Radial artery versus saphenous vein as the second conduit for coronary artery bypass surgery: A meta-analysis

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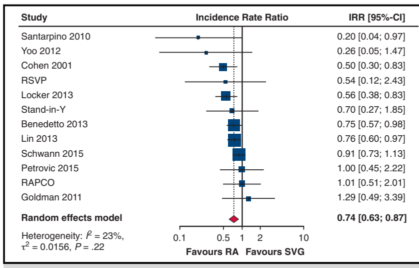
ABSTRACT

Objective: Individual studies may be limited by sample size to detect differences in late survival between radial artery (RA) or saphenous vein graft (SVG) as a second conduit for coronary artery bypass surgery. Here we undertook a meta-analysis of the best evidence available on the comparison of early and late clinical outcomes of the RA and the SVG.

Methods: MEDLINE and EMBASE were searched for studies comparing use of the RA versus SVG for isolated coronary artery bypass surgery. Time-to-event outcomes for long-term mortality, repeat revascularization, and myocardial infarction (MI) were extracted as incidence rate ratios (IRR) with 95%confidence intervals (95% CI). Odds ratios (OR) were extracted for perioperative mortality, stroke, and MI. A random effects meta-analysis was performed. Sensitivity analyses included leave-one-out-analyses and meta-regression.

Results: Among 1201 articles, 14 studies (20,931 patients) were included (mean follow-up: 6.6 years). Operative mortality was 1.25% in the RA versus 1.33% in the SVG group (OR, 0.93; 95% CI, 0.68-1.28). No difference in perioperative MI (OR, 0.96; 95% CI, 0.59-1.56) or stroke (OR, 0.70; 95% CI, 0.43-1.13) was found between RA and SVG. Long-term mortality (mean follow-up 6.6 years) was 24.5% in RA versus 34.2% in SVG group (IRR, 0.74; 95% CI, 0.63-0.87, $P < .001$). No difference in follow-up MI or repeat revascularization was found (IRR, 0.76; 95% CI, 0.42-1.36 and IRR, 0.68; 95% CI, 0.42-1.09 respectively). At meta-regression, RA survival advantage was independent of age, sex, diabetes, and ventricular function.

Conclusions: Compared with the SVG, using the RA as the second conduit is associated with a 26% relative risk reduction in mortality at 6.6-year follow-up. (J Thorac Cardiovasc Surg 2019;157:1819-25)



Forest plot for long-term mortality (expressed as incidence rate ratio).

Central Message

As compared with SVG, the use of the RA as the second conduit for CABG is associated with a 26% relative risk reduction in mortality at a mean follow-up of 6.6 years.

Perspective

This meta-analysis compares the radial artery (RA) versus the saphenous vein graft (SVG) for coronary artery bypass grafting (CABG) on clinically important outcomes. A total of 14 studies (20,931 patients) represents the best-available evidence on the comparison of the early and late clinical endpoints of the RA and the SVG for CABG.

See Commentary on page 1826.

Previous meta-analyses of the radial artery (RA) and saphenous vein graft (SVG) as a second conduit have focused on graft patency and have shown better mid-term patency rate for the RA.[1] No previous aggregate meta-analysis has focused on the comparison of clinical outcomes after coronary artery bypass surgery (CABG). Evidence comparing the clinical results of the RA and SVG exist only from single-center observational studies. The outcomes of those studies may be heavily influenced by the individual surgeon's expertise with the RA and potential baseline differences in the patients selected for RA grafting such that a broader and more generalizable

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Abbreviations and Acronyms

- CABG = coronary artery bypass surgery
- CI = confidence interval
- HR = hazard ratio
- IRR = incidence rate ratio
- MI = myocardial infarction
- OR = odds ratio
- RA = radial artery
- RCT = randomized clinical trial
- SVG = saphenous vein graft

estimate of the clinical effect of the use of the RA for CABG at the moment is unclear.

The present meta-analysis is aimed at overcoming these limitations by aggregating data from both randomized clinical trials (RCTs) and adjusted observational studies to determine the best evidence regarding the comparison of the early and late clinical outcomes of the RA and the SVG used for CABG.

METHODS

This systematic review and meta-analysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.[2,3]

Data Sources and Systematic Literature Review

A medical librarian developed searches to identify studies that compared the survival after CABG using the RA and the SVG. Ovid's version of MEDLINE (In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1946 to Present), Ovid EMBASE (1974 to present), and The Cochrane Library (Wiley) were searched. Searches used subject headings and keywords for the following terms: "radial artery graft," "coronary artery bypass," "saphenous vein graft," and "internal mammary-coronary artery anastomosis." The full search strategy for Ovid MEDLINE is available in the Appendix 1. There were no publication date restrictions.

The inclusion criteria were English-language full-length articles, follow-up >30 days, direct comparison of survival of patient receiving the RA and the SVG, and isolated CABG. In addition, we hand-searched recent meta-analyses and reviews on this topic for potential additional studies. In case of overlapping studies or studies from the same or overlapping cohorts reporting different outcomes, the largest series was included for each outcome. Studies in which additional arterial grafts were used in addition to the RA or that compared multiple arterial revascularization strategies were excluded unless it was possible to extract specific data of the subgroups who received only the RA or the SVG.

Data Extraction and Quality Assessment

Data extraction was performed independently by 2 investigators (A.A. and M.K.). In case of discrepancies, they were resolved by consultation with the first and senior author. The following variables were included: study demographics (sample size, number of centers, publication year, study period, design, and country), patient demographics and comorbidities in the unmatched and eventually matched population (age, sex, diabetes, ejection fraction, chronic obstructive pulmonary disease, and percentage of RA target vessel stenosis), and details of the surgical procedure.

The quality of the included observational studies was assessed using The Risk Of Bias In Non-randomized Studies–of Interventions assessment tool[4] and the included RCTs were assessed using the Cochrane Collaboration's Risk of Bias tool.[5]

Outcomes

The primary outcome was all-cause long-term mortality. The secondary outcomes were perioperative (30 days or in-hospital) mortality, perioperative myocardial infarction (MI), and stroke, follow-up MI, and repeat revascularization.

Data Synthesis and Analysis

The efficacies of RA versus SVG were compared directly in pairwise random effects meta-analyses by pooling data from the included studies using "meta" and "metafor" packages[6,7] in R (version 3.3.3, R Project; R Foundation for Statistical Computing, Vienna, Austria). We pooled the short-term binary outcomes using odds ratio (OR) with 95% confidence interval (CI) using the generic inverse variance method.[8] To account for potentially different follow-up durations between the groups, late outcomes were analyzed using the natural logarithm of the incident rate ratio (IRR, the ie, number of deaths per population at-risk per unit time). We estimated the IRR through several means depending on the available study data. When hazard ratios (HRs) were provided, we took the natural logarithm of the HR; the standard error was derived from the 95% CI or log rank *P* value.[9] When HRs were not reported, we estimated IRR through either (1) the Kaplan–Meier curves using GetData Graph Digitizer software 2.26 (http://getdata-graph-digitizer.com/) or (2) the reported events and accumulated group-specific person-years of follow-up as previously described.[10-12] When differential follow up durations by group were not provided, relative risk was used. For two studies (Yoo 2012 and RSVP)[13,14] individual patients' data were used. Details of IRR calculation for the primary outcome are provided in Table E1[13-24] in Appendix 1.

In addition, for the 9 studies that provided Kaplan–Meier curves for long-term survival (Benedetto and Codispoti 2013, Cohen and colleagues 2001, Lin and colleagues 2013, Locker and colleagues 2013, Petrovic and colleagues 2015, Santarpino and colleagues 2010, Schwann and colleagues 2015, RAPCO, Stand-in-Y),[15-23] individual patient survival data were reconstructed using an iterative algorithm applied to solve the Kaplan–Meier equations that were originally used to produce the published graphs. This algorithm uses digitized Kaplan–Meier curve data to find numerical solutions to the inverted Kaplan–Meier equation.[25] The algorithm assumes constant censoring. The reconstructed patient survival data were then aggregated to form combined survival curves.

Heterogeneity was reported as low (I^2 = 0%-25%), moderate (I^2 = 26%-50%), high (I^2 > 50%), consistent with guidelines.[26] Publication bias was assessed visually by funnel plot and quantitatively by the Egger test. Crude outcomes were calculated by aggregating crude numbers of events from the individual studies. The SVG graft group was used as the reference group in all the analyses. Statistical significance was assumed for $P < .05$.

Sensitivity Analyses

Subgroup analysis was used to compare RCTs and observational studies for the primary outcome. A leave-one-out analysis was performed to examine the impact of individual studies on the robustness of the primary and secondary outcomes. Univariate meta-regression for the primary outcome was performed for of age, sex, diabetes, left ventricular function, and percentage of RA target vessel stenosis. The same meta-regression models were also applied for the differences between the RA and SVG arm in the unmatched population to test for potential unmatched confounders related to treatment allocation bias (see Appendix 1). As an

TABLE 1. Demographics of the included studies (matched groups are considered in case of observational studies)

Study	Arm	Age, y, mean ± SD	Female, n (%)	DM, n (%)	EF, mean ± SD	COPD, n (%)	RA TVS
Benedetto and Codispoti, 2013[15]	RA	64 ± 10	178 (22)	82 (10.1)	NR*	92 (11.4)	NR
	SVG	65 ± 10	157 (19.4)	98 (12.1)	NR*	83 (10.3)	
Cohen et al, 2001[16]	RA	60.7 ± 8.8	76 (15.9)	160 (33.5)	NR	23 (4.8)	NR
	SVG	61.2 ± 8.7	152 (15.9)	238 (24.9)	NR	40 (4.2)	
Goldman et al, 2011[24]	RA	61 ± 8	1 (1)	154 (42)	NR	NR	>70%
	SVG	62 ± 8	5 (1)	153 (42)	NR	NR	
Lin et al, 2013[17]	RA	70.6 ± 8.7	79 (30.4)	101 (38.8)	53.6 ± 13.5	33 (12.7)	NR
	SVG	70.9 ± 9.8	77 (29.4)	91 (33.5)	53.3 ± 15.6	39 (15)	
Locker et al, 2013[18]	RA	NR	NR	NR	NR	NR	NR
	SVG	59 ± 10	187 (16.2)	221 (19.2)	58 ± 13	86 (7.5)	
Petrovic et al, 2015[19]	RA	56.3 ± 6.1	27 (27)	39 (39)	48.8 ± 10.7	9 (9)	≥80%
	SVG	57.1 ± 6.5	27 (27)	43 (43)	48 ± 10.8	8 (8)	
Santarpino et al, 2010[20]	RA	NR	NR	NR	NR	NR	>80%
	SVG	NR	NR	NR	NR	NR	
Schwann et al, 2015[21]	RA	62.7	803 (27)	1107 (37.3)	44.7	605 (20.4)	NR
	SVG	62.7	780 (26.3)	1132 (38.1)	44.7	577 (19.5)	
Tranbaugh et al, 2010[27]	RA	60.8 ± 8.1	203 (23.5)	314 (36.4)	48.3 ± 11.8	187 (21.7)	>70%
	SVG	60.8 ± 9.2	185 (22.5)	332 (38.3)	47.7 ± 13.2	173 (20.1)	
RAPCO (Hayward et al, 2008)[22]	RA	72.9 (62.3-83.5)†	10 (14)	27 (37)	NR*	NR	≥70%
	SVG	73.2 (64.0-82.4)	13 (16)	37 (46)	NR*	NR	
Stand-in-Y (Nasso et al, 2009)[23]	RA	70.5 ± 3.1	88 (43.1)	74 (36.1)	NR*	58 (28.2)	≥70%
	SVG	69.7 ± 3.5	85 (41.6)	78 (38.1)	NR*	57 (27.7)	
Yoo et al, 2012[13]	RA	72.7 ± 3.2	18 (51.4)	15 (42.9)	NR*	NR	NR
	SVG	74.6 ± 3.8	11 (44.0)	13 (52.0)	NR*	NR	
RSVP (Collins et al, 2008)[14]	RA	58 ± 6	3 (4)	15 (18)	NR	NR	≥70%
	SVG	59 ± 7	2 (3)	10 (17)	NR	NR	
Muneretto et al, 2004[28]	RA	77.3 ± 3	35 (43.7)	39 (48.7)	NR	NR	≥70%
	SVG	76.8 ± 2	37 (46.2)	36 (45.0)	NR	NR	

SD, Standard deviation; *DM*, diabetes mellitus; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *RA*, radial artery; *TVS*, target vessel stenosis; *NR*, not reported; *SVG*, saphenous vein graft. *EF reported as categories. †Median (interquartile range).

exploratory analysis, the same meta-regression model was also applied to operative mortality (see Appendix 1).

RESULTS

Among the 1201 screened articles, a total of 14 studies[13-24,27,28] (20,931 patients; 6671 RA and 14,260 SVG) were included (7 RCTs [n = 1924] and 7 observational studies [n = 19,007 patients]). The weighted mean follow-up was 6.6 years (Figure E1 in Appendix 1).

Four of the 14 studies were multicenter. Three studies were from the United States, 2 each from Italy and the United Kingdom, and 1 each from Canada, Korea, and Serbia. Demographics of the included studies are shown in Tables 1 and 2 and Table E2 in Appendix 1.

The Risk Of Bias In Non-randomized Studies–of Interventions assessment tool (version for cohort-type studies)[4] and Cochrane Collaboration's Tool for RCTs are shown in the Online Data Supplement and Table E3 in Appendix 1, respectively. All observational studies included were matched or adjusted and were of high quality and low risk of bias. The RCTs were also found to be of low risk of bias.

The number of patients in the individual studies ranged from 35 to 4404 patients in the RA group and from 25 to 8069 in the SVG group. The mean age ranged from 56.3 to 77.3 years in the RA group and from 57.1 to 76.8 in the SVG group. The majority of patients were male, with female patients ranging from 1% to 51.4% in the RA group and from 1% to 46.2% in the SVG group. Most patients had normal or low-normal ejection fraction (range 44.7%-58%).

Long-term mortality, repeat revascularization, and MI were reported in 12, 6, and 6 studies respectively (19,046, 1769, and 1692 patients). For short-term outcomes, mortality was

TABLE 2. Demographics of the included studies: Part 2

Study	Type	Center	Period	UNM RA	UNM SVG	UNM Total	MAT RA	MAT SVG	MAT Total	FU, y mean ± SD	Max FU, y
Benedetto and Codispoti, 2013[15]	Obs.	Papworth Hospital, Cambridge, England	1996-2012	936	8069	9005	809	809	1618	6.4 ± 3.6	13.6
Cohen et al, 2001[16]	Obs.	Sunnybrook and Women's College Health Sciences Centre, Toronto, Canada	1994-1999	478	2369	2847	478	956	1434	–	3
Goldman et al, 2011[24]	RCT	Multicenter	2003-2009	366	367	733	–	–	–	–	1
Lin et al, 2013[17]	Obs.	Cedars-Sinai Medical Center in Los Angeles, California	1997-2001	–	–	–	260	260	520	9.4 (5.7-11.9)*	12
Locker et al, 2013[18]	Obs.	Mayo Clinic, Rochester, Minn	1993-2009	168	7281	7449	–	–	–	7.6 ± 4.6	18.3
Petrovic et al, 2015[19]	RCT	Belgrade University School of Medicine, Belgrade, Serbia	2001-2003	100	100	200	–	–	–	–	8
Santarpino et al, 2010[20]	Obs.	Magna Graecia University of Catanzaro, Italy	2003-2007	150	180	330	–	–	–	3.17 ± 0.07	4.8
Schwann et al, 2015[21]	Obs.	Multicenter	1994-2011	4404	6709	11,261	2966	2966	5932	–	15
Tranbaugh et al, 2010[27]	Obs.	Beth Israel Medical Center, New York, NY	1995-2009	1560	2711	4271	862	862	1724	7.7 (0.1-13.8)*	14
RAPCO (Hayward et al, 2008)[22]	RCT	Austin Hospital, Victoria, Australia	1996-2002	73	80	153	–	–	–	6.2	10.8
Stand-in-Y (Nasso et al, 2009)[23]	RCT	Anthea Hospital, Bari, Italy; and Villa Azzurra Hospital, Rapallo, Italy	2003-2006	202	202	404	–	–	–	2.0 ± 0.8	–
Yoo et al, 2012[13]	RCT	Severance Hospital, Yonsei University Health System, Seoul, Korea	2008-2009	35	25	60	–	–	–	0.7	–
RSVP (Collins et al, 2008)[14]	RCT	Royal Brompton and Harefield NHS Trust, London, UK	1998-2000	82	60	142	–	–	–	5	–
Muneretto et al, 2004[28]	RCT	University of Brescia Medical School, Brescia, Italy	2000-2002	80	80	160	–	–	–	1.3 ± 0.3	–

UNM, Unmatched group; *RA*, radial artery; *SVG*, saphenous vein graft; *MAT*, matched group; *FU*, follow-up; *SD*, standard deviation; *Obs.*, observational study; *RCT*, randomized controlled trial. *Median and interquartile range.

reported in 11 studies (11,533 patients), stroke in 7 studies (3883 patients) and MI in 7 studies (6574 patients).

Primary Outcome

At a weighted mean follow-up of 6.6 years, mortality was 24.5% in RA group versus 34.2% in SVG group (IRR, 0.74; 95% CI, 0.63-0.87, $P < .001$) (Figure 1). Reconstructed Kaplan–Meier overall survival for RA versus SVG among included studies is shown in Figure E2 and Table E4 in Appendix 1.

Leave-one-out analysis supported the robustness of this finding (Figure E3, *A*, in Appendix 1). Funnel plot showed no publication bias (Egger test intercept was -0.72 ± 0.56, $P = .23$, Figure E3, *B*, in Appendix 1).

Subgroup analysis based on the study type revealed lower mortality in RA compared with SVG in observational studies but not in RCTs (IRR 0.71; 95% CI, 0.58- 0.87 and IRR, 0.88; 95% CI, 0.60-1.31) respectively (Figure E4 in Appendix 1).

Secondary Outcomes

Operative mortality was 1.25% in RA group versus 1.33% in SVG group (OR, 0.93; 95% CI, 0.68-1.28). No difference in perioperative MI or stroke was found (OR, 0.96; 95% CI, 0.59-1.56 and OR, 0.70; 95% CI, 0.43-1.13, respectively) (Figure E5 in Appendix 1).

No difference in follow-up MI or repeat revascularization was found between groups at a weighted mean follow-up of

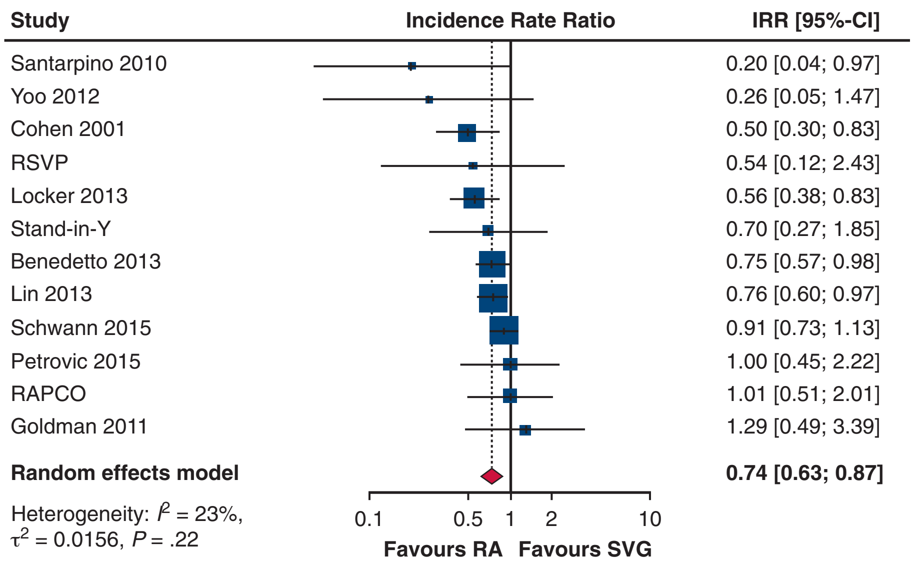

FIGURE 1. Forest plot for long-term mortality (expressed as incidence rate ratio [*IRR*]). *CI*, Confidence interval; *RA*, radial artery, *SVG*, saphenous vein graft.

3 and 2.8 years, respectively (IRR, 0.76; 95% CI, 0.42-1.36 and IRR, 0.68; 95% CI, 0.42-1.09, Table 3; Figure 2). However, when excluding the VA trial (limited to 1-year follow-up) the RA was associated with a significantly lower risk of repeat revascularization (Figure E6 in Appendix 1).

Meta-Regression

The survival advantage for the RA was independent from age (beta = 0.005, P = .79), percentage of females (beta = 0.005, P = .65), diabetes mellitus (beta = 0.009, P = .15), left ventricular ejection fraction (bet a = −0.04, P = .21), and RA target vessel stenosis severity (beta = −0.06, P = .37) (Figure E7 in Appendix 1). The results of the meta-regression model in the unmatched populations confirmed the results of the main analysis (Table E5 in Appendix 1). No effect of the explored variables on operative mortality was found (Table E6 in Appendix 1).

DISCUSSION

Together with the right internal thoracic artery, the RA is the most commonly used complementary arterial graft for CABG. The easy accessibility, possibility of simultaneous harvesting with other arterial conduits, optimal caliber, and length make the RA an almost-ideal conduit for CABG. Compared with the right internal thoracic artery, the RA also has the additional advantage of easier technical manipulation without an increase in the risk of sternal complications.[29]

The patency rate of the RA has been shown to be significantly better than that of the SVG at mid- and long-term follow-up. Two large angiographic randomized trials and several meta-analyses have in fact shown that the occlusion rate of SVG grafts is significantly greater than that of the RA, especially after the fourth postoperative year.[1,14,30] In the angiographic comparison with the longest follow-up published to date, we have described a more than 2-fold increase in the risk of graft occlusion at 20 years using the SVG instead of the RA as a conduit.[31]

Recently, in a pooled patient-level analysis of all the RCTs that have compared the 2 conduits we have reported a significantly lower risk of the composite of death, MI,

TABLE 3. Outcomes summary

Outcomes	Number of patients (mean follow-up)	Number of studies	Point estimate* 95% CI	Overall effect P value	Heterogeneity (I^2, P value)
Long-term mortality	19,046 (6.63 y)	12	0.74 (0.63- 0.87)	<.001	23.1%, P = .22
Follow-up RR	1769 (2.84 y)	6	0.68 (0.42-1.09)	.11	12.6%, P = .33
Follow-up MI	1769 (2.99 y)	6	0.76 (0.42- 1.36)	.35	0%, P = .94
Operative mortality	11,533	11	0.93 (0.68-1.28)	.67	0%, P = .93
Perioperative stroke	3883	7	0.70 (0.43-1.13)	.14	0%, P = .74
Perioperative MI	6574	7	0.96 (0.59- 1.56)	.86	0%, P = .89

CI, Confidence interval; *RR*, repeated revascularization; *MI*, myocardial infarction. *Incidence rate ratio was used for long-term outcomes whereas odds ratio was used for perioperative outcomes.

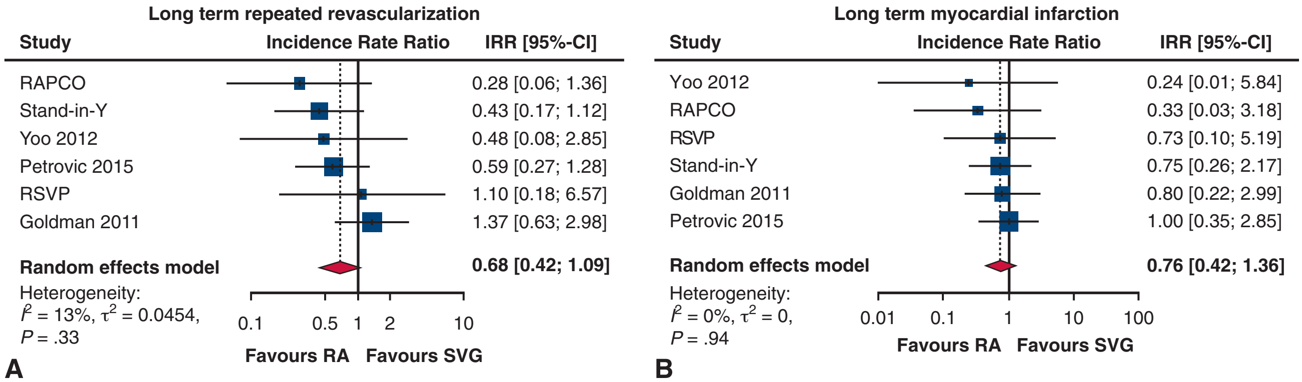

FIGURE 2. Forest plots of long-term secondary outcomes: A, Long-term repeat revascularization; B, long-term myocardial infarction (both expressed as incidence rate ratio [*IRR*]). *CI*, Confidence interval; *RA*, radial artery, *SVG*, saphenous vein graft.

and/or repeat revascularization 5 years after surgery.[32] No statistically significant difference in mortality was found.

Regarding long-term survival, in the largest single-center observational study comparing the RA and the SVG, Schwann and colleagues[21] reported on 11,261 patients and found significantly better survival at 15 years in the RA group. In a similar study on 8622 patients, Locker and colleagues[18] reported a 44% reduction in the risk of death at late 7.6 years follow-up in patients who received an RA instead of SVG.

However, the published evidence on the clinical effect of using the RA for CABG is mainly derived single-center observational studies from institutions which are very experienced with the use of arterial conduits. Previously published meta-analyses have focused on RCTs and angiographic outcomes. Thus, to our knowledge, this is the first meta-analysis to estimate the clinical effect of using the RA for CABG including outcomes from RCTs and matched or adjusted observational studies. To circumvent issues in generalizability by including only single-institution studies, which can vary considerably based on local factors and experience with the RA, we included data from 14 RCTs and observational studies involving 20,931 patients in aggregate with a mean follow-up of 6.6 years. The key finding is that the use of the RA is associated with a significant reduction in mortality at follow-up without an increase in the operative mortality or morbidity. The beneficial effect of the use of the RA is independent of age, sex, diabetes status, and left ventricular function. The differences in results for the secondary outcomes between this meta-analysis and our previous analysis of individual patient data are due to the different inclusion criteria (only studies with a follow-up >2 years were included in our previous study) and in the statistical approach used for aggregate versus individual patient analyses.

Limitations

The results of this meta-analysis must be interpreted in the context of some important limitations. The inclusion of observational studies raises the possibility of bias from unmatched confounders due to treatment allocation by the operating surgeons.[12] For this reason, we decided to limit our analysis to adjusted and matched observational studies, although we acknowledge that even the best matching techniques can be inadequate to minimize the effect of treatment allocation bias in studies of this type. It is important, and somewhat reassuring, to note that in our analysis, the patients' profile of the 2 arms in the unmatched population was very similar. It is possible that, as the use of the RA is generally perceived to be associated with less morbidity than bilateral internal thoracic artery, the confounders that we have described in studies comparing single and double internal thoracic arteries[12] are somewhat reduced in the studies comparing the RA and the SVG. In addition, we have used meta-regression to evaluate the variation of the results of the RA versus SVG comparison according to the difference in preoperative profile of the unmatched arms and found that the survival benefit associated with the RA was confirmed in every scenario.

This study shares the limitation of the analyses of aggregate data. There may be difference in surgical techniques, perioperative protocols, definition of nonfatal outcomes, and secondary prevention strategies among the included studies. However, only moderate heterogeneity was found across the different series, suggesting that these differences, if present, had only a marginal effect on the primary outcome. Finally, the analyses on repeat revascularization and late MI included only few studies and were very likely underpowered.

In conclusion, our analysis of the aggregated evidence comparing the RA and SVG for CABG showed that the use of the arterial conduit was associated with a statistically significant 26% relative reduction in the risk of death at a mean follow-up of 6.6 years without significant increase in the operative risk. Our results, combined with the large amount of evidence of better patency rate and clinical outcome for the RA compared with the SVG, suggests that the RA should be used in preference to the SVG at least in patients in whom it is technical appropriate and with long life expectancy.

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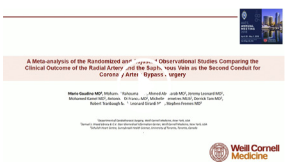

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: radial artery, saphenous vein, coronary artery bypass surgery, CABG, meta-analysis

APPENDIX 1

Full search strategy	
Ovid MEDLINE Epub Ahead of Print, in-process and other non-indexed citations, Ovid MEDLINE Daily and Ovid MEDLINE: 1946 to Present (Searched on 08/22/2017)	
Line #	Search term
1	Radial Artery/tr [Transplantation]
2	Radial Artery/ and (Transplantation/ or Transplants/)
3	((radial arter* or arteria radialis or radialis artery) and (transplant* or graft*)).tw.
4	or/1-3
5	Coronary Artery Bypass/
6	(aorta adj2 bypass).tw.
7	CABG.tw.
8	(aortic coronary bypass or aorticocoronary anastomosis).tw.
9	(aorto coronary adj2 (bypass or graft)).tw.
10	(aortocoronary adj2 (anastomosis or bypass or shunt or graft)).tw.
11	(coronary adj2 (bypass or graft)).tw.
12	(Total arterial revascularization or total arterial revascularisation or Multiple arterial revascularization or multiple arterial revascularisation).tw.
13	or/5-12
14	Saphenous Vein/tr [Transplantation]
15	Saphenous Vein/ and (Transplantation/ or Transplants/)
16	((Saphenous Vein* or SVG or saphena vein or saphenous venos system or vena saphena) and (transplant* or graft*)).tw.
17	Internal Mammary-Coronary Artery Anastomosis/
18	((Right Internal Mammary Artery or RIMA or Coronary Internal Mammary Artery or arteria mammaria interna or arteria thoracica interna or internal thoracic artery or mammary internal artery) and (transplant* or graft* or anastomosis)).tw.
19	(cardiac muscle revascularisation or cardiac muscle revascularization or coronary revascularisation or coronary revascularization or heart muscle revascularisation or heart myocardium revascularisation or heart revascularisation or heart revascularization or internal mammary arterial anastomosis or internal mammary arterial implantation or internal mammary artery anastomosis or internal mammary artery graft or internal mammary artery implant or internal mammary artery implantation or internal mammary-coronary artery anastomosis or myocardial revascularisation or myocardial revascularization or myocardium revascularisation or myocardium revascularization or transmyocardial laser revascularisation or transmyocardial laser revascularization or vineberg operation).tw.
20	or/14-19
21	4 and 13 and 20
22	Editorial/ or Letter/ or Comment/ or Meeting abstract/
23	(conference paper or conference proceeding* or conference abstract* or meeting abstract or editorial or letter or comment).pt.
24	22 or 23
25	21 not 24
26	limit 25 to English language

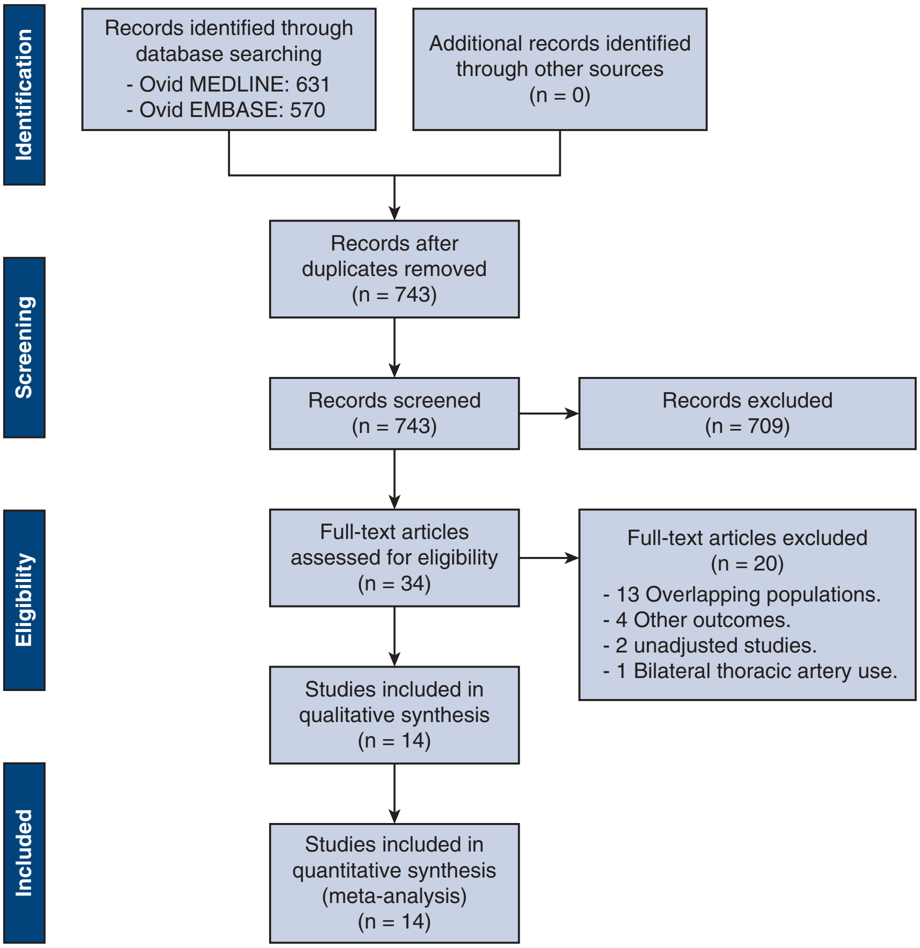

FIGURE E1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram.

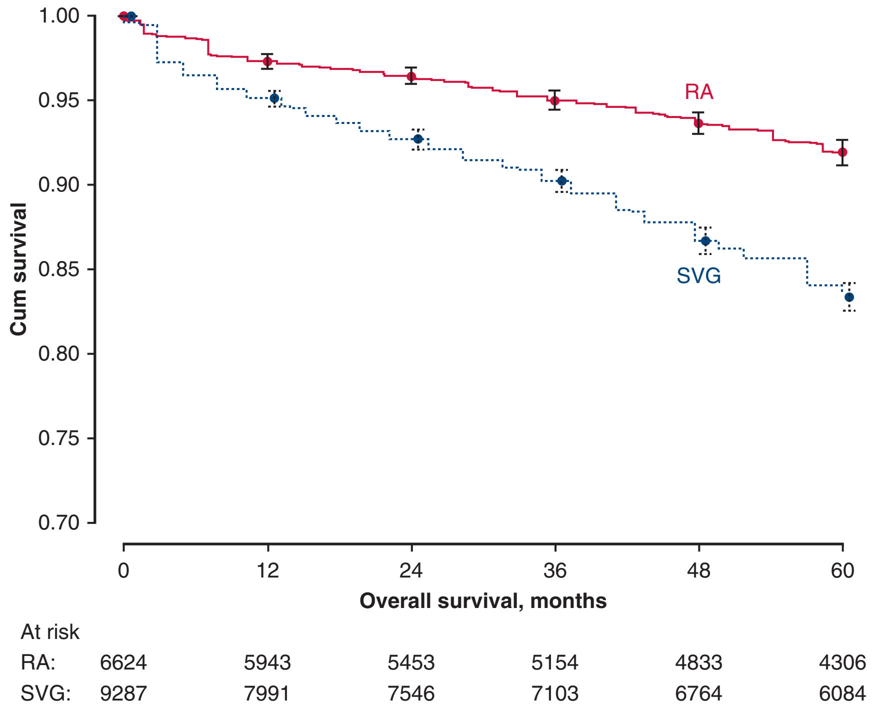

FIGURE E2. Reconstructed Kaplan–Meier overall survival for RA versus SVG among included studies with error bars denoting 95% confidence intervals ($P < .001$). *RA*, Radial artery; *SVG*, saphenous vein graft.

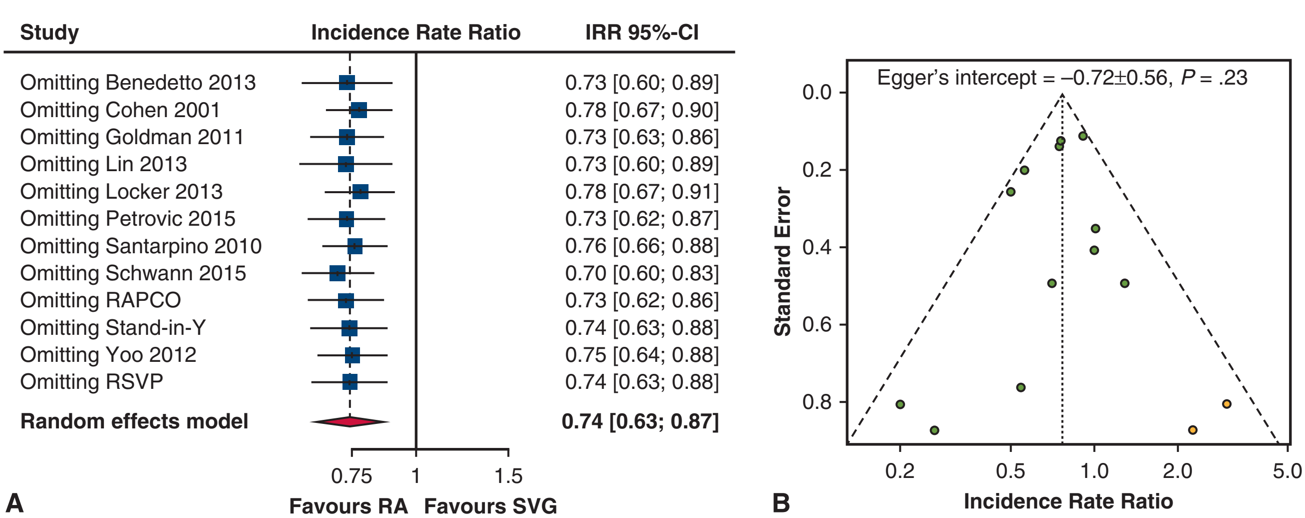

FIGURE E3. Primary outcomes: (A) Leave-one-out analysis and (B) Funnel plot with trim-and-fill method and Egger test results. *IRR*, Incidence rate ratio; *CI*, confidence interval; *RA*, radial artery; *SVG*, saphenous vein graft.

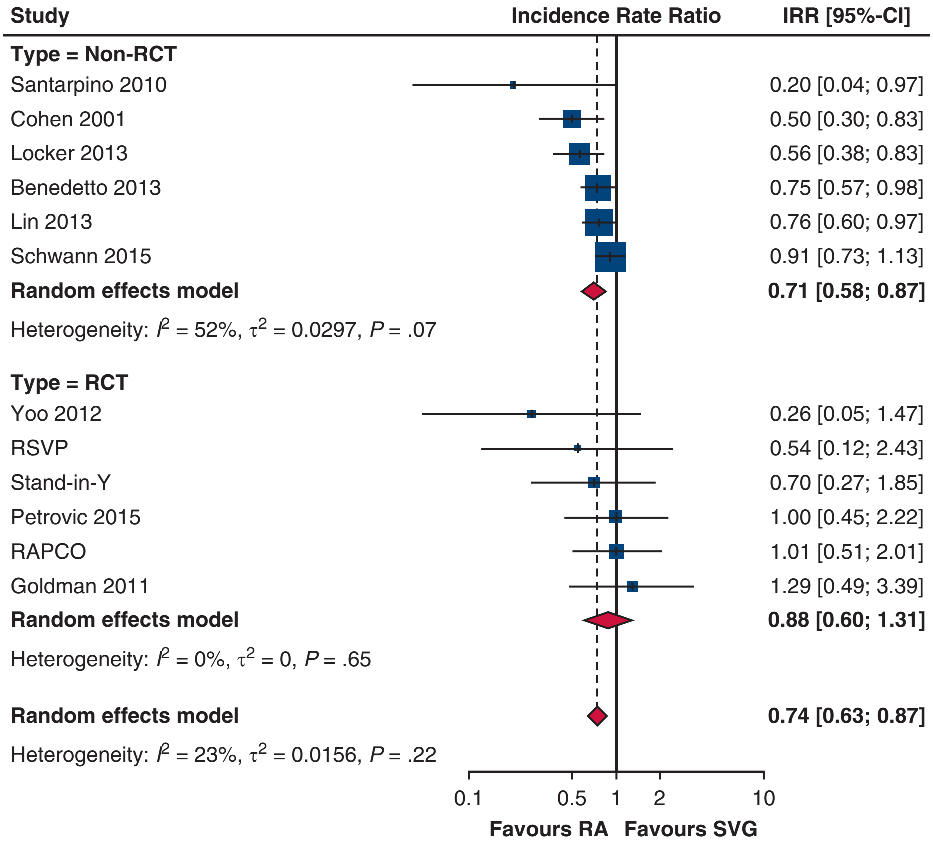

FIGURE E4. Forest plot of late mortality in RA versus SVG according to study type (non-RCT vs RCTs). *IRR*, Incidence rate ratio; *CI*, confidence interval; *Non-RCTs*, nonrandomized observational clinical trials; *RCT*, randomized clinical trials; *RA*, radial artery; *SVG*, saphenous vein graft.

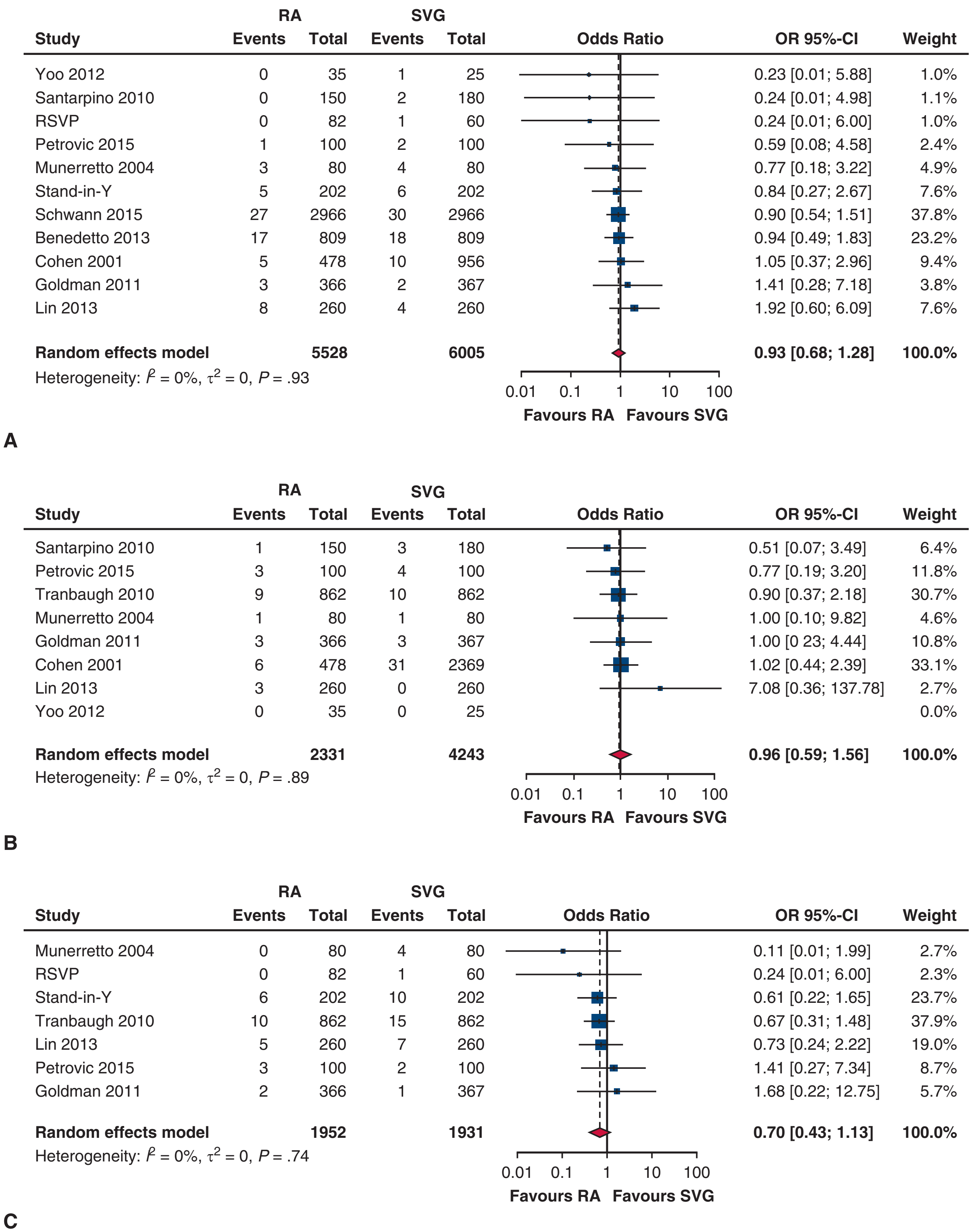

FIGURE E5. Forest plots for short term secondary outcomes: (A) operative mortality, (B) perioperative myocardial infarction and, (C) perioperative stroke (all expressed as OR). *RA*, Radial artery; *SVG*, saphenous vein graft; *OR*, odds ratio; *CI*, confidence interval.

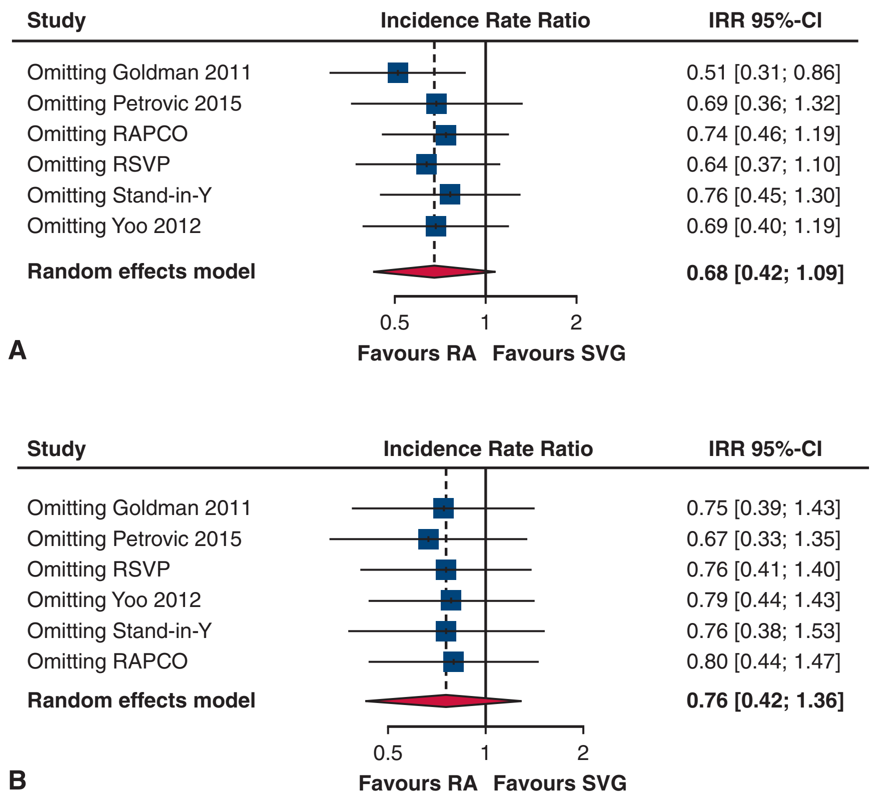

FIGURE E6. Leave-one-out analysis of (A) long-term repeated revascularization and (B) long-term myocardial infarction. *IRR*, Incidence rate ratio; *CI*, confidence interval; *RA*, radial artery; *SVG*, saphenous vein graft.

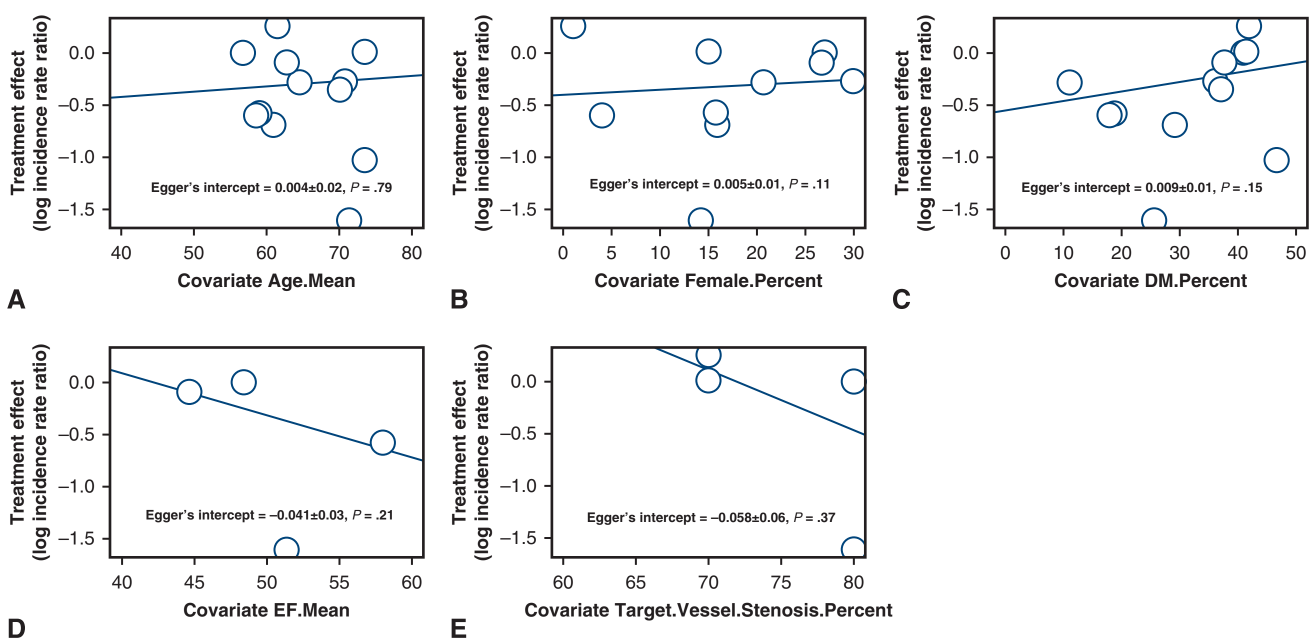

FIGURE E7. Meta-regression for the primary outcome (long-term mortality): (A) mean age; (B) Female sex percentage; (C) DM percentage; (D) mean EF; and (E) target vessel stenosis percentage. *DM*, Diabetes mellitus; *EF*, ejection fraction.

TABLE E1. Long term mortality: Summary of the statistics calculation

First author/ acronym	Type	Follow-up, y	RA total	SVG total	RA events	KM nonevent rate RA	SVG events	KM nonevent rate SVG	Log rank *P* value	IRR	LN(IRR)	SE [LN (IRR)]	IRR calculation method
Benedetto and Codispoti, 2013[15]	Non-RCT	6.4*	809	809						0.75	−0.29	0.14	HR
Cohen et al, 2001[16]	Non-RCT	3†	478	956	19	0.96	76	0.92	0.64	0.50	−0.69	0.26	KM
Goldman et al, 2011[24]	RCT	1†	366	367	9		7			1.29	0.25	0.49	Events (RR)
Lin et al, 2013[17]	Non-RCT	9.4*	260	260						0.76	−0.27	0.12	HR
Locker et al, 2013[18]	Non-RCT	7.6*	168	7281						0.56	−0.58	0.20	HR
Petrovic et al, 2015[19]	RCT	8†	100	100	12		12			1.00	0.00	0.41	Events (RR)
Santarpino et al, 2010[20]	Non-RCT	3.17*	150	180		0.95		0.75	0.046	0.20	−1.61	0.81	KM
Schwann et al, 2015[21]	Non-RCT	15†	2966	2966						0.91	−0.09	0.11	HR
RAPCO (Hayward et al, 2008)[22]	RCT	6.2*	113	112						1.01	0.01	0.35	HR (inverted)
Stand-in-Y (Nasso et al, 2009)[23]	RCT	2.01*	201	202	7		10			0.70	−0.35	0.49	Events (RR)
Yoo et al, 2012[13]	RCT	0.67*	35	25						0.265	−1.328	0.874	HR from IPD
RSVP (Collins et al, 2008)[14]	RCT	5*	82	60						0.544	−0.609	0.763	HR from IPD

IRR: If survival curve nonevent rate proportions are available, then IRR= (1/RA nonevent rate)/(1/SVG nonevent rate). If the actual number of patients with events and group-specific patient-years of follow-up are available, then IRR = [RA event patients/RA patient-years of follow-up]/[SVG event patients/SVG patient-years of follow-up]. SE[LN(IRR)]: If HR and 95% confidence intervals were reported, then it was calculated as LN(Upper 95% CI) – LN(Lower 95% CI))/3.92. If the survival curve *P* value was available, then it was calculated as LN(IRR)/NORMSINV (*P* value/2) where NORMSINV is a function in Microsoft Excel. If only actual events were available, then it was calculated as SE[LN(IRR)] = SQRT (1/RA event patients + 1/SVG event patients), where SQRT is a function in Microsoft Excel (see Yanagawa et al[10]). *RA*, Radial artery; *SVG*, saphenous vein graft; *KM*, Kaplan–Meier; *IRR*, incidence rate ratio; *LN(IRR)*, natural logarithm of incidence rate ratio; *SE*, standard error; *RCT*, randomized clinical trial; *HR*, hazard ratio; *RR*, relative risk; *IPD*, individual patient-level data. *Mean follow-up. †Maximum follow-up.

TABLE E2. Demographics of the included observational studies (unmatched groups)

Study	Arm	Age, y, mean SD	Female, n (%)	DM, n (%)	EF, mean SD	COPD, n (%)
Benedetto and Codispoti, 2013[15]	RA	65.0 ± 10.0	191 (20.4)	95 (10.1)	NR*	110 (11.8)
	SVG	68.0 ± 9.0	1452 (18.0)	928 (11.5)	NR*	880 (10.9)
Cohen et al, 2001[16]	RA	NR	NR	NR	NR	NR
	SVG	NR	NR	NR	NR	NR
Lin et al, 2013[17]	RA	NR	NR	NR	NR	NR
	SVG	NR	NR	NR	NR	NR
Locker et al, 2013[18]	RA	NR	NR	NR	NR	NR
	SVG	68.0 ± 9.0	(24.8)	(33.5)	55.0 ± 14.0	(11.7)
Santarpino et al, 2010[20]	RA	72.2 ± 9.9	20 (13.3)	49 (32.6)	53.5 ± 9.9	24 (13.3)
	SVG	70.5 ± 9.6	26 (14.4)	36 (20.0)	49.2 ± 10.7	27 (18.0)
Schwann et al, 2015[21]	RA	60.2 ± 9.7	1026 (34.4)	1694 (37.2)	49 ± 11	779 (17.1)
	SVG	67.3 ± 9.9	2305 (34.4)	2541 (37.9)	48 ± 12	1748 (26.1)
Tranbaugh et al, 2010[27]	RA	57.1 ± 8.5	270 (17.3)	551 (35.3)	48.2 ± 11.4	282 (18.1)
	SVG	68.4 ± 9.3	933 (34.4)	1038 (38.3)	46.1 ± 13.2	881 (32.5)

SD, Standard deviation; *DM*, diabetes mellitus; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *RA*, radial artery; *NR*, not reported; *SVG*, saphenous vein graft. *EF reported as categories.

TABLE E3. Cochrane collaboration's tool for the included randomized trials

Risk of bias	Authors' judgment	Support for judgment
Goldman et al, 2011[24]		
Random sequence generation	Low risk	Patients were assigned in a 1:1 ratio to RA or SVG using permuted blocks randomization.
Allocation concealment	Unclear	No info.
Blinding of participants and personnel	NA	Blinding not applicable.
Blinding of outcome assessment	Low risk	The central angiography readers were blinded as to which patients had radial artery grafts vs saphenous vein grafts.
Incomplete outcome data	Low risk	Five hundred thirty-three patients (73%) had 1-y angiograms.
Selective reporting	Low risk	All expected outcomes reported.
Other bias	Low risk	No other sources of bias to report.
Petrovic et al, 2015[19]		
Random sequence generation	Unclear	Patients were randomized in 1:1 fashion to receive either LITA and RA grafts or LITA and SVGs.
Allocation concealment	Unclear	No info.
Blinding of participants and personnel	NA	Blinding not applicable.
Blinding of outcome assessment	Unclear	No info.
Incomplete outcome data	Low risk	All patients were followed for 8 y or until death.
Selective reporting	Low risk	All expected outcomes reported.
Other bias	Low risk	No other sources of bias to report.
Stand-in-Y (Nasso et al, 2009)[23]		
Random sequence generation	Low risk	Patients randomized with the aid of a computerized algorithm
Allocation concealment	Unclear	No info
Blinding of participants and personnel	NA	Blinding not applicable
Blinding of outcome assessment	Unclear	No info
Incomplete outcome data	Low risk	Three patients were lost at follow-up.
Selective reporting	Low risk	All expected outcomes reported
Other bias	Low risk	No other sources of bias to report
Yoo et al, 2012[13]		
Random sequence generation	Unclear	Sixty patients were allocated in a random ratio of 1:1 to 2 groups.
Allocation concealment	Unclear	No info.
Blinding of participants and personnel	NA	Blinding not applicable.
Blinding of outcome assessment	Unclear	No info.
Incomplete outcome data	Unclear	No info.
Selective reporting	Low risk	All expected outcomes reported.
Other bias	Low risk	No other sources of bias to report
RSVP (Collins et al, 2008)[14]		
Random sequence generation	Low risk	Randomization codes were obtained by use of a random number generator sequence.
Allocation concealment	Low risk	Sealed in brown envelopes that were sequentially numbered.
Blinding of participants and personnel	NA	Blinding not applicable.
Blinding of outcome assessment	Unclear	No info.
Incomplete outcome data	Low risk	Follow-up angiography was performed in 103 of the 134 patients alive and not withdrawn from the study (77%).
Selective reporting	Low risk	All expected outcomes reported.
Other bias	Low risk	No other sources of bias to report.
Muneretto et al, 2004[28]		
Random sequence generation	Unclear	The patients were randomly assigned to group 1 or group 2.
Allocation concealment	Unclear	No info.
Blinding of participants and personnel	NA	Blinding not applicable.
Blinding of outcome assessment	Unclear	No info.
Incomplete outcome data	Low risk	We evaluated 76 patients (98%) in group 1 and 76 patients (100%) in group 2 by means of clinical visits and cycloergometric tests. Angiographic evaluation was performed in 89.6% and 88.1% of hospital survivors in groups 1 and 2, respectively.

(Continued)

TABLE E3. Continued

Risk of bias	Authors' judgment	Support for judgment
Selective reporting	Low risk	All expected outcomes reported.
Other bias	Low risk	No other sources of bias to report.
RAPCO (Hayward et al, 2008)[22]		
Random sequence generation	Low risk	The choice of the second conduit was determined by random assignment. Random numbers were generated from the Minitab statistical package (Minitab, Inc, State College, Pa)
Allocation concealment	Low risk	Numbers were placed in sealed envelopes.
Blinding of participants and personnel	NA	Blinding not applicable.
Blinding of outcome assessment	Unclear	No info.
Incomplete outcome data	Low risk	Survival was confirmed with the National Death Index, a register of all deaths.
Selective reporting	Low risk	All expected outcomes reported.
Other bias	Low risk	No other sources of bias to report.

RA, Radial artery; *SVG*, saphenous vein graft; *N/A*, not available; *LITA*, left internal thoracic artery.

TABLE E4. Estimate survival at 1 and 5 years and at the end of follow-up from reconstructed Kaplan–Meier curves

Graft	HR 1 y	HR 5 y	HR end of follow-up
RA	97.2% (96.8%-97.6%)	91.9 (91.2%-92.7%)	69.0% (67.1%-71.0%) at 169.6 mo
SVG	95.1% (94.7%-95.6%)	83.4% (82.6%-84.2%)	50.1% (48.7%-51.6%) at 167.99 mo

Ranges in parentheses are 95% confidence intervals. *HR*, Hazard ratio; *RA*, radial artery; *SVG*, saphenous vein graft.

TABLE E5. Results of meta-regression for the primary outcome

Variable source	Variables	Meta-regression results
Matched	Mean age	Beta = 0.0049, P = .7850
Matched	Female % (mean)	Beta = −0.0048, P = .6480
Matched	Diabetes % (mean)	Beta = 0.0092, P = .1511
Matched	Mean EF%	Beta = −0.0405, P = .2135
Matched	RA % target vessel stenosis	Beta = −0.0578, P = .3658
Unmatched	Mean age	Beta = 0.0049, P = .7850
Unmatched	Mean age absolute difference	Beta = −0.0490, P = .3379
Unmatched	Female % (mean)	Beta = 0.0132, P = .4267
Unmatched	Female % absolute difference	Beta = −0.0058, P = .8773
Unmatched	Diabetes % (mean)	Beta = 0.0136, P = .2667
Unmatched	Diabetes % absolute difference	Beta = −0.0267, P = .0252
Unmatched	Mean EF%	Beta = −0.5344, P = .0602
Unmatched	Mean EF% absolute difference	Beta = −0.4593, P = .0598

EF, Ejection fraction; *RA*, radial artery.

TABLE E6. Results of meta-regression for operative mortality

Variable source	Variables	Meta-regression results
Matched	Mean age	Beta = 0.0030, P = .9364
Matched	Female % (mean)	Beta = −0.0052, P = .7578
Matched	Diabetes % (mean)	Beta = 0.0001, P = .9922
Matched	Mean EF%	Beta = −0.1648, P = .3762
Matched	RA % target vessel stenosis	Beta = −0.0806, P = .4317

EF, Ejection fraction; *RA*, radial artery.