] the quest for the second-best arterial conduit to supplement the left internal thoracic artery (LITA) continues.[2] In particular, it is still to be

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Abbreviations and Acronyms

BMI = body mass index
CABG = coronary artery bypass grafting
COPD = chronic obstructive pulmonary disease
CVA = cerebrovascular accident
CX = circumflex artery
IABP = intra-aortic balloon pump
LAD = left anterior descending artery
LITA = left internal thoracic artery
OPCAB = off-pump coronary artery bypass
PS = propensity score
PSM = propensity score matching
RA = radial artery
RCA = right coronary artery
RCT = randomized controlled trial
RITA = right internal thoracic artery
SMD = standardized mean difference
SV = saphenous vein

determined whether the use of the right internal thoracic artery (RITA) confers a survival advantage when compared with the radial artery (RA).[3] To date, only a single randomized controlled trial (RCT)[3] has been published in the literature, largely underpowered to detect any difference in long-term survival between the RITA and RA groups. Several observational studies comparing RITA with RA have been reported with conflicting findings.[4-12] Propensity score matching (PSM)-based analysis of observational data is emerging as an attractive alternative in view of the paucity of evidence from RCT, and can be relied upon as evidence when RCTs are not possible.[4] Recently, general recommendations have been proposed for conducting PSM.[13-15] We aimed to compare short-term outcomes and long-term survival in patients receiving RITA versus RA as second arterial conduit by conducting a single-center 15-year outcomes PSM comparison in accordance with current recommendations.

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 (NICOR) NACSA registry on June 1, 2015, for all isolated first-time CABG procedures performed at the Bristol Heart Institute, Bristol, United Kingdom, from April 1996 to April 2015. Reproducible cleaning algorithms were applied to the database, which are regularly updated as required. Briefly, duplicate records and nonadult cardiac surgery entries were removed; transcriptional discrepancies harmonized; and clinical conflicts and extreme values corrected or removed. The data are 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. Of 15,119 isolated first-time cases of CABG performed during the study period, we selected patients who met the following criteria: multivessel coronary disease including left main and/or left anterior descending artery (LAD) coronary disease; requiring at least 2 grafts; CABG performed using the following strategies: LITA used in situ to graft the LAD territory and RA to graft the non-LAD territory with or without additional saphenous vein (SV) grafts (RA group) or both LITA and RITA with or without additional SV grafts as required in both groups (Figure E1). Patients receiving both the RITA and the RA (n = 275) were excluded from the present analysis. In the present series, the RITA and the RA were used only in cases where target stenosis was ≥75%. The RA was used as a free graft directly connected to the ascending aorta. The internal thoracic artery was harvested as a pedicle in all cases and was used as an in situ graft that remained proximally connected to its respective subclavian artery or as a free graft proximally connected to other internal thoracic artery.

Pretreatment Variables and Study Endpoints

The effect of adding the RA as a third arterial conduit instead of SV was adjusted for the following variables: age, gender, body mass index (BMI); previous myocardial infarction, previous percutaneous coronary intervention (PCI); diabetes mellitus orally treated or on insulin; chronic obstructive pulmonary disease (COPD); current smoking; serum creatinine ≥200 mmol/L, previous cerebrovascular accident (CVA); peripheral vascular disease; preoperative atrial fibrillation; left main disease; non-LAD vessel diseased including diagonal; circumflex artery (CX); right coronary artery (RCA); left ventricle ejection fraction, non-elective priority, off-pump coronary artery bypass (OPCAB), procedure performed by resident versus attending surgeon and logistic euroSCORE.

Short-term endpoints were 30-day mortality, need for postoperative intra-aortic balloon pump (IABP), re-exploration for bleeding, renal replacement therapy, and sternal wound reconstruction. Long-term end-point was all-cause mortality, which is a robust and unbiased index for comparative studies because no adjudication is required.[16] Information about death was obtained from the institutional database and the National General Register Office for all patients. Follow-up was completed for all patients (100%).

Statistical Analysis

For baseline characteristics, variables are summarized as mean for continuous variables and proportion for categorical variables. Multiple imputation was used to address missing data (Table E1 and Figure E2) (available from: 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 based on pretreatment covariates as independent variables, with treatment type (RITA vs RA) as a binary dependent variable according to current recommendations.[13,15] The resulting propensity score represented the probability of a patient receiving the RITA as second arterial conduit. Because the PS model achieved a good discriminatory power (C-statistic = 0.74; Figure E3), no attempt was made to include interactions or nonlinear terms. Pairs of patients receiving RITA and RA were derived using greedy 1:1 matching with a caliper of width of 0.2 standard deviation of the logit of the PS[14] (available from: http://CRAN.Rproject.org/package=nonrandom). The quality of the match was assessed by comparing selected pretreatment variables in propensity-score-matched patients using the standardized mean difference (SMD), by which an absolute standardized difference of greater than 10% is suggested to represent meaningful covariate imbalance.[13-15] Analytic methods for the estimation of the treatment effect in the matched sample were selected. McNemar's test was used to compare postoperative complication rates in the 2 groups.[13] In the primary Kaplan-Meier analysis, comparing late survival between the 2 groups, it was found that the curves crossed thus showing that the proportional hazards assumption was violated and the hazard was not constant with time. To evaluate the trends in this Kaplan-Meier curve, time-segmented Cox regression models before and after the curves crossed,[17] stratified on the matched pairs,[18] were used to investigate the effect of treatment (RITA vs RA) on early and late mortality phases. This

TABLE 1. Pretreatment variables distribution in the RITA group and in the unmatched and matched RA group

	RITA (N = 764)		Unmatched RA (N = 1990)		PSM RA (N = 764)			
Variable	**n**	**%**	**n**	**%**	**n**	**%**	**SMD before PSM**	**SMD after PSM**
Age								
Mean, y ± SD	57 ± 9		61 ± 9		58 ± 8		−44.6	−4.1
<60 y	501	65.6	859	43.2	453	59.3		
60-69 y	213	27.9	797	40.1	254	33.2		
70-79 y	41	5.4	303	15.2	55	7.2		
≥80 y	9	1.2	31	1.6	2	0.3		
Female								
No	710	92.9	1727	86.8	711	93.1	−20.5	−0.5
Yes	54	7.1	263	13.2	53	6.9		
BMI								
Mean, kg/m^2 ± SD	28 ± 3		29 ± 4		28 ± 4		−23.7	−2.9
<30 kg/m^2	597	78.1	1318	66.2	568	74.3		
≥30 kg/m^2	167	21.9	672	33.8	196	25.7		
MI								
No	447	58.5	1096	55.1	443	58.0	−6.9	−1.1
Yes	317	41.5	894	44.9	321	42.0		
PCI								
No	725	94.9	1883	94.6	726	95.0	1.2	0.6
Yes	39	5.1	107	5.4	38	5.0		
DM								
No	725	94.9	1635	82.2	715	93.6	−35.4	−1.1
Orally treated	17	2.2	212	10.7	34	4.5		
On insulin	22	2.9	143	7.2	15	2.0		
Current smoking								
No	631	82.6	1677	84.3	621	81.3	−4.5	−3.4
Yes	133	17.4	313	15.7	143	18.7		
Creatinine >200 mmol/L								
No	760	99.5	1986	99.8	763	99.9	5.4	6.9
Yes	4	0.5	4	0.2	1	0.1		
COPD								
No	726	95.0	1813	91.1	728	95.3	−15.5	−1.2
Yes	38	5.0	177	8.9	36	4.7		
CVA								
No	754	98.7	1939	97.4	752	98.4	−9.1	−2.2
Yes	10	1.3	51	2.6	12	1.6		
PVD								
No	716	93.7	1853	93.1	718	94.0	2.4	1.1
Yes	48	6.3	137	6.9	46	6.0		
AF								
No	754	98.7	1938	97.4	752	98.4	−9.4	−2.2
Yes	10	1.3	52	2.6	12	1.6		
LVEF								
≥50%	646	84.6	1587	79.7	647	84.7	−13.4	0
30%-49%	109	14.3	359	18.0	107	14.0		
<30%	9	1.2	44	2.2	10	1.3		
Preoperative IABP								
No	763	99.9	1988	99.9	763	99.9	−0.9	0
Yes	1	0.1	2	0.1	1	0.1		
OPCAB								
No	421	55.1	617	31.0	380	49.7	−50.2	−9.8
Yes	343	44.9	1373	69.0	384	50.3		
Non-elective priority								
No	427	55.9	1176	59.1	421	55.1	6.5	1.6
Yes	337	44.1	814	40.9	343	44.9		

(Continued)

TABLE 1. Continued

Variable	RITA (N = 764) n	RITA (N = 764) %	Unmatched RA (N = 1990) n	Unmatched RA (N = 1990) %	PSM RA (N = 764) n	PSM RA (N = 764) %	SMD before PSM	SMD after PSM
Performed by resident								
No	419	54.8	1423	71.5	435	56.9	35.1	4.2
Yes	345	45.2	567	28.5	329	43.1		
Logistic euroSCORE								
Mean ± SD	2% ± 2%		2% ± 3%		2% ± 2%		−19.2	−0.7
<1.0%	233	30.5	369	18.5	220	28.8		
1.0%-1.9%	318	41.6	816	41.0	336	44.0		
2%-2.9%	114	14.9	391	19.6	124	16.2		
≥3.0%	99	13.0	414	20.8	84	11.0		
Year of surgery								
1996-1999	289	37.8	160	8.0	99	13.0	−33.3	−7.8
2000-2004	190	24.9	743	37.3	338	44.2		
2005-2009	133	17.4	835	42.0	274	35.9		
2010-2015	152	19.9	252	12.7	53	6.9		
LMS								
No	587	76.8	1502	75.5	576	75.4	3.2	3.4
Yes	177	23.2	488	24.5	188	24.6		
LAD								
No	4	0.5	25	1.3	4	0.5	7.8	0
Yes	760	99.5	1965	98.7	760	99.5		
RCA								
No	220	28.8	701	35.2	220	28.8	13.8	0
Yes	544	71.2	1289	64.8	544	71.2		
CX								
No	151	19.8	379	19.0	136	17.8	1.8	5
Yes	613	80.2	1611	81.0	628	82.2		
DIA								
No	599	78.4	1511	75.9	598	78.3	−5.9	−0.3
Yes	165	21.6	479	24.1	166	21.7		

RITA, Right internal thoracic artery; *RA*, radial artery; *PSM*, propensity score matching; *SMD*, standardized mean difference; *SD*, standard deviation; *BMI*, body mass index; *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; *OPCAB*, off-pump coronary artery bypass grafting; *LMS*, left main stem; *LAD*, left anterior descending artery; *RCA*, right coronary artery; *CX*, circumflex artery; *DIA*, diagonal.

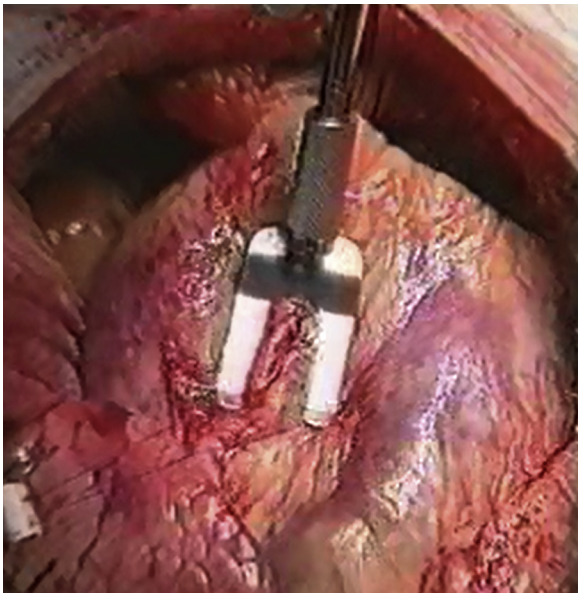
approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets (available from: http://CRAN.R-project.org/package=survival). The Schoenfeld residuals test was used to confirm the nonviolation of the proportional hazard assumption in the 2 separate Cox models. Subgroup analysis on late mortality according to the experimental conduit target, RITA configuration, and OPCAB use was carried out by mains of covariate adjustment using the PS on the overall sample to account for the relatively small sample size. Finally, because of the different distribution in OPCAB rate across the years (Figure E4), the treatment effect was adjusted for the interaction between OPCAB and year of surgery. Because of the highly selected low-risk population, frailty models were not used. All P values less than .05 were considered to indicate statistical significance. All statistical analysis was performed using R statistical software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The study population included 764 low-risk patients who received RITA with (n = 482) or without (282) additional SV grafts and 1990 patients who received the RA with (n = 1206) or without (784) additional SV grafts. The distribution of patient characteristics before and after PS matching is summarized in Table 1. In the unmatched group, RA tended to present a higher burden of comorbidities. In particular they were more likely to be older and female and to have a BMI ≥ 30, COPD, and diabetes (both orally treated and on insulin) and impaired left ventricular function. OPCAB rate was higher in the RA group (Video 1). After matching the 764 matched pairs, the groups were comparable for all pretreatment variables (SMD < 10, Figure 1).

Arterial Graft Configuration

The mean number of grafts performed was 2.87 ± 0.76 in the RITA group versus 2.80 ± 0.70 and 2.87 ± 0.70 in the unmatched (P = .003) and matched (P = .1) RA groups, respectively. Graft targets in the unmatched and matched groups are summarized in Table 2. The RITA was used to graft the CX territory in 319 (42%) cases, the RCA territory in 245 (32%) cases, and the LAD territory in 200 (26%)



VIDEO 1. Radial artery grated to the circumflex artery during off-pump coronary artery bypass. Video available at: http://www.jtcvsonline.org/article/S0022-5223(16)31099-6/addons.

cases. Overall, the CX territory was grafted using an internal thoracic artery in 519 (68%) cases. The RA was used to graft the CX territory in 1530 (77%) cases and 565 (74%) cases, the RCA territory in 460 (23%) cases and 199 (26%) cases in the unmatched and matched RA groups, respectively. The RITA was used as a Y-graft in 144 cases and as in situ graft in the remaining 620 cases.

Short-Term Outcomes

Short-term outcomes in the matched samples are summarized in Table 3. The 2 groups were comparable in terms of 30-day mortality, incidence of CVA, and need for renal replacement therapy. However, we found a trend towards a higher rate of re-exploration for bleeding, sternal wound reconstruction, and need for postoperative IABP in the RITA group, although the overall incidence of these complications was relatively low. Hospital stay length tended to be increased in the RITA group. Short-term outcomes in the unmatched RA group are reported in Table E2.

Mortality

In the PS-matched group, mean time to follow-up was 10.2 ± 4.5 years (maximum 17.3 years) and 10.1 ± 5.1 and 10.3 ± 3.7 years in the RITA and matched RA groups, respectively ($P = .31$). A total of 85 and 106 deaths were recorded in the RITA and RA groups, respectively. Survival probabilities at 5, 10, and 15 years were 96.4% ± 0.7% versus 95.4% ± 0.7%, 91.0% ± 1.1% versus 89.1% ± 1.2%, and 82.4% ± 1.9% versus 77.2% ± 2.5% in the RITA and RA groups respectively. The 2 survival curves crossed at 4 years (96.9 ± 0.6 years, Figure 2). During the first 4 years, RITA and RA were

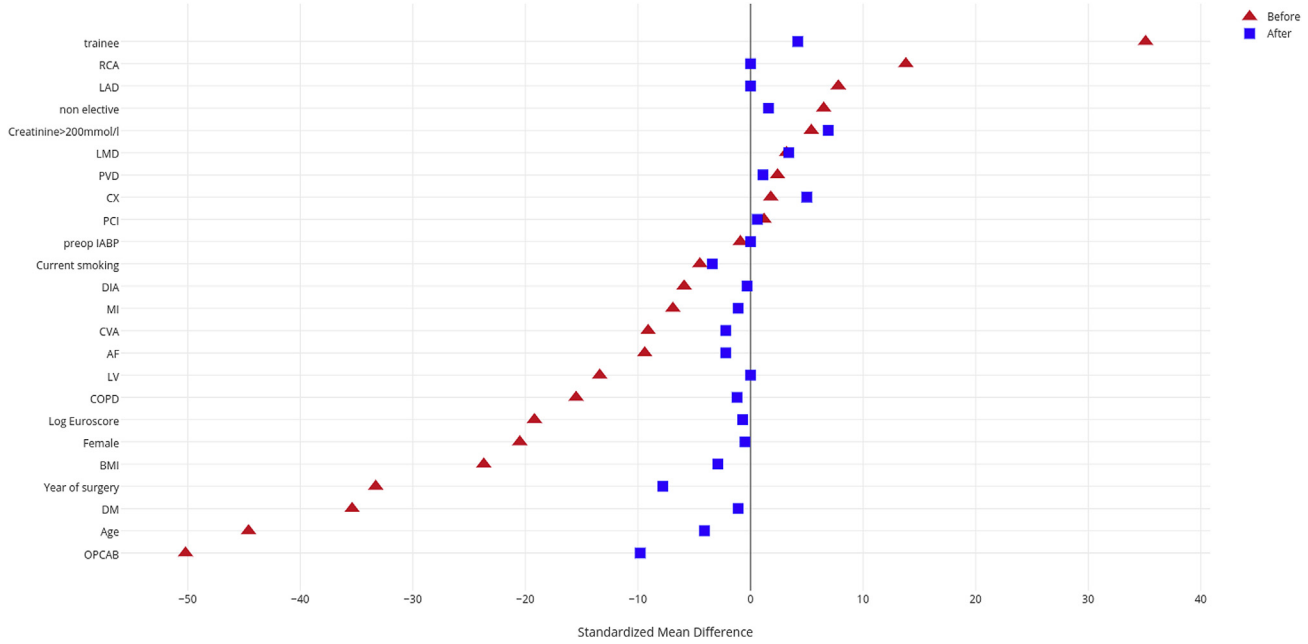


FIGURE 1. Graphic visualization of standardized mean difference before after propensity score matching. *RCA*, Right coronary artery; *LAD*, left anterior descending artery; *LMD*, left main disease; *PVD*, peripheral vascular disease; *CX*, circumflex artery; *PCI*, percutaneous coronary intervention; *IABP*, intra-aortic balloon pump; *DIA*, diagonal; *MI*, myocardial infarction; *CVA*, cerebrovascular accident; *AF*, atrial fibrillation; *LV*, left ventricle; *COPD*, chronic obstructive pulmonary disease; *BMI*, body mass index; *DM*, diabetes mellitus; *OPCAB*, off-pump coronary artery bypass grafting.

TABLE 2. Arterial graft target and configuration

RITA target (N = 764)	RA target unmatched (N = 1990)	RA target matched (N = 764)
RCA as in situ graft = 198 (26%)*	RCA = 460 (23%)*	RCA = 197 (26%)*
RCA as free graft = 47 (6%)*†	CX = 1530 (77%)*	CX = 567 (74%)*
CX as in situ graft (retroaortic) = 232 (31%)*	Sequential grafts = 130 (6.5%)	Sequential grafts = 46 (6.0%)
CX as free graft = 87 (11%)*†		
LAD as in situ graft = 190 (25%)‡		
LAD as free graft = 10 (1%)†‡		
Sequential grafts = 46 (6.0%)		

RITA, Right internal thoracic artery; *RA*, radial artery; *RCA*, right coronary artery; *CX*, circumflex artery; *LAD*, left anterior descending artery. *LITA was used to graft the LAD as an in situ graft. †RITA proximally connected to the LITA (Y-graft). ‡LITA was used to graft the CX as an in situ graft.

comparable in terms of mortality (hazard ratio [HR], 1.00; 95% confidence interval [CI], 0.56-1.78; $P = .98$). However, after 4 years RITA was associated with a significant reduction in late mortality (HR, 0.67; 95% CI, 0.48-0.95; $P = .02$). Schoenfeld residuals test excluded proportional hazard assumption violation ($P = .93$, Figure E5). The survival rates in the unmatched RA group are reported in Figure E6.

Subgroup analysis on late mortality (after 4 years). Subgroup analysis suggested that the RITA was superior to the RA in term of late survival when the experimental conduit was used to graft the left coronary system (HR, 0.69; 95% CI, 0.47-0.99; $P = .04$), but not the right coronary system (HR, 0.98; 95% CI, 0.59-1.62; $P = .93$) (Figure 3). In cases with the experimental conduit grafted on the right coronary system only, neither in situ RITA (HR, 0.76; 95% CI, 0.42-1.36; $P = .1$) nor free RITA (HR, 1.78; 95% CI, 0.89-3.56; $P = .3$) were significantly associated with a better late survival when compared with the RA (Figure E7).

On the other hand, in cases with the experimental conduit grafted on the left coronary system only, we could not demonstrate any significant difference between free RITA over in situ RITA (HR, 0.55; 95% CI, 0.21-1.43; $P = .22$; Figure 4). No significant difference in late mortality could be demonstrated between the RITA grafted to the CX (with LITA to LAD) when compared with the RITA grafted to the LAD territory (with LITA to CX) (HR, 0.71; 95% CI, 0.34-1.43; $P = .33$). When patients receiving sequential grafts were excluded, the use of RITA to graft the left coronary system was still found to be superior to the RA (HR, 0.65; 95% CI, 0.43-0.99; $P = .04$). Finally the protective effect of RITA over RA on late mortality was confirmed when adjusted for the interaction between

TABLE 3. Short-term outcomes

	RITA (N = 764)		PSM RA (N = 764)		
Outcome	**n**	%	**n**	%	***P* value**
Mortality within 30 d					
No	758	99.2	762	99.7	.26
Yes	6	0.8	2	0.3	
Re-exploration for bleeding					
No	737	96.5	753	98.6	.01
Yes	27	3.5	11	1.4	
Postoperative CVA					
No	759	99.3	759	99.3	1
Yes	5	0.7	5	0.7	
Postoperative RRT					
No	752	98.4	758	99.2	.24
Yes	12	1.6	6	0.8	
Postoperative IABP					
No	754	98.7	762	99.7	.04
Yes	10	1.3	2	0.3	
SW reconstruction					
No	757	99.1	763	99.9	.07
Yes	7	0.9	1	0.1	
Length of hospital stay					
Mean ± SD	7.1 ± 5.1		6.6 ± 3.7		.05
<10 d	676	88.5	691	90.4	
≥10 d	88	11.5	73	9.6	

RITA, Right internal thoracic artery; *PSM*, propensity score matching; *RA*, radial artery; *CVA*, cerebrovascular accident; *RRT*, renal replacement therapy; *IABP*, intra-aortic balloon pump; *SW*, sternal wound; *SD*, standard deviation.

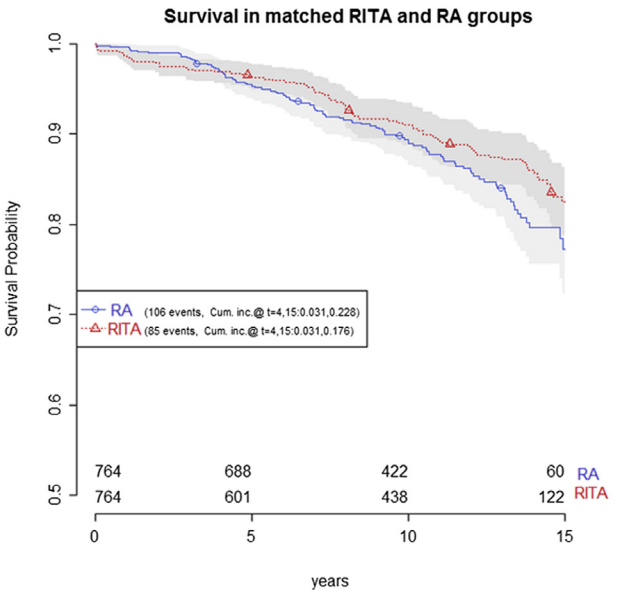


FIGURE 2. Kaplan-Meier survival curve probabilities in the right internal thoracic artery (*RITA*) and the radial artery (*RA*) groups in the propensity-score-matched population.

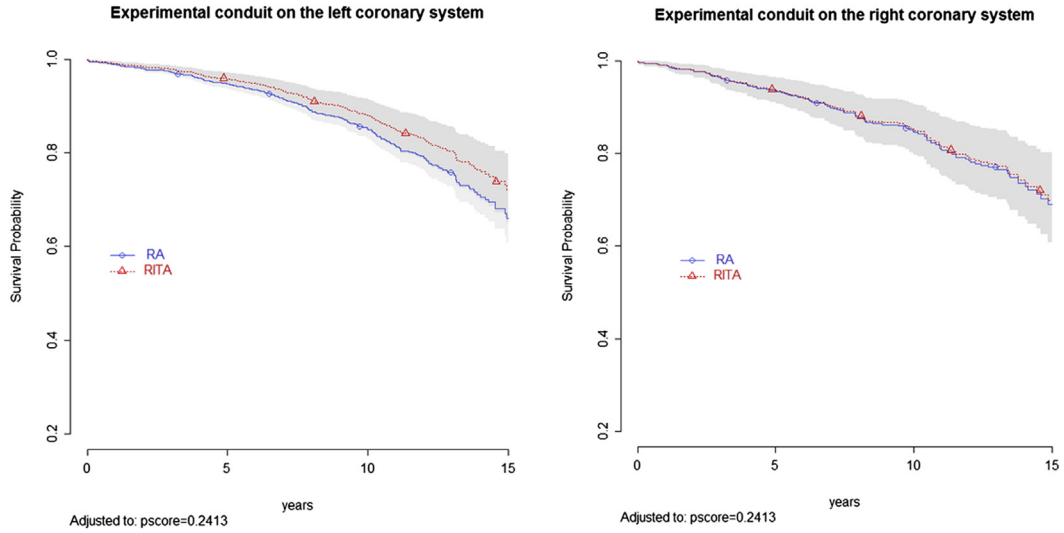


FIGURE 3. Propensity-score-adjusted Cox model survival curve probabilities in the right internal thoracic artery (*RITA*) and the radial artery (*RA*) groups according to the experimental conduit target.

OPCAB and era of surgery (HR, 0.73; 95% CI, 0.54-0.99; $P = .04$).

DISCUSSION

The present single-center long-term PSM analysis showed that, in a low-risk population, the use of the RITA when compared with the RA as second arterial conduit was associated with superior long-term survival in patients undergoing CABG. The trend towards a survival benefit from the RITA was evident only after 4 years from the index operation. We found that the RITA was associated with improved late survival only when the experimental conduit was used to graft the left coronary system. When used to graft the left coronary system, free RITA and in situ RITA showed comparable long-term survival. Survival after RITA to LAD graft did not significantly differ from RITA to CX graft.

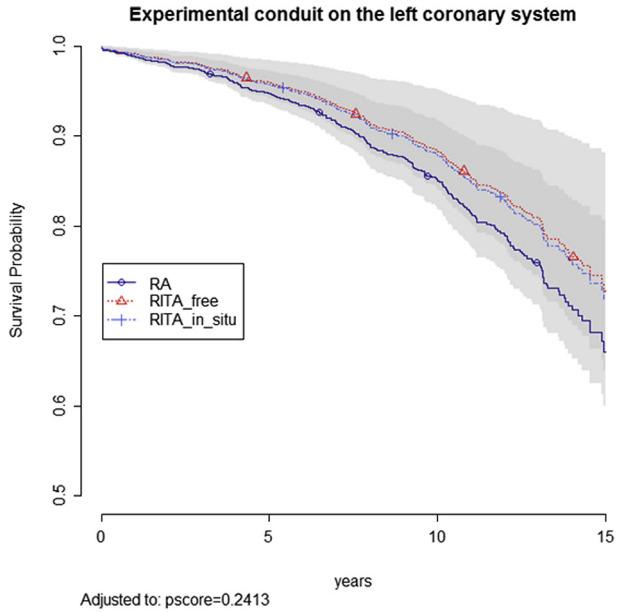


FIGURE 4. Propensity-score-adjusted Cox model survival curve probabilities in the right internal thoracic artery (*RITA*) and the radial artery (*RA*) groups with the experimental conduit grafted to the left coronary system according to different RITA graft configuration.

The use of the RITA over the RA did not significantly increase operative mortality (within 30 days), the incidence of postoperative CVA, or the need for renal replacement therapy. However, we found a trend towards an increased incidence of re-exploration for bleeding, IABP requirement, sternal wound complication requiring reconstruction, and prolonged hospital stay length in patients receiving the RITA. However, the overall incidence of these complications was particularly low, partially due to the low-risk profile of the study population.

Despite the slow initial adoption, multiple arterial grafting is now widely advocated by the cardiovascular community.[1] The use of both RITA and RA has been shown to be associated with better long-term survival when compared with the traditional strategy using a single internal thoracic artery and additional SV grafts.[9] Controversy still remains on whether the use of the RA as a second arterial conduit achieves the same long-term benefits as that documented with the use of the RITA.[5-12] The lack of clear evidence, the potentially increased sternal wound complication rate, and the perceived technical complexity when using bilateral internal thoracic arteries often results in the RA as the preferred second conduit of choice.[1] The only randomized direct comparison in the literature is the

Radial Artery Patency and Clinical Outcome,[3] which randomized 196 patients to receive the RITA grafts and 193 patients to receive the RA grafts. No significant differences in terms of angiographic patency or clinical outcome were found at midterm follow-up. However, the trial was largely underpowered to detect significant differences in survival between the 2 groups.

PSM is emerging as an attractive alternative in view of the paucity of evidence from RCT.[4] Recently, conflicting results on the superiority of the RITA over the RA have been reported by several PSM studies. Schwann and colleagues[9] reported on 551 propensity-matched RITA and RA, and their conclusions supported the equipoise between RITA and RA as the second-best arterial conduit. However, it should be noted that their analysis showed a clear trend towards a better survival by using RITA over RA (HR, 1.35; 95% CI, 0.98-1.81). Shi and colleagues[10] performed a PSM on 318 matched pairs of patients receiving RITA versus RA. They demonstrated a marginally significant survival benefit from RITA (HR, 0.78; 95% CI, 0.60-1.00; $P = .048$). On the contrary, Tranbaugh and colleagues[11] reported on 528 pairs who received either a RA or a free RITA to bypass the circumflex coronary. Ten-year survival was 85% for patients receiving RA and 80% for patients receiving RITA, which was not statistically significant ($P = .06$). RA patency (83.9%) was similar to RITA patency (87.4%) ($P = .15$). It should be noted that, in their series, Tranbaugh and colleagues used the RITA as free graft directly connected to the aorta in 42% of cases, and the caliper mismatch between the aorta and the RITA might have affected its patency thus neutralizing its superior patency.

By conducting a single-center 15-year PSM on 764 pairs of patients receiving the RITA versus the RA as the second arterial conduit, we found that the use of the RITA is associated with a significant risk reduction of mortality after 4 years, but that this benefit is more likely to be relevant only when the RITA is used to graft the left coronary system. These findings are supported by previous studies that suggested that, for bilateral ITA grafting to improve long-term outcomes over single ITA-to-LAD grafting, the second ITA should bypass the CX rather than the RCA.[19-21] Schmidt and colleagues[19] observed a long-term survival of 93% when both ITAs were 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 ($P = .02$). Carrel and colleagues[20] and Pick and colleagues[21] have separately reported that using both ITAs to graft left-sided coronaries may increase survival over single ITA revascularization. These observations may reflect the lower patency of ITA grafts when used to bypass the RCA system compared with left-sided coronary arteries. Grafts to the 3 different coronary artery territories have different patency rates that have been clearly demonstrated for individual ITA grafts.[22] Robinson and colleagues[23] recently reported on postdischarge angiography of 296 free RITA as Y-grafts, including a total of 1174 individual anastomoses: there were 428 anterior wall (36.5%), 411 lateral wall (35.0%), and 335 inferior wall (28.5%) anastomoses. The patency rates for these were 90.6%, 83.9%, and 62.3%, respectively.

In contrast, Kurlansky and colleagues[24] compared 1479 RITA used to revascularize the left coronary system with 736 RITA used to graft the right coronary system, and they found similar survival after a mean follow-up of 12 years. In their series, in situ grafting was used in most of the cases (approximately 98% of arteries grafted) and, when using the RITA to the RCA, efforts were made to graft severely stenosed vessels and distal branches rather than the main RCA. In this context, Sabik at al.[25] were able to document equivalent long-term results with the use of the RITA, whether applied to the left or right coronary system. Their findings of similar survival whether the RITA was used to bypass the RCA or CX system were attributable to careful patient selection. In fact, 2 important factors used in selecting the RCA as the site for the RITA: (1) stenosis 70% to 90% with viable myocardium in its distribution; and (2) freedom from distal stenosis. They were, therefore, likely to graft a RCA with a RITA only when the likelihood of the RITA graft remaining patent, and thus effectiveness was high.

We could not demonstrate a superiority of in situ over Y-graft RITA configuration when the RITA was used to graft the left coronary system. This result is supported by a recent study by Hwang and colleagues[26] on 398 patients who underwent OPCAB with in situ RITA (n = 164) graft or free RITA y-composite graft (n = 234) used to graft the left coronary system. They found that the 5-year patency rate was 92.5% versus 92.4% for in situ RITA and free RITA grafts, respectively ($P = .97$). Finally, we found that in situ RITA to LAD was a valid alternative to in situ LITA to LAD when performing CABG using bilateral ITAs grafting on the left coronary system being associated with similar survival rates. The RITA to LAD strategy represents an easily reproducible and technically less-demanding strategy compared with other configurations. The RITA is biologically identical to the LITA, and excellent angiographic results have been reported for RITA to LAD grafts.[22] Tatoulis and colleagues[22] reported a 95% 10-year patency rate for 149 RITA to LAD grafts, and this result was comparable with LITA to LAD grafts (96%). In a previous series, we demonstrated a similar survival rate and freedom from reintervention between RITA to LAD versus LITA to LAD in the context of bilateral ITA grafting.[27]

Although in this low-risk population, operative morbidity and mortality was particularly low in both groups, we found that the use of RITA was associated with an increased risk of re-exploration for bleeding, need for IABP, sternal wound reconstruction, and prolonged hospital stay length. Inability

to control bleeding from branches of the retrocaval and retroaortic routed RITA, which are in spasm at the time of closure and bleed later because of vasodilatation, as well as an increased number of potential bleeding sites due to construction of the Y-graft, are some of the plausible reasons for the higher rate of re-exploration in the RITA group.[28] Moreover, retrocaval and transverse sinus routing of the RITA might compromise graft flow because of undetected kinks, graft overstretching, or rotation, which can partially account for the increased need for IABP.[28] Finally, the use of RITA was confirmed to increase the risk of sternal wound reconstruction. In the present series, a pedicled harvesting technique was used in all cases and this might account for this result and better results are anticipated by using a skeletonized technique.[29] Taking into account the observed increased complications rate associated with the RITA, and based on the observation that the beneficial effect on survival from the RITA may be delayed by as much as 7 to 10 years,[30] it seems reasonable to consider the RA as a valid option in older patients or patients with a greater number of risk factors such as diabetes and obesity.[31]

The present analysis has intrinsic limitations. The main limitation of our study is that no follow-up data were available to compare the groups with respect to the cause of death (cardiac vs noncardiac), recurrence of angina, need for repeated revascularization, or graft patency. Therefore, we can only speculate that the mechanism beyond the better long-term survival observed in our RITA group is related to the better patency rate of the RITA over the RA. Propensity technique 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).

In conclusion, we found that in a highly selected low-risk group of patients, the use of the RITA as a second arterial conduit instead of the RA, was associated with better survival when used to graft the left but not the RCA. This gain in long-term survival may be at the expense of short-term morbidity.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

References

1. Tranbaugh RF, Lucido DJ, Dimitrova KR, Hoffman DM, Geller CM, Dincheva GR, et al. Multiple arterial bypass grafting should be routine. *J Thorac Cardiovasc Surg*. 2015;150:1537-45.
2. Benedetto U, Raja SG, Albanese A, Amrani M, Biondi-Zoccai G, Frati G. Searching for the second best graft for coronary artery bypass surgery: a network meta-analysis of randomized controlled trials. *Eur J Cardiothorac Surg*. 2015; 47:59-65.
3. Hayward PA, Gordon IR, Hare DL, Matalanis G, Horrigan ML, Rosalion A, et al. Comparable patencies of the radial artery and right internal thoracic artery or saphenous vein beyond 5 years: results from the Radial Artery Patency and Clinical Outcomes trial. *J Thorac Cardiovasc Surg*. 2010;139:60-5.
4. Lonjon G, Boutron I, Trinquart L, Ahmad N, Aim F, Nizard R, et al. Comparison of 100 treatment effect estimates from prospective nonrandomized studies with 101 propensity score analysis and randomized controlled trials of surgical procedures. *Ann Surg*. 2014;259:18-25.
5. Navia D, Vrancic M, Piccinini F, Camporrotondo M, Thierer J, Gil C, 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*. 2014;147:632-8.
6. Pevni D, Mohr R, Paz Y, Kramer A, Ben-Gal Y, Nesher N, et al. Long-term outcome of revascularization with composite T-grafts: is bilateral mammary grafting better than single mammary and radial artery grafting? *J Thorac Cardiovasc Surg*. 2016;151:1311-9.
7. Raja SG, Benedetto U, Jothidasan A, Jujjavarapu RK, Ukwu UF, De Robertis F, et al. Right internal mammary artery versus radial artery as second arterial conduit in coronary artery bypass grafting: a case-control study of 1526 patients. *Int J Surg*. 2015;16:183-9.
8. Ruttmann E, Fischler N, Sakic A, Chevtchik O, Alber H, Schistek R, et al. Second internal thoracic artery versus radial artery in coronary artery bypass grafting: a long-term, propensity score-matched follow-up study. *Circulation*. 2011;124:1321-9.
9. Schwann TA, Hashim SW, Badour S, Obeid M, Engoren M, Tranbaugh RF, et al. Equipoise between radial artery and right internal thoracic artery as the second arterial conduit in left internal thoracic artery-based coronary artery bypass graft surgery: a multi-institutional study. *Eur J Cardiothorac Surg*. 2016;49:188-95.
10. Shi WY, Hayward PA, Tatoulis J, Rosalion A, Newcomb AE, Fuller JA, et al. Are all forms of total arterial revascularization equal? A comparison of single versus bilateral internal thoracic artery grafting strategies. *J Thorac Cardiovasc Surg*. 2015;150:1526-34.
11. Tranbaugh RF, Dimitrova KR, Lucido DJ, Hoffman DM, Dincheva GR, Geller CM, et al. The second best arterial graft: a propensity analysis of the radial artery versus the free rightinternal thoracic artery to bypass the circumflex coronary artery. *J Thorac Cardiovasc Surg*. 2014;147:133-40.
12. Tsuneyoshi H, Komiya T, Shimamoto T, Sakai J, Hiraoka T, Kawashima T, et al. The second best arterial graft to the left coronary system in off-pump bypass surgery: a propensity analysis of the radial artery with a proximal anastomosis to the ascending aorta versus the right internal thoracic artery. *Gen Thorac Cardiovasc Surg*. 2015;63:335-42.
13. Austin PC. A tutorial and case study in propensity score analysis: an application to estimate the effect of in-hospital smoking cessation counseling on mortality. *Multivariate Behav Res*. 2011;46:119-51.
14. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat*. 2011;10:150-61.
15. Collins GS, Le Manach Y. Comparing treatment effects between propensity scores and randomized controlled trials: improving conduct and reporting. *Eur Heart J*. 2012;33:1867-9.
16. Lauer MS, Blackstone EH, Young JB, Topol EJ. Cause of death in clinical research: time for a reassessment? *J Am Coll Cardiol*. 1999;34:618-20.
17. Myers WO, Blackstone EH, Davis K, Foster ED, Kaiser GC. CASS Registry long term surgical survival. Coronary Artery Surgery Study. *J Am Coll Cardiol*. 1999; 33:488-98.
18. Cummings P, McKnight B, Greenland S. Matched cohort methods for injury research. *Epidemiol Rev*. 2003;25:43-50.
19. Schmidt SE, Jones JW, Thornby JI, Miller CC III, Beall AC Jr. Improved survival with multiple left-sided bilateral internal thoracic artery grafts. *Ann Thorac Surg*. 1997;64:9-14.
20. Carrel T, Horber P, Turina MI. Operation for two-vessel coronary artery disease: midterm results of bilateral ITA grafting versus unilateral ITA and saphenous vein grafting. *Ann Thorac Surg*. 1996;62:1289-94.
21. Pick AW, Orszulak TA, Anderson BJ, Schaff HV. Single versus bilateral internal mammary artery grafts: 10-year outcome analysis. *Ann Thorac Surg*. 1997;64: 599-605.
22. Tatoulis J, Buxton BF, Fuller JA. The right internal thoracic artery: the forgotten conduit—5,766 patients and 991 angiograms. *Ann Thorac Surg*. 2011;92:9-17.
23. Robinson BM, Paterson HS, Naidoo R, Dhurandhar V, Denniss AR. Bilateral internal thoracic artery composite Y grafts: analysis of 464 angiograms in 296 patients. *Ann Thorac Surg*. 2016;101:974-80.

24. Kurlansky PA, Traad EA, Dorman MJ, Galbut DL, Zucker M, Ebra G. Location of the second internal mammary artery graft does not influence outcome of coronary artery bypass grafting. *Ann Thorac Surg*. 2011;91:1378-83.
25. Sabik JF III, Stockins A, Nowicki ER, Blackstone EH, Houghtaling PL, Lytle BW, et al. Does location of the second internal thoracic artery graft influence outcome of coronary artery bypass grafting? *Circulation*. 2008;118:S210-5.
26. Hwang HY, Kim JS, Cho KR, Kim KB. Bilateral internal thoracic artery in situ versus y-composite graftings: five-year angiographic patency and long-term clinical outcomes. *Ann Thorac Surg*. 2011;92:579-85.
27. Raja SG, Benedetto U, Husain M, Soliman R, De Robertis F, Amrani M. 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;148:1275-81.
28. Bonacchi M, Prifti E, Battaglia F, Frati G, Sani G, Popoff G. In situ retrocaval skeletonized right internal thoracic artery anastomosed to the circumflex system via transverse sinus: technical aspects and postoperative outcome. *J Thorac Cardiovasc Surg*. 2003;126:1302-13.
29. Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Pawlaczyk R, et al; Arterial Revascularization Trial investigators. Pedicled and skeletonized single and bilateral internal thoracic artery grafts and the incidence of sternal wound complications: insights from the Arterial Revascularization Trial. *J Thorac Cardiovasc Surg*. 2016;152:270-6.
30. Benedetto U, Amrani M, Raja SG. Harefield Cardiac Outcomes Research Group. Guidance for the use of bilateral internal thoracic arteries according to survival benefit across age groups. *J Thorac Cardiovasc Surg*. 2014;148:2706-11.
31. Raza S, Sabik JF III, Masabni K, Ainkaran P, Lytle BW, Blackstone EH. Surgical revascularization techniques that minimize surgical risk and maximize late survival after coronary artery bypass grafting in patients with diabetes mellitus. *J Thorac Cardiovasc Surg*. 2014;148:1257-64.

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

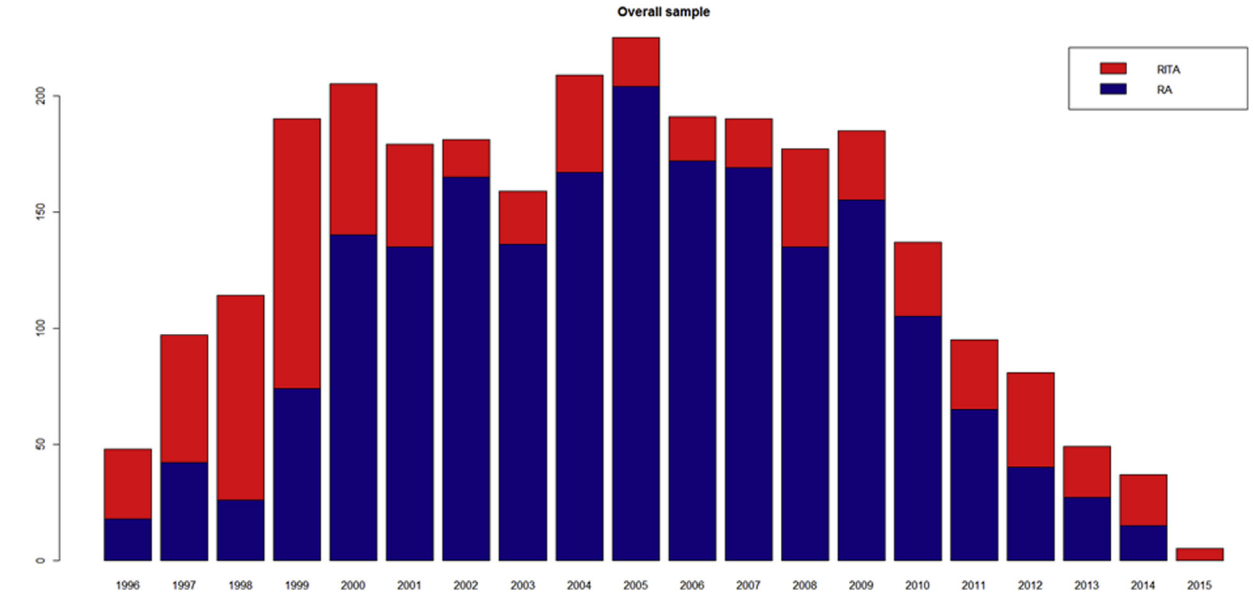


FIGURE E1. Number of procedures per year performed by using the RITA or the RA as second arterial conduit during the study period. *RITA*, Right internal thoracic artery; *RA*, radial artery.

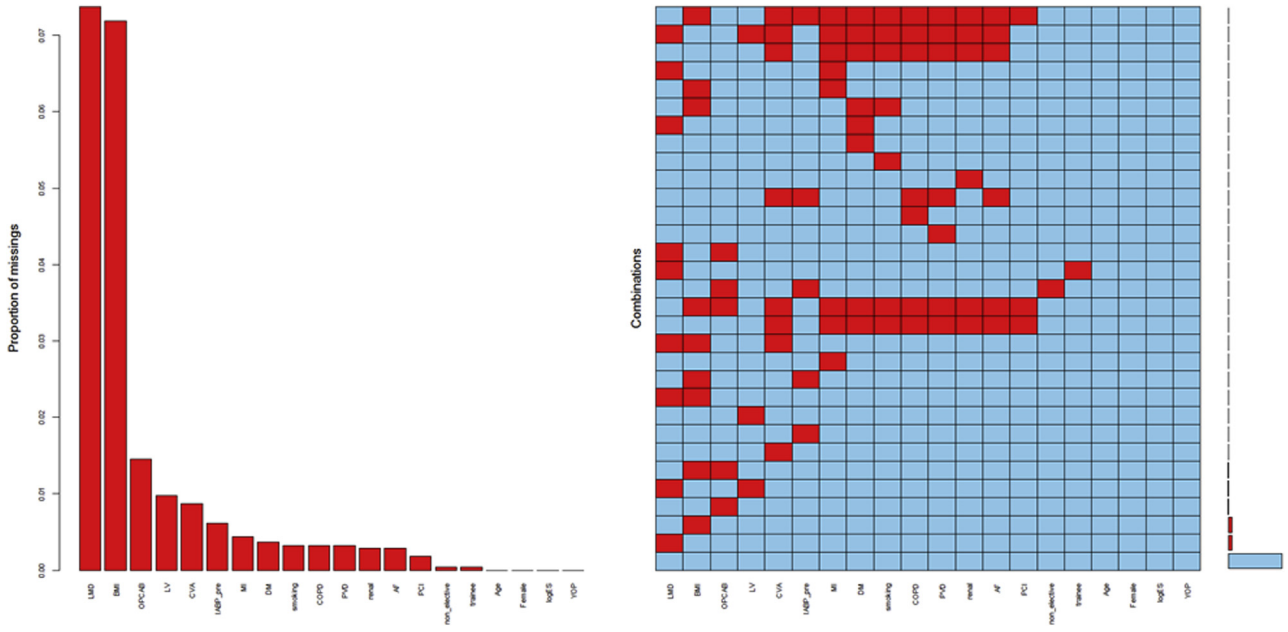


FIGURE E2. Graphic visualization of missing data rates and combinations. *LMD*, Left main disease; *BMI*, body mass index; *OPCAB*, off-pump coronary artery bypass grafting; *LV*, left ventricle; *CVA*, cerebrovascular accident; *IABP*, intra-aortic balloon pump; *MI*, myocardial infarction; *DM*, diabetes mellitus; *COPD*, chronic obstructive pulmonary disease; *PVD*, peripheral vascular disease; *AF*, atrial fibrillation; *PCI*, percutaneous coronary intervention; *YOP*, year of procedure.

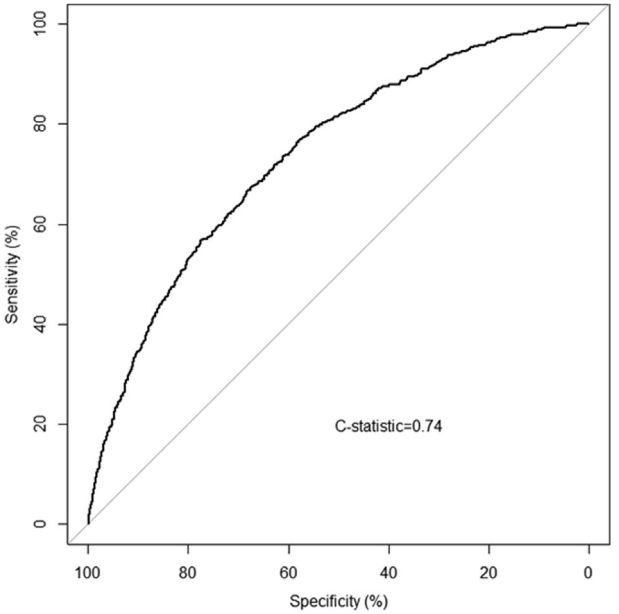


FIGURE E3. Area under the curve for the propensity score model.

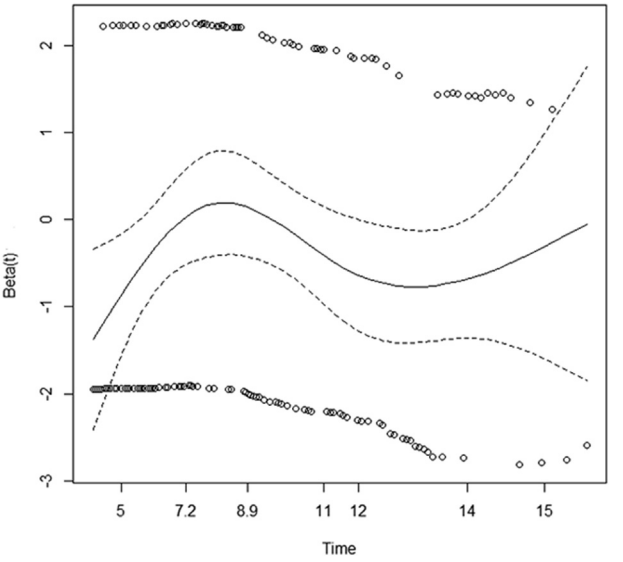


FIGURE E5. Schoenfeld residuals visualization to check the proportional hazard assumption for the treatment variable on late mortality (beyond 4 years).

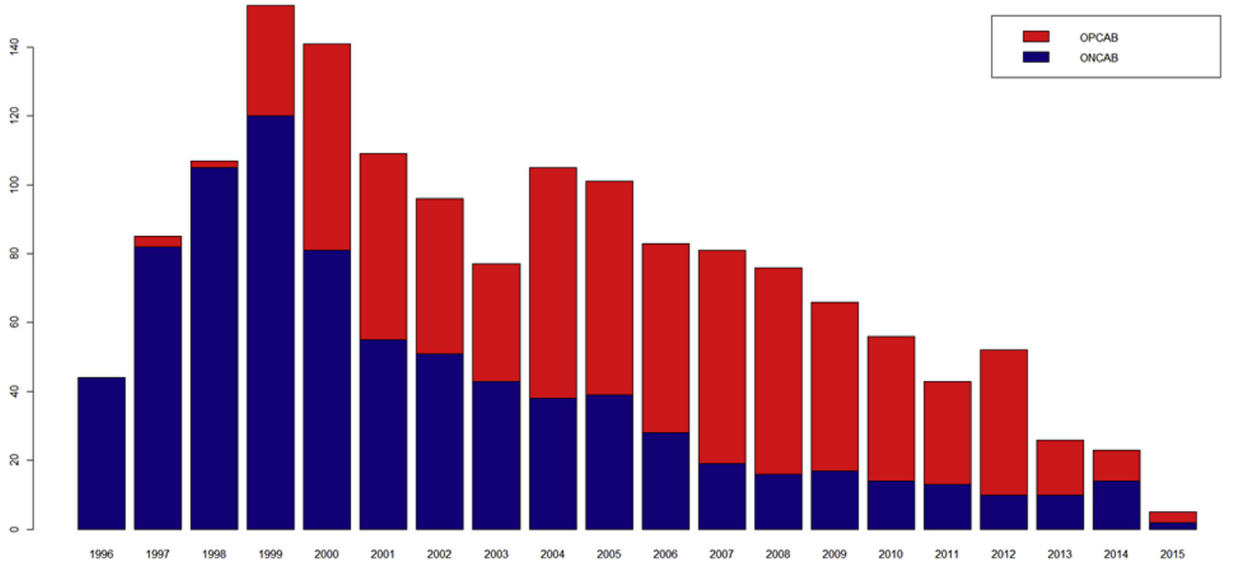


FIGURE E4. Number of procedures per year performed off-pump during in the study population. *OPCAB*, Off-pump coronary artery bypass; *ONCAB*, on-pump coronary artery bypass.

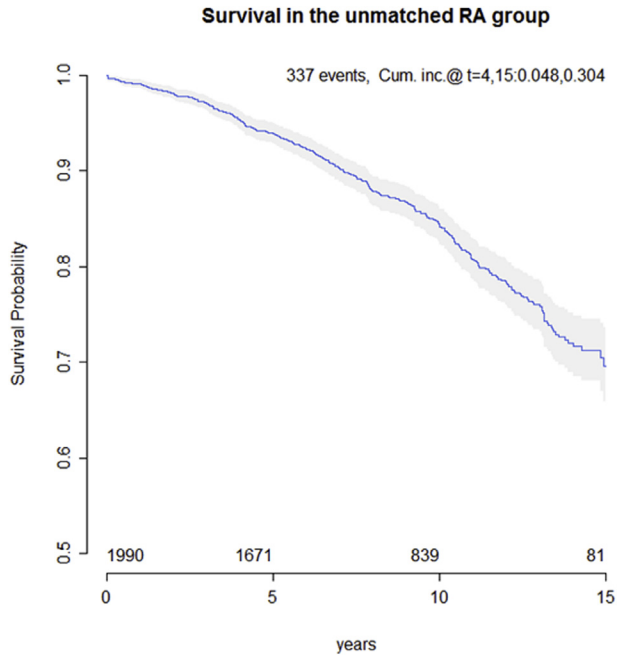


FIGURE E6. Kaplan-Meier survival curve probabilities in the unmatched radial artery (*RA*) groups.

TABLE E1. Missing data rate

Variable	Count	%
Age	0	0
Female	0	0
MI	12	0.4
PCI	5	0.2
DM	10	0.4
Current smoking	9	0.3
Creatinine >200 mmol/L	8	0.3
COPD	9	0.3
CVA	24	0.9
PVD	9	0.3
AF	8	0.3
LMS	203	7.3
LVEF	27	0.9
Preoperative IABP	17	0.6
OPCAB	40	1.4
Non-elective priority	1	0.03
BMI	198	7.1
Performed by resident	1	0.03
Logistic euroSCORE	0	0
Year of surgery	0	0
LAD	0	0
DIA	0	0
CX	0	0
RCA	0	0

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; *LMS*, left main stem; *LVEF*, left ventricular ejection fraction; *IABP*, intra-aortic balloon pump; *OPCAB*, off-pump coronary artery bypass grafting; *BMI*, body mass index; *LAD*, left anterior descending artery; *DIA*, diagonal; *CX*, circumflex artery; *RCA*, right coronary artery.

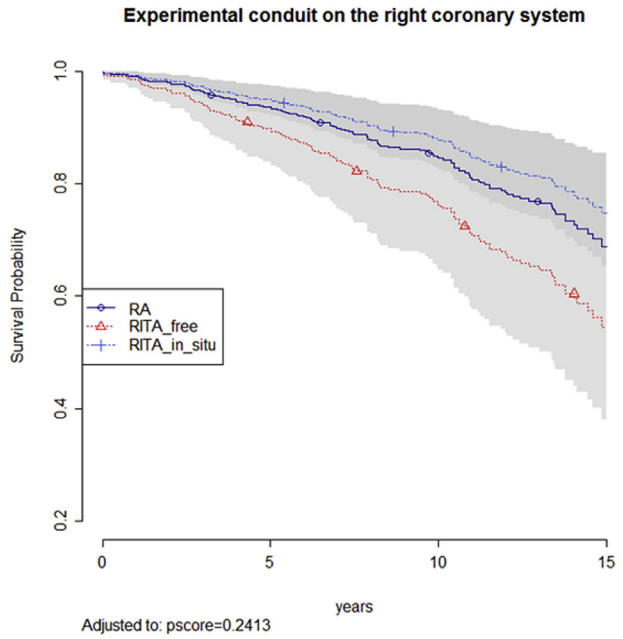


FIGURE E7. Propensity-score-adjusted Cox model survival curve probabilities in the right internal thoracic artery (*RITA*) and the radial artery (*RA*) groups with the experimental conduit grafted to the right coronary system according to different RITA graft configuration.

TABLE E2. Short-term outcomes in the unmatched RA group

	Unmatched RA (N = 1990)	
Outcome	**N**	%
Mortality within 30 d		
No	1982	99.6
Yes	8	0.4
Re-exploration for bleeding		
No	1956	98.3
Yes	34	1.7
Postoperative CVA		
No	1977	99.3
Yes	13	0.7
Postoperative RRT		
No	1972	99.1
Yes	18	0.9
Postoperative IABP		
No	1972	99.1
Yes	18	0.9
SW reconstruction		
No	1981	99.5
Yes	9	0.5
Length of hospital stay		
Mean, d ± SD	7.1 ± 6.1	
<10 d	1759	88.4
≥10 d	231	11.6

RA, Radial artery; *CVA*, cerebrovascular accident; *RRT*, renal replacement therapy; *IABP*, intra-aortic balloon pump; *SW*, sternal wound; *SD*, standard deviation.