Radial Artery Versus Right Internal Thoracic Artery Versus Saphenous Vein as the Second Conduit for Coronary Artery Bypass Surgery: A Network Meta-Analysis of Clinical Outcomes

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Background—There remains uncertainty regarding the second-best conduit after the internal thoracic artery in coronary artery bypass grafting. Few studies directly compared the clinical results of the radial artery (RA), right internal thoracic artery (RITA), and saphenous vein (SV). No network meta-analysis has compared these 3 strategies.

Methods and Results—MEDLINE and EMBASE were searched for adjusted observational studies and randomized controlled trials comparing the RA, SV, and/or RITA as the second conduit for coronary artery bypass grafting. The primary end point was all-cause long-term mortality. Secondary end points were operative mortality, perioperative stroke, perioperative myocardial infarction, and deep sternal wound infection (DSWI). Pairwise and network meta-analyses were performed. A total of 149 902 patients (4 randomized, 31 observational studies) were included (RA, 16 201, SV, 112 018, RITA, 21 683). At NMA, the use of SV was associated with higher long-term mortality compared with the RA (incidence rate ratio, 1.23; 95% CI, 1.12–1.34) and RITA (incidence rate ratio, 1.26; 95% CI, 1.17–1.35). The risk of DSWI for SV was similar to RA but lower than RITA (odds ratio, 0.71; 95% CI, 0.55–0.91). There were no differences for any outcome between RITA and RA, although DSWI trended higher with RITA (odds ratio, 1.39; 95% CI, 0.92–2.1). The risk of DSWI in bilateral internal thoracic artery studies was higher when the skeletonization technique was not used.

Conclusions—The use of the RA or the RITA is associated with a similar and statistically significant long-term clinical benefit compared with the SV. There are no differences in operative risk or complications between the 2 arterial conduits, but DSWI remains a concern with bilateral ITA when skeletonization is not used. **(*J Am Heart Assoc*. 2019;8:e010839. DOI: 10.1161/JAHA.118.010839.)**

Key Words: arterial conduits • coronary artery bypass • coronary artery bypass graft surgery • saphenous vein graft

One of the most important unresolved questions in contemporary coronary artery bypass (CABG) surgery is the choice of the conduit to complement the internal thoracic to left anterior descending artery anastomosis.

The radial artery (RA), the right internal thoracic artery (RITA), and the saphenous vein (SV) are all currently being used routinely, although the majority of the surgeons favor the SV.

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Accompanying Tables S1 through S4 and Figures S1 through S5 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.010839

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Clinical Perspective

What Is New?

- The use of the radial artery or the right internal thoracic artery is associated with a similar and statistically significant long-term clinical benefit compared with the saphenous vein.
- There are no differences in operative risk or complications between the two arterial conduits, but deep sternal wound infection remains a concern with bilateral internal thoracic artery when skeletonization is not used.

What Are the Clinical Implications?

- The results of our study support the superiority of the use of a second arterial over venous graft, and suggest the equivalence in long-term and perioperative outcomes among RITA and radial artery.

Abundant observational evidence suggests a survival benefit for the use of arterial grafts, and the current guidelines encourage a wider use of the RA or the RITA, especially in patients with a long life expectancy.[1–4] However, the reported benefit of arterial grafts has not been confirmed in a large randomized controlled trial (RCT) , and it has been hypothesized that the survival benefit seen in observational studies may be due to unmatched confounders and treatment allocation bias.[5,6] An important additional unresolved question is the relative role of the RITA and RA. Although the RITA is biologically identical to the left internal thoracic artery, data comparing the patency rate and clinical outcome of the 2 arterial grafts has been contradictory and inconclusive.[7,8]

Network meta-analysis (NMA) with adjusted indirect comparison among treatments is a useful technique to reduce the potential for heterogeneity or allocation biases, in particular when analyzing both RCTs and observational studies.[9]

To date, the only published NMA comparing the SV, RITA and RA as the second conduit in CABG focused only on angiographic patency and not on clinical outcomes.[10] Due to the well-known discrepancy between occlusion of grafts to non–left anterior descending arteries and clinical outcomes,[11] a similar analysis focusing on clinical end points is of particular relevance to the surgical community.

Here, we performed an NMA with the aim to specifically investigate the differences in late survival (primary outcome) and other clinical outcomes according to the type of second graft used for CABG.

Material and Methods

The authors declare that all supporting data are available within the article and its online supplementary files. This systematic review and NMA follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.[12]

Data Sources and Systematic Literature Review

Ovid's version of MEDLINE and EMBASE were searched from inception to February 2018 (full search strategy attached in Table S1). Inclusion criteria were English language publications, adjusted or matched observational studies or RCTs comparing RA and/or SV and/or RITA as the second conduit for CABG. In addition, we searched recent meta-analyses and reviews on this topic for potential additional studies. All citations were reviewed by 3 investigators independently (A.A., A.D.F., and M.R.), and any disagreements were resolved by consensus. In case of overlapping studies, the largest series were included.

Data Extraction and Quality Assessment

Data extraction was performed independently by 2 investigators (A.A. and A.D.F.). The following variables were included: study demographics (sample size, number of centers, institutions involved, publication year, study period, design and country, length of follow-up), patient demographics (age, sex, diabetes mellitus, and ejection fraction) and procedural (use of skeletonization) and postoperative data. The quality of the included studies was assessed by the Newcastle–Ottawa Scale (Table S2).[13] Only RCTs and observational studies of high quality (Newcastle–Ottawa Scale score >6) were included in the final analysis.

Outcomes

The primary outcome was all-cause long-term mortality. The secondary outcomes were operative mortality, perioperative stroke, perioperative myocardial infarction (MI), and deep sternal wound infection (DSWI), as defined in the original articles.

Two levels of analyses were conducted for all outcomes: (1) pairwise meta-analysis between arterial grafts (with either RITA or RA) and SV and between RITA and RA, and (2) network meta-analyses between RITA, RA, and SV.

Data Synthesis and Analysis

Pairwise meta-analysis

Late outcomes were pooled as the natural logarithm of the incident rate ratio (IRR) to account for potentially different follow-up durations between the groups. We estimated the IRR through several means depending on the available study data. When hazard ratios for matched (preferentially)/adjusted cohorts were provided, we took the natural logarithm

of the hazard ratio; the standard error was derived from the 95% CI or log rank *P* value.[14] When Kaplan–Meier curves were present, we estimated the event rates from the curves using GetData Graph Digitizer software 2.26 (http://getdata-graph-digitizer.com/). In case of missing Kaplan–Meier curves, we used the reported event rates in order to calculate the IRR, as previously described.[15,16] Short-term binary outcomes were pooled using log odds ratio (OR) with 95% CI using the generic inverse variance method.[9] Random effect meta-analysis was performed using meta and metafor packages in R (version 3.3.3 R Project for Statistical Computing).[17,18] Heterogeneity was reported as low (I^2=0–25%), moderate (I^2=26–50%), or high (I^2 >50%).[19] In random-effects meta-analysis, the extent of variation among the effects observed in different studies (between-study variance) is referred to as tau^2 (ie, the variance of the true effect size parameters across the population of studies). Tau^2 reflects the amount of true variance (heterogeneity), while tau is the estimated standard deviation of underlying true effects across studies, and they are used to describe the distribution of true effects; if there is no variance between studies, tau^2 is low (or zero).[20–22] We reported tau^2 values throughout tables and figures, as appropriate.

Sensitivity analysis using leave-one-out analysis and publication bias assessment by funnel plot and Egger's test were conducted for the primary outcome. Subgroup analysis was used to compare the relative results of RITA and RA versus SV. Meta-regression was used to explore the effect of age, sex, diabetes mellitus, and preoperative ejection fraction on the IRR for the primary outcome.

Network meta-analysis

Network (multiple-treatment) meta-analysis was conducted in R (version 3.3.3 R Project for Statistical Computing) using the "netmeta" statistical package based on the method described by Rücker.[23–25] Inconsistency was evaluated with Cochran's Q.[26] Pooled log IRRs with 95% CIs was used to determine the relative effect estimates of late outcomes. ORs with 95% CIs were used for the binary outcomes. A random-effects model was preferentially used to improve the model fit, but results using a fixed model were also reported.

Inconsistency in NMA was evaluated by conducting conventional pairwise meta-analyses and testing consistency by comparing the direct and indirect evidence. The consistency equation used was $\mu BC=\mu AC-\mu AB$, where μAB is the treatment effect for treatment B compared with treatment A.[27,28] We used Cochran's Q statistic to assess inconsistency, and the presence of $P<0.05$ signifies inconsistency. Statistical significance (at the 5% level) was declared when 95% CI did not cross the line of no effect. For the primary outcome, a network meta-regression was used to relate the size of treatment effect to potential effect modifiers (mean age, percentage of female, percentage of patients with diabetes mellitus, and mean preoperative ejection fraction). Network meta-regression was conducted using the logit transformation method with random-effects model with no priori. The logit transformation was used as suggested by other authors.[29,30]

Results

Description of the Included Studies and of the Population

A total of 2455 studies were retrieved and 35 met inclusion criteria and were included in the final meta-analysis (Figure S1). Seven studies were international and multicenter; 11 studies were from the United States; 4 from Canada, 3 each from Italy and the United Kingdom; 2 each from Japan and Australia, and 1 each from Austria, Serbia, and Argentina (Tables 1 and 2).[31–65]

A total of 149 902 patients were included (RA, 16 201; SV, 112 018; and RITA, 21 683) from 4 RCTs (n=1932) and 31 observational studies (n=147 970). Demographics of the included studies are shown in Tables 1 and 2.

The number of patients in the individual studies ranged from 182 to 48 241 (91–4577 in the RA group, 91–46 343 in the SV group, and 118–2215 in the RITA group). The mean age ranged from 56.0 to 72.1 (56.3–72.1 years in the RA group, 57.1–70.6 years in the SV group, and 56.2–69.2 in the RITA group). Female sex ranged from 1.1 to 43.8% (1.0–43.1% in the RA group, 1.1–41.6% in the SV group, and 7.3–43.8% in the SV group). Most patients had a normal or low-normal ejection fraction (range 42–59.4%). The incidence of diabetes mellitus ranged from 5.1 to 53.2% (6.5–45.1% in the RA group, 12.0–43.8% in the SV group, and 5.1–53.3% in the RITA group).

Pairwise Meta-Analysis

The main results of the pairwise meta-analysis are summarized in Table 3.

At a mean follow-up of 6.9 years, the use of any arterial graft (RA or RITA) was associated with lower long-term mortality compared with the use of the SV (IRR, 0.80; 95% CI, 0.75–0.85). There was a significantly higher risk of DSWI (OR 1.27; 95% CI, 1.05–1.54) in the arterial graft group. Operative mortality (OR, 0.68; 95% CI, 0.55–0.83), perioperative MI (OR, 0.77; 95% CI, 0.64–0.92) and perioperative stroke (OR, 0.80; 95% CI, 0.65–0.98) were lower in the arterial graft group.

The use of the RA was associated with lower long-term mortality (IRR, 0.81; 95% CI, 0.73–0.90) at a mean follow-up of 8.1 years compared with the SV. Operative mortality (OR, 0.66; 95% CI, 0.46–0.95) and perioperative stroke (OR, 0.73; 95% CI, 0.54–1.00) were lower in the RA group, while the risk of perioperative MI (OR, 0.67, 95% CI, 0.42–1.07), and DSWI were similar (OR, 1.10; 95% CI, 0.80–1.51).

Table 1. Characteristics of the Included Studies

Author/Year	Study Period	Mean/Median SD Follow-Up (Years)	Hospitals/Centers	Type
Benedetto 2013[31]	1996–2012	6.4±3.6	Papworth Hospital, Cambridge, England	PSM
Benedetto 2014[32]	2001–2013	4.0±3.2	Harefield Hospital, London, United Kingdom	PSM
Benedetto 2017[33]	1996–2015	10.2±4.5	Bristol Heart Institute, United Kingdom	PSM
Buxton 1998[34]	1985–1995	4.3	Austin and Repatriation Medical Center, University of Melbourne, Victoria, Australia	Adjusted
Calafiore 2004[35]	1986–1999	Overall: 7.3±4.8 RITA: 7.1±5.0 SV: 7.5±4.7	University Hospital, Torino, Italy and "G D'Annunzio" University, Chieti, Italy	PSM
Carrier 2009[36]	1995–2007	10.0	Montreal Heart Institute, Montreal, Quebec, Canada	Adjusted
Cohen 2001[37]	1994–1999	Max 3.0	Sunnybrook and Women's College Health Sciences Centre, Toronto, Canada	PSM
Dewar 1995[38]	1984–1992	4.0	Vancouver Hospital and Health Sciences Centre, University of British Columbia, Vancouver, Canada	PSM
Goldman 2011[39]	2003–2009	Max 1.0	Multicenter	RCT
Goldstone 2018[40]	2006–2011	Median arterial: 5.3 (IQR: 3.8–6.7) Median venous: 5.2 (IQR: 3.7–6.6)	Multicenter	PSM
Grau 2015[41]	1994–2013	Overall: 10.5±5.0 RITA: 10.9±5.0 SV: 10.1±5.0	Columbia University College of Physicians and Surgeons, Ridgewood, NJ, United States	PSM
Hayward 2013 (RAPCO)[42]	1996–2004	6 (1.8–10.4)	University of Melbourne, Victoria, Australia	RCT
Ioannidis 2001[43]	1993–1996	NR	Multicenter	Adjusted
Janiec 2017[44]	2001–2015	SV: 9.3 (4.2) RA: 10.7 (4.1) RITA: 5.5 (5.0)	Multicenter	Adjusted
Kurlansky 2010[45]	1972–1994	Overall: 11.0±0.5 RITA: 12±.0.7.0 SV: 11.0±1.0	Florida Heart Research Institute, Miami, FL, United States	Adjusted
LaPar 2015[46]	2001–2013	30.0 days	VCSQI database, Virginia, United States	PSM
Lin 2013[47]	1997–2001	9.4 (5.7–11.9)	Cedars-Sinai Medical Center in Los Angeles, CA	PSM
Locker 2013[48]	1993–2009	7.6	Mayo Clinic, Rochester, MN, United States	Adjusted
Lytle 2004[49]	1971–1989	RITA: 16.2±2.4 SV: 16.3±2.5	The Cleveland Clinic Foundation, Cleveland, OH, United States	PSM
Nasso 2009[50]	2003–2006	24.1±9.8 months	Multicenter	RCT
Navia 2016[51]	1996–2014	Median: 5.5 (IQR: 2.6–8.8)	Instituto Cardiovascular de Buenos Aires, Buenos Aires, Argentina	PSM
Parsa 2013[52]	1984–2009	NR	Duke University Medical Center, Durham, NC, United States	Adjusted
Petrovic 2015[53]	2001–2003	Max 8.0	Belgrade University School of Medicine, Belgrade, Serbia	RCT
Pusca 2008[54]	1997–2006	NR	Emory University School of Medicine, Atlanta GA, United States	Adjusted
Rosenblum 2016[55]	2003–2013	Median: 2.8 (1.1–4.9)	Emory University School of Medicine, Atlanta, GA, United States	PSM
Ruttman 2011[56]	2001–2010	Overall: 57.7 (3.0–112.0) months RITA: 32.7 (3–111.0) RA: 67.3 (3–112.0)	Innsbruck Medical University, Austria	PSM
Santarpino 2010[57]	2003–2007	3.17±0.07	Magna Graecia University of Catanzaro, Italy	Adjusted

Continued

Table 1. Continued

Author/Year	Study Period	Mean/Median SD Follow-Up (Years)	Hospitals/Centers	Type
Schwann 2016[58]	1987–2011	4.7	Multicenter	PSM
Stevens 2004[59]	1985–1995	Overall: 11.0±3.0 RITA: 8.0±2.0 SV: 12.0±3.0	Montreal Heart Institute, Montreal, Quebec, Canada	Adjusted
Tarelli 2001[60]	1988–1990	Overall: 9.2 RITA: 9.2±2.8 SV: 9.1±2.5	Varese Hospital, Varese, Italy	PSM
Tranbaugh 2010[61]	1995–2009	7.7 (0.1–13.8)	Beth Israel Medical Center, New York, NY, United States	PSM
Tranbaugh 2017[62]	1995–2012	RA: 8.8±4.0 RITA: 8.9±4.9 SV: 9.1	Multicenter	Adjusted
Tsuneyoshi 2015[63]	2000–2013	6.1±7.8	"Kurashiki Central Hospital, Okayama, Japan"	PSM
Yoshida 2017[64]	1997–2007	7.5±4.4	Fukui Cardiovascular Center, Shinbo, Fukui, Japan	PSM
Zacharias 2004[65]	1996–2002	3.7±1.9	Mercy St Vincent Medical Center, Toledo, OH, United States	PSM

IQR indicates interquartile range; NR, not reported; PSM, propensity score matched; RA, radial artery; RAPCO, Radial Artery Patency and Clinical Outcomes randomized trial; RCT, randomized controlled trial; RITA, right internal thoracic artery; SV, saphenous vein; VCSQI, Virginia Cardiac Services Quality Initiative.

The use of the RITA was associated with lower long-term mortality (IRR, 0.80; 95% CI, 0.73–0.86) at mean 8.5 years follow-up compared with SV. Perioperative MI (OR, 0.79; 95% CI, 0.65–0.96) and operative mortality (OR, 0.68; 95% CI, 0.53–0.87) were lower in the RITA arm. There was no difference in perioperative stroke (OR, 0.85; 95% CI, 0.62–1.16), while the risk of DSWI higher in the RITA group (OR, 1.33; 95% CI, 1.04–1.69).

When directly comparing the 2 arterial grafts, the use of RITA was associated with similar long-term mortality (IRR, 0.96; 95% CI, 0.83–1.11) at 7.1 years' mean follow-up compared with the RA. The risk of perioperative MI (OR, 0.32; 95% CI, 0.03–3.13) and perioperative stroke (OR, 0.87; 95% CI, 0.45–1.68) were similar between the 2 arterial grafts. There was a significantly higher risk of DSWI (OR, 2.22; 95% CI, 1.09–4.54) and operative mortality (OR, 1.76, 95% CI, 1.21–2.55) in the RITA group. When limiting the analysis to the studies where the skeletonization technique was used for ITA harvesting, no difference in DSWI between the RA and RITA groups was found (Figure S2).

A subgroup analysis for the primary outcome comparing the results of RCT versus non-RCT studies is provided in Figure S3.

Leave-one-out analysis was robust for the primary outcome in the main analysis (arterial grafts versus SV (Figure S4A). Funnel plot Egger's test intercept for the primary outcome in arterial versus venous comparison was −0.64±0.46, P=0.17 (Figure S4B).

Network Meta-Analysis

The results of the NMA are summarized in Figure and Tables S3 and S4.

The use of the SV was associated with higher late mortality (IRR, 1.23; 95% CI, 1.12–1.34) and operative mortality (OR, 1.71; 95% CI, 1.17–2.52) compared with the RA. The risk of perioperative MI (OR, 1.32; 95% CI, 0.84–2.07), perioperative stroke (OR, 1.30; 95% CI, 0.90–1.88), and DSWI (OR, 0.98; 95% CI, 0.67–1.46) was not statistically different when compared with the RA.

The use of the SV was associated with higher late mortality (IRR, 1.26; 95% CI, 1.17–1.35), operative mortality (OR, 1.45; 95% CI, 1.14–1.84), and perioperative MI (OR, 1.30; 95% CI, 1.06–1.61) compared with the RITA. The risk of perioperative stroke (OR, 1.24; 95% CI, 0.93–1.64) was not statistically different, and the risk of DSWI (OR, 0.71; 95% CI, 0.55–0.91) was lower with the SV compared with the RITA.

The use of the RITA was associated with similar late mortality (IRR, 0.98; 95% CI, 0.89–1.07) and perioperative MI (OR, 1.01; 95% CI, 0.62–1.65) compared with the RA. There was a trend toward higher risk of DSWI in the RITA group (OR, 1.39; 95% CI, 0.92–2.1), while operative mortality and stroke were similar for the 2 arteries.

At network meta-regression, mean age, percentage of female, percentage of patients with diabetes mellitus, and mean preoperative ejection fraction were not found to significantly modify the treatment effect (Figure S5).

Discussion

The balance between possible better long-term clinical and angiographic outcomes of arterial grafts and the potential risk of harvesting site complications and the increased technical complexity associated with their use has been the center of a continuous debate over the past 25 years.[66] Also, the relative

Table 2. Patient Demographics and Surgical Details

Author/ Year	Total Number			Age, y (Mean±SD)			Sex (Female) N (%)			Ejection Fraction (Mean±SD)			COPD N (%)			Diabetes Mellitus N (%)			RA Target Vessel Stenosis (%)	OPCAB/ ONCAB Details
	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA		
RA vs SV studies																				
Benedetto 2013[31]	809	809	···	64±10	65±10	···	178 (22)	157 (19.4)	···	NR	NR	···	83 (10.3)	92 (11.4)	···	82 (10.1)	98 (12.1)	···	NR	OPCAB: RA, 27.8% SV, 25.5%
Cohen 2001[37]	478	956	···	60.7±8.8	61.2±8.7	···	76 (15.9)	152 (15.9)	···	NR	NR	···	40 (4.2)	23 (4.8)	···	160 (33.5)	238 (24.9)	···	NR	NR
Goldman 2011[39]	366	367	···	61±8	62±8	···	1 (1)	5 (1)	···	NR	NR	···	NR	NR	···	154 (42)	153 (42)	···	>70	OPCAB: RA, 11% SV, 13%
Lin 2013[47]	260	260	···	70.6±8.7	70.6±8.7	···	79 (30.4)	77 (29.4)	···	NR	NR	···	39 (15.0)	33 (12.7)	···	101 (38.8)	91 (33.5)	···	NR	OPCAB: RA, 16.5% SV, 18.1%
Petrovic 2015[53]	100	100	···	56.3±6.1	57.1±6.5	···	27 (27)	27 (27)	···	48.8±10.7	48.0±10.8	···	8 (8)	9 (9)	···	39 (39)	43 (43)	···	>80	NR
Santarpino 2010[57]	150	180	···	72.19±9.9	70.52±9.586	···	20 (11.1)	49 (27.2)	···	53.5±9.92	49.2±10.7	···	27 (18)	24 (13.3)	···	49 (27.2)	36 (24)	···	>80	OPCAB: RA, 28.9% SV, 24%
Tranbaugh 2010[61]	862	862	···	60.8±8.1	60.8±9.2	···	203 (23.5)	185 (22.5)	···	48.3±11.8	47.7±13.2	···	173 (20.1)	187 (21.7)	···	314 (36.4)	332 (38.3)	···	>70	OPCAB: SV, 4.1% RA, 1.3%
Yoshida 2017[64]	91	91	···	64±8.8	64.7±9.7	···	21 (23.1%)	22 (24.2%)	···	NR	NR	···	NR	NR	···	35 (38.5)	38 (41.8)	···	87.2± 13.2%	OPCAB: RA, 30.9% SV: 26.1%
Zacharias 2004[65]	925	925	···	63±10	63±10	···	268 (28.1)	271 (28.5)	···	49±10	49±10	···	174 (18.3)	177 (18.6)	···	326 (34.2)	327 (34.3)	···	From <70 to >90	NR
RITA vs SV studies																				
Benedetto 2014[32]	···	750	750	···	NR (Ranges)	NR (Ranges)	···	(21.2)	(10.8)	···	<50% in 22.1%	<50% in 13.2%	···	10.6	7.7	···	31.5	15.9	···	OPCAB: RITA, 71.7% SV, 72.5%
Buxton 1998[34]	···	1557	1269	···	64.9±9	58.6±9	···	(22)	(10.6)	···	<50% in 24.2%	<50% in 4.9%	···	NR	NR	···	19.9	6.8	···	NR
Calafiore 2004[35]	···	570	570	···	60.8±9.0	60.7±8.3	···	(17.5)	(19.3)	···	59.3±13.8	59.4±13.1	···	3	2.8	···	24.2	24.2	···	OPCAB: RITA, 32.5% SV, 24.2%
Carrier 2009[36]	···	5420	1235	···	68±8	61±9	···	29	16	···	NR	NR	···	NR	NR	···	31	21	···	NR
Dewar 1995[38]	···	765	377	···	NR	NR	···	16.6	15.4	···	NR	NR	···	NR	NR	···	19.3	17.7	···	NR
Grau 2015[41]	···	1006	1006	···	62±9	60±9	···	12.1	10.4	···	50±12	51±11	···	5.9	5.1	···	13.3	11	···	OPCAB: RITA, 49.2% SV 49.2%
Ioannidis 2001[43]	···	830	867	···	65.2 (9.8)	62.0±10.3	···	37.3	22.6	···	42.0 (13.1)	46.5±13.7	···	19.3	13	···	38.4	25.6	···	All ONCAB
Kurlansky 2010[45]	···	2369	2215	···	67.5±9.4	62.9±10.0	···	25.7	14.9	···	CAT	CAT	···	NR	NR	···	27.3	20.8	···	All ONCAB
LaPar 2015[46]	···	1333	1333	···	59±10	56±10	···	18.7	14.3	···	55 (50–60)	55 (50–60)	···	11.4	10.7	···	34.9	18.2	···	NR
Lytle 2004[49]	···	1152	1152	···	57.8±8.3	57.5±8.1	···	14	12	···	NR	NR	···	NR	NR	···	12	12	···	NR
Navia 2016[51]	···	485	485	···	NR	63.7±9.1	···	NR	9.8	···	NR	NR	···	NR	4.2	···	NR	25.9	···	ONCAB: RITA, 0.4% SV, 61%

Continued

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Table 2. Continued

Author/ Year	Total Number			Age, y (Mean±SD)			Sex (Female) N (%)			Ejection Fraction (Mean±SD)			COPD N (%)			Diabetes Mellitus N (%)			RA Target Vessel Stenosis (%)	OPCAB/ ONCAB Details
	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA	RA	SV	RITA		
Parsa 2013[52]	···	16 881	728	···	64 (median)	59 (median)	···	28.5	19.8	···	52% (median)	51% (median)	···	8.2	3.9	···	29.9	14.7	···	NR
Pusca 2008[54]	···	10 212	599	···	62.9 (10.7)	58.0±0.34	···	2810 (27.5)	17.4	···	50.1 (12.7)	51.6±11.4	···	1564 (15.3) 7	12	···	3725 (36.5)	25.2	···	OPCAB: SV, 39% RITA, 90%
Rosenblum 2016[55]	···	306	306	···	63.8±10.6	59.0±10.1	···	28.7	15.5	···	51.7±12.4	52.2±11.0	···	6.3	1.8	···	43.8	27.6	···	ONCAB: SV, 33.7% RITA: 18.8%
Stevens 2004[59]	···	2547	1835	···	63±9	57±9	···	25	12	···	NR	NR	···	6	4	···	18	12	···	NR
Tarelli 2001[60]	···	150	150	···	59.3±8.3	56.5±8.2	···	17.3	7.3	···	54.5±13.5	57.2±13.6	···	NR	NR	···	24.7	11.3	···	NR (presumably all ONCAB)
RA vs RITA studies																				
Benedetto 2017[33]	764	···	764	58±8	···	57±9	53 (6.9)		54 (7.1)	CAT	···	CAT	36 4.7	···	38 5.0	49 (6.5)	···	39 (5.1)	>75	OPCAB: RA, 69% RITA, 44.9%
Hayward 2013 (RAPCO)[42]	198	···	196	59.2 (37.9–71.0)	···	59.5 (36.2–70.9)	23 (12)	···	18 (9)	NR	···	NR	NR	···	NR	22 (11%)	···	20 (10%)	>70	All ONCAB
Ruttman 2011[56]	277	···	277	57.8±9.0	···	56.6±9.6	28 (10.1)	···	28 (10.1)	52.9±12.1	···	54.9±10.8	92 (33.2)	···	92 (33.2)	62 (22.4)	···	59 (21.3)	NR	NR
Tsuneyoshi 2015[63]	118	···	118	67.9±10	···	68.3±8	30 (25)	···	22 (19)	CAT	···	CAT	2 (1.6)	···	2 (1.6)	53 (45)	···	63 (53)	"Severe"	All OPCAB
RA vs SV vs RITA studies																				
Goldstone 2018[40]	4268	5813	1574	62.1±10.5	62.5±10.4	61.7±10.3	614 (14.5)	916 (15.8)	229 (14.3)	55.5±12.0	55.6±12.0	56.1±12.0	629 (14.8)	856 (14.7)	250 (15.6)	1525 (35.7)	2066 (35.5)	528 (33.7)	NR	NR
Janiec 2017[44]	1036	46 343	862	64.5 (9.7)	66.4 (8.4)	63.9 (9.0)	277 (26.7%)	8879 (19.2%)	146 (16.9%)	CAT	CAT	CAT	39 (5.7%)	2551 (6.9%)	59 (7.7%)	212 (20.7%)	11 077 (24.3%)	206 (24.0%)	NR	OPCAB: SV, 2.4% RA, 2.4% RITA 6.7%
Locker 2013[48]	169	1153 (Matched)	589	NR	59±10	NR	NR	187 (16.2)	NR	NR	58±13	NR	NR	86 (7.5)	NR	NR	221 (19.2)	NR	NR	OPCAB: SV, 4.4% MultArt, 3.3%
Nasso 2009[50]	202	202	201	70.5±3.1	69.7±3.5	69.2±3.9	87 (43.1)	84 (41.6)	88 (43.8)	CAT		CAT	57 (28.2)	56 (27.7)	55 (27.4)	73 (36.1)	77 (38.1)	76 (37.8)	>70	All ONCAB
Schwann 2016[58]	551	551	551	58.4±10.2	60.6±10.3	59.5±9.7	72 (13)	97 (18)	77 (14)	52±10	54±10	53±11	46 (8.3)	39 (7.1)	41 (7.4)	100 (18)	94 (17)	93 (17)	>75	ONCAB: RITA, 98% RA, 96% SV, 95%
Tranbaugh 2010[61]	4577	7073	1674	60.3±9.7	67.4±9.9	64.9±10.3	1033 (22.6)	2448 (34.6)	460 (27.5)	49.1±10.9	47.2±12.9	46.4±14.3	781 (17.1)	1804 (25.5)	149 (8.9)	702 (37.2)	2704 (38.2)	597 (35.7)	LCX:>70 RCA:>90	OPCAB: SV, 3.5% RA, 3.0% RITA, 1.4%

CAT indicates reported as categories; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; EF, ejection fraction; LCX, left circumflex artery territory; MultiArt, multiple arterial grafting group; NR, not reported; ONCAB, on-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; RA, radial artery; RCA, right coronary artery territory; RITA, right internal thoracic artery; SV, saphenous vein.

Table 3. Outcomes Summary of the Pairwise Meta-Analysis

Model	Studies*	Point Estimate†	95% CI	Overall Effect (Z-Value, *P* Value)	Heterogeneity (I^2, *P* Value)	Tau^2	Interpretation
Long term mortality							
RA/SV	11	0.81	0.73 to 0.90	···	47, 0.04	0.0110	Better in RA
RITA/SV	17	0.80	0.73 to 0.86	···	73, <0.01	0.0136	Better in RITA
RITA/RA	9	0.96	0.83 to 1.11	···	57, 0.02	0.0204	ND
ART/SV	28	0.80	0.75 to 0.85	−6.93, <0.0001	66, <0.01	0.0115	Better in ART
Perioperative DSWI							
RA/SV	8	1.10	0.80 to 1.51	···	0, 0.48	0	ND
RITA/SV	14	1.33	1.04 to 1.69	···	24, 0.20	0.0463	Higher in RITA
RITA/RA	6	2.22	1.09 to 4.54	···	40, 0.14	0.2795	Higher in RITA
ART/SV	21	1.27	1.05 to 1.54	2.41, 0.0159	14, 0.27	0.0264	Higher in ART
Perioperative mortality							
RA/SV	7	0.66	0.46 to 0.95	−2.27, 0.0234	29, 0.21	0.0599	Better in RA
RITA/SV	17	0.68	0.53 to 0.87	−3.11, 0.0019	56,	0.1327	Better in RITA
RITA/RA	7	1.76	1.21 to 2.55	2.98, 0.0029	11.7, 0.34	0.0310	Better in RA
ART/SV	24	0.68	0.55 to 0.83	−3.79, 0.0002	49.1, 0.004	0.1043	Better in ART
Perioperative stroke							
RA/SV	7	0.73	0.54 to 1.00	···	0, 0.72	0	Better in RA
RITA/SV	11	0.85	0.62 to 1.16	···	36, 0.11	0.0875	ND
RITA/RA	5	0.87	0.45 to 1.68	···	29, 0.23	0.1653	ND
ART/SV	18	0.80	0.65 to 0.98	−2.11, 0.0350	14, 0.29	0.0266	Better in arterial
Perioperative MI							
RA/SV	7	0.67	0.42 to 1.07	···	0, 0.56	0	ND
RITA/SV	8	0.79	0.65 to 0.96	···	0, 0.65	0	Better in RITA
RITA/RA	2	0.32	0.03 to 3.13	···	61.1, 0.11	1.67	ND
ART/SV	15	0.77	0.64 to 0.92	−2.82, 0.0048	0, 0.73	0	Better in ART

ART indicates all arterial grafts; DSWI, deep sternal wound infections; MI, myocardial infarction; ND, no difference; RA, radial artery; RITA, right internal thoracic artery; SV, saphenous vein.
*Articles reporting the outcomes in RA, RITA, and SV cohorts were included as 3 studies (RA/SV, RITA/SV, and RITA/RA).
†Incidence rate ratio was used for long-term mortality, while odds ratio was used for operative mortality and perioperative outcomes.

efficacy of the RITA and RA as the second arterial grafts remains controversial.[7]

Several pairwise meta-analyses on the topic have been published previously.[1,67,68] However, pairwise meta-analyses have known limitations in terms of heterogeneity of the included studies and potential for treatment allocation bias. NMAs have been proposed to overcome the limitations of the pairwise comparison, especially when summarizing the evidence of RCTs and observational studies.[9,69] It has been suggested that NMA can be superior to classical pairwise analyses, especially in case of comparison of a new treatment to a standard one.[70]

This is the first NMA specifically addressing the differences in clinical outcomes according to the type of second graft used for CABG. The only published network meta-analysis on the subject focused only on the patency rates of conduits and did not include clinical outcomes.[10] Due to the demonstrated absence of a consistent correlation between angiographic failure and clinical events,[11] a deeper understanding of the clinical impact of the type of second conduit used for CABG seems of major relevance.

The results of our study support the superiority of the use of a second arterial over venous graft, and suggest the equivalence in long-term and perioperative outcomes between the RITA and RA.

The superior midterm patency rate of arterial grafts (especially the RA) has been convincingly demonstrated in RCTs and observational studies.[50,71–74] A large amount of observational evidence also suggests a clinical benefit in terms of survival and event-free survival for the use of the RA

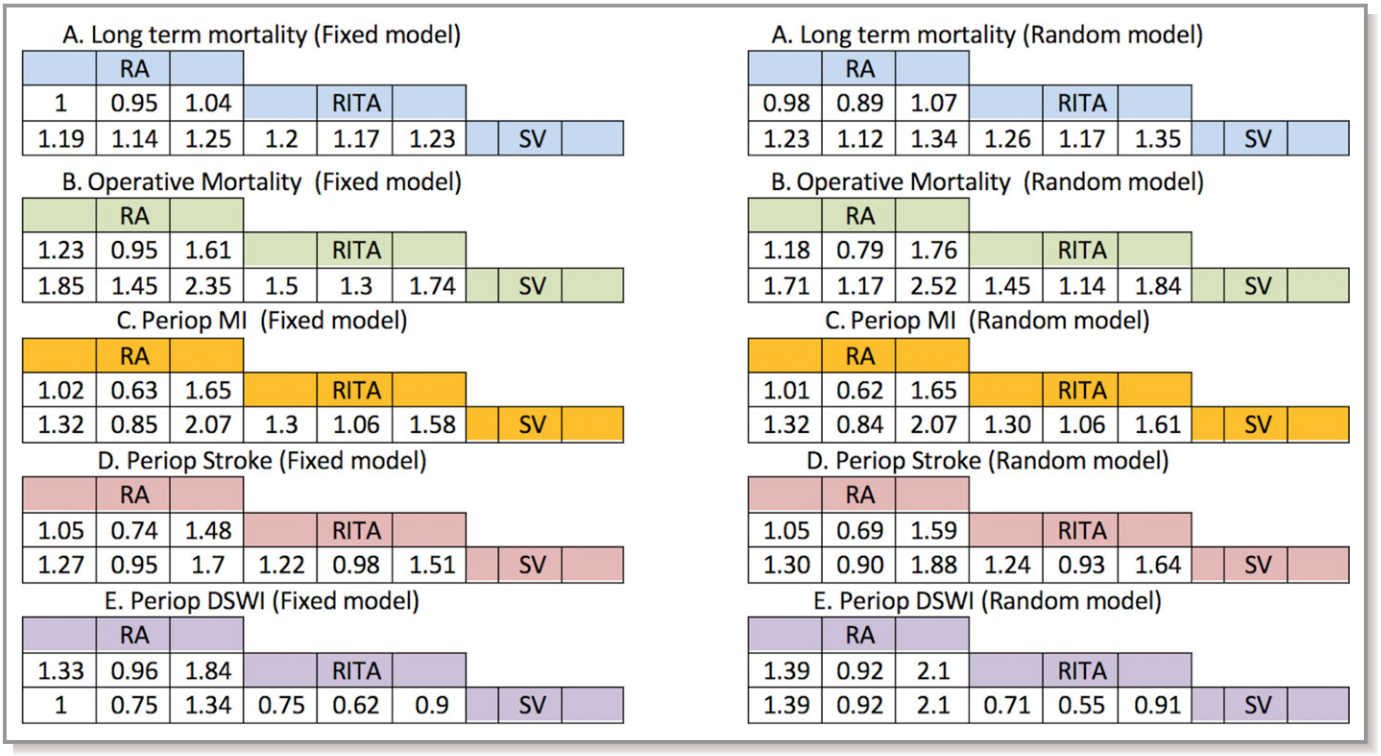

Figure. Full network meta-analytic estimates (expressed as incidence rate ratio [IRR] and odds ratio [OR] with 95% credible interval) for the different outcomes using random and fixed models respectively. **A**, Long-term mortality (SV is associated with higher long-term mortality compared with RA; IRR=1.23, 95%CI=1.12–1.34; τ^2=0.0127; I^2=64%); **B**, Operative mortality (SV is associated with higher operative mortality compared with RA expressed as OR, 1.71; 95% CI. 1.17–2.52; τ^2=0.1219; I^2=48.7%); **C**, Perioperative MI (SV is associated with similar perioperative MI compared with RA expressed as OR=1.32, 95%CI=0.84–2.07; τ^2=0.0041; I^2=2.1%); **D**, Perioperative stroke (SV is associated with similar perioperative stroke compared with RA expressed as OR=1.30, 95%CI=0.90–1.88; τ^2=0.0573; I^2=22%); **E**, Perioperative DSWI (SV is associated with similar perioperative DSWI compared with RA expressed as OR=0.98, 95%CI=0.67–1.46; τ^2=0.0671; I^2=25.4%I). DSWI indicates deep sternal wound infections; MI, myocardial infarction; RA, radial artery; RITA, right internal thoracic artery; SV, saphenous vein.

or the RITA instead of the SV as the second graft.[1,7,75,76] However, we have recently shown how unmatched confounders are present even in the best comparative observational studies and suggested that a treatment allocation bias may be responsible for the better clinical outcome of patients receiving more than 1 arterial graft.[6]

This type of bias is potentially present even in the present meta-analysis, but the additional power and precision of NMA in defining relations and interactions between treatments from the aggregated estimates of all the available evidence should permit a more efficient comparison among different strategies.[9]

Our results are in line with those of a recent patient-level meta-analysis on the comparison between the RA and the SV.[76] However, at first sight, our results appear to contradict the overall neutral findings of the ART (Arterial Revascularization Trial), where on the primary intention-to-treat analysis, there was no difference in survival between single and bilateral ITA grafts at 10 years (in press). However, 40% of patients in the ART received a different treatment from that initially proposed and an as-treated analysis showed a significant survival benefit in patients receiving >1 arterial graft, consistent with the results of the current study. Difference in sample size and length of follow-up and the fact that in observational studies the revascularization strategy is based on surgical judgment and not mandated by protocol are possible explanations for these apparent contradictions.

A key finding of this study is the demonstration of equivalence between the RITA and RA with respect to all the short- and long-term clinical outcomes. Of note, in our analysis, the relative survival benefit of the RITA and RA compared with the SV were identical (SV versus RITA and RA, IRR, 1.26; 95% CI, 1.17–1.35). Although there was a trend toward higher risk of DSWI with RITA, this risk became nonsignificant in a subgroup analysis of studies where the skeletonization of ITA was employed. This finding is in accordance with what was reported by previous meta-analyses[7] and by a post hoc analysis of the ART.[77]

The literature on the comparison between the RITA and RA is discordant. We previously published a pairwise meta-analysis of the propensity-matched studies comparing the 2

arterial grafts and found that the use of the RITA was associated with a 25% relative reduction in the risk of long-term mortality.[7] The reason underlying the discrepancy between our previous meta-analysis and the present findings is probably related to the different sample size (149 902 patients with 6.9 years of follow-up for the present analysis versus 15 374 patients and a range of 45–168 months of follow-up for the previous pairwise comparison). Also, our previous analysis did not include 2 recent large studies comparing the 2 arterial grafts.[33,78] Finally, the use of NMA and direct/indirect comparisons allow for better precision around estimates compared with pairwise comparisons.

Of note, in a large study the Society of Thoracic Surgeons National Database of >1.4 million patients, Schwann et al[8] showed significantly higher perioperative mortality and risk of DSWI using the RITA, but not the RA, versus the SV as the second graft—findings that were also demonstrated in the present study. The authors also described a significant volume-to-outcome relation for the use of the RITA but not of the RA. Similarly, in a meta-analysis of 34 bilateral internal thoracic artery (BITA) series and 27 000 BITA patients, we recently identified a highly significant BITA use-to-outcome relationship for long-term survival and incidence of DSWI that was independent from the well-known CABG volume/outcome effect.[78] These findings suggest that BITA grafting may be more technically demanding than the use of the single internal thoracic artery and that a volume/outcome relation can explain the marginally increased operative risk in the RITA arm.

A key point when using the RA for CABG is the degree of target vessel stenosis. It has been shown that the patency rate of RA grafts is strongly influenced by the degree of target coronary stenosis.[79–81] In fact, a target vessel stenosis >70% was a common criterion for using the RA in the studies included in this meta-analysis (Table 2).

This study shares the usual limitations of meta-analyses of observational studies.[82] Despite statistical adjustment and the use of NMA, between-studies heterogeneity remains a source of bias. Important details such as the etiology of follow-up of death, the protocols used to reduce the risk of DSWI (with the exception of skeletonization of the ITA), and the incidence of repeat revascularization were not systematically retrievable and could not be included in our analyses.

Additionally, we recognize that despite including only adjusted studies, the presence of unmeasured confounders and treatment allocation biases cannot be excluded.[6] However, the NMA approach utilized and the low-moderate-grade heterogeneity found across the studies should have attenuated these biases.

In conclusion, in an NMA of adjusted observational and randomized studies comparing the RA, the RITA, and the SV as the second conduit for CABG, we found that the use of the RITA or the RA was associated with a similar long-term clinical benefit compared with the use of the SV. No differences in late and operative mortality and postoperative complications was found between the 2 arterial conduits, although DSWI remains a concern after BITA grafting if skeletonization is not used.

Disclosures

None.

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Supplemental Material

Table S1. Search strategy.

Ovid MEDLINE® (Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® - 1946 to Present); Searched on 02/22/2018	
Line #	**Search term**
1	Coronary Artery Bypass/
2	(aorta adj2 bypass).tw.
3	CABG.tw.
4	(aortic coronary bypass or aorticocoronary anastomosis).tw.
5	(aorto coronary adj2 (bypass or graft)).tw.
6	(aortocoronary adj2 (anastomosis or bypass or shunt or graft)).tw.
7	(coronary adj2 (bypass or graft)).tw.
8	(Total arterial revascularization or total arterial revascularisation or Multiple arterial revascularization or multiple arterial revascularisation).tw.
9	or/1-8
10	Radial Artery/
11	(radial arter* or arteria radialis or radialis artery).tw.
12	10 or 11
13	Saphenous Vein/
14	(Saphenous Vein* or SVG or saphena vein or saphenous venos system or vena saphena).tw.
15	13 or 14
16	Internal Mammary-Coronary Artery Anastomosis/
17	(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).tw.
18	(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.
19	16 or 17 or 18
20	9 and (12 or 15 or 19)

21	((second or 2nd) adj3 (conduit* or graft*)).tw.
22	(multi-vessel* or multivessel* or multiple vessel* or multi-vein* or multiple vein* or multi-arter* or multiple arter*).tw.
23	21 or 22
24	20 and 23
25	limit 24 to English language

Table S2. Newcastle-Ottawa scale for the included studies.

Author / Year	Selection	Comparability	Outcome/Exposure	Total
Benedetto 2013[1]	****	**	***	*********
Benedetto 2014[2]	****	**	***	*********
Benedetto 2017[3]	****	**	***	*********
Buxton 1998[4]	****	**	**	********
Calafiore 2004[5]	****	**	***	*********
Carrier 2009[6]	****	**	***	*********
Cohen 2001[7]	****	**	*	*******
Dewar 1995[8]	****	**	**	********
Goldman 2011[9]	****	**	*	*******
Goldstone 2017[10]	****	**	***	*********
Grau 2015[11]	****	**	***	*********
Hayward 2013 (RAPCO)[12]	****	**	***	*********
Ioannidis 2001[13]	****	**	*	*******
Janiec 2017[14]	****	**	***	*********
Kurlansky 2010[15]	****	**	***	*********
LaPar 2015[16]	****	**	*	*******
Lin 2013[17]	****	**	***	*********
Locker 2013[18]	****	*	***	********
Lytle 2004[19]	****	**	***	*********
Nasso 2009[20]	****	**	*	*******
Navia 2016[21]	****	**	***	*********
Parsa 2013[22]	****	**	***	********
Petrovic 2015[23]	****	**	***	********
Pusca 2008[24]	****	**	***	*********
Rosenblum 2016[25]	****	**	***	********
Ruttman 2011[26]	****	**	**	********
Santarpino 2010[27]	****	**	***	********
Schwann 2016[28]	****	**	***	*********
Stevens 2004[29]	****	**	***	********

Tarelli 2001[30]	****	**	***	********
Tranbaugh 2010[31]	****	**	***	*********
Tranbaugh 2017[32]	****	**	***	*********
Tsuneyoshi 2015[33]	****	**	***	*********
Yoshida 2017[34]	****	**	***	*********
Zacharias 2004[35]	****	**	**	********

Table S3. Comparison of direct and indirect estimates to assess inconsistency within network loops for the outcomes.

Long term mortality

Fixed effect model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
RA:RITA	9	0.47	0.00	-0.01	0.02	-0.03	-0.57	0.5712
RA:SV	11	0.62	-0.18	-0.17	-0.19	0.03	0.57	0.5712
RITA :SV	17	0.91	-0.18	-0.18	-0.16	-0.03	-0.57	0.5712

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
RA:RITA	9	0.53	0.02	0.03	0.02	0.01	0.11	0.9113
RA:SV	11	0.65	-0.21	-0.21	-0.20	-0.01	-0.11	0.9113
RITA :SV	17	0.82	-0.23	-0.23	-0.24	0.01	0.11	0.9113

Perioperative mortality

Fixed effect model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
RA:RITA	7	0.67	-0.21	-0.61	0.61	-1.22	-4.23	< 0.0001
RA:SV	7	0.91	-0.61	-0.51	-1.73	1.22	2.78	0.0054
RITA :SV	17	0.98	-0.40	-0.41	-0.11	-0.30	-0.50	0.6182

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
RA:RITA	7	0.72	-0.17	-0.50	0.68	-1.18	-2.59	0.0095
RA:SV	7	0.82	-0.54	-0.36	-1.34	0.97	1.90	0.0575
RITA :SV	17	0.97	-0.37	-0.39	0.51	-0.90	-1.16	0.2459

Perioperative MI

Fixed effect model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
RA:RITA	2	0.11	-0.02	1.12	-0.17	1.29	1.66	0.0963
RA:SV	7	0.90	-0.28	-0.40	0.88	-1.29	-1.66	0.0963
RITA :SV	8	0.98	-0.26	-0.24	-1.52	1.29	1.66	0.0963

Random effects model:

comparison	k	prop	nma	direct	indir.	Diff	z	p-value
RA:RITA	2	0.12	-0.01	1.12	-0.16	1.28	1.65	0.0990
RA:SV	7	0.90	-0.28	-0.40	0.88	-1.28	-1.65	0.0990
RITA :SV	8	0.98	-0.27	-0.24	-1.52	1.28	1.65	0.0990

Perioperative Stroke	Fixed effect model: comparison k prop nma direct indir. Diff z p-value RA:RITA 5 0.59 -0.05 -0.01 -0.09 0.08 0.22 0.8248 RA:SV 7 0.91 -0.24 -0.31 0.45 -0.75 -1.44 0.1489 SV:RITA 11 0.96 0.20 0.17 0.78 -0.61 -1.15 0.2519 Random effects model: comparison k prop nma direct indir. Diff z p-value RA:RITA 5 0.59 -0.05 0.06 -0.20 0.26 0.60 0.5485 RA:SV 7 0.87 -0.26 -0.34 0.26 -0.60 -1.09 0.2775 SV:RITA 11 0.94 0.21 0.17 0.95 -0.78 -1.25 0.2117
Perioperative DSWI	Fixed effect model: comparison k prop nma direct indir. Diff z p-value RA:RITA 6 0.63 -0.29 -0.54 0.15 -0.69 -2.00 0.0455 RA:SV 8 0.86 0.00 0.09 -0.54 0.63 1.49 0.1373 SV:RITA 14 0.95 -0.29 -0.26 -0.79 0.54 1.28 0.2001 Random effects model: comparison k prop nma direct indir. Diff z p-value RA:RITA 6 0.62 -0.33 -0.63 0.15 -0.77 -1.80 0.0726 RA:SV 8 0.79 0.02 0.18 -0.60 0.78 1.59 0.1124 SV:RITA 14 0.94 -0.35 -0.29 -1.19 0.89 1.65 0.0987

k - Number of studies providing direct evidence
prop - Direct evidence proportion
nma - Estimated treatment effect (logIRR or log OR) in network meta-analysis
direct - Estimated treatment effect (logIRR or log OR) derived from direct evidence
indir. - Estimated treatment effect (logIRR or log OR) derived from indirect evidence
Diff - Difference between direct and indirect treatment estimates
z - z-value of test for disagreement (direct versus indirect)
p-value - p-value of test for disagreement (direct versus indirect)

RA, radial artery; RITA, right internal artery; SV, saphenous vein.

Table S4. Rank scores with probability rank of different graft groups with the greatest reduction in outcomes within the different treatment groups (RITA, RA and SV) where the closer to one equates to the probability the therapy leads to the greatest reduction.

Long term mortality	P-score (fixed)	P-score (random)
	RITA 0.7875	0.8466
	RA 0.7125	0.6534
	SV 0.0000	0.0000
Perioperative mortality	P-score (fixed)	P-score (random)
	RA 0.9699	0.8967
	RITA 0.5301	0.6012
	SV 0.0000	0.0021
Perioperative MI	P-score (fixed)	P-score (random)
	RITA 0.7293	0.7361
	RA 0.7143	0.7052
	SV 0.0564	0.0587
Perioperative stroke	P-score (fixed)	P-score (random)
	RA 0.7746	0.7532
	RITA 0.6797	0.6704
	SV 0.0457	0.0764
Perioperative DSWI	P-score (fixed)	P-score (random)
	SV 0.7522	0.7638
	RA 0.7254	0.7056
	RITA 0.0224	0.0306

RA, radial artery; RITA, right internal artery; SV, saphenous vein.

Figure S1. PRISMA flow chart of study selection.

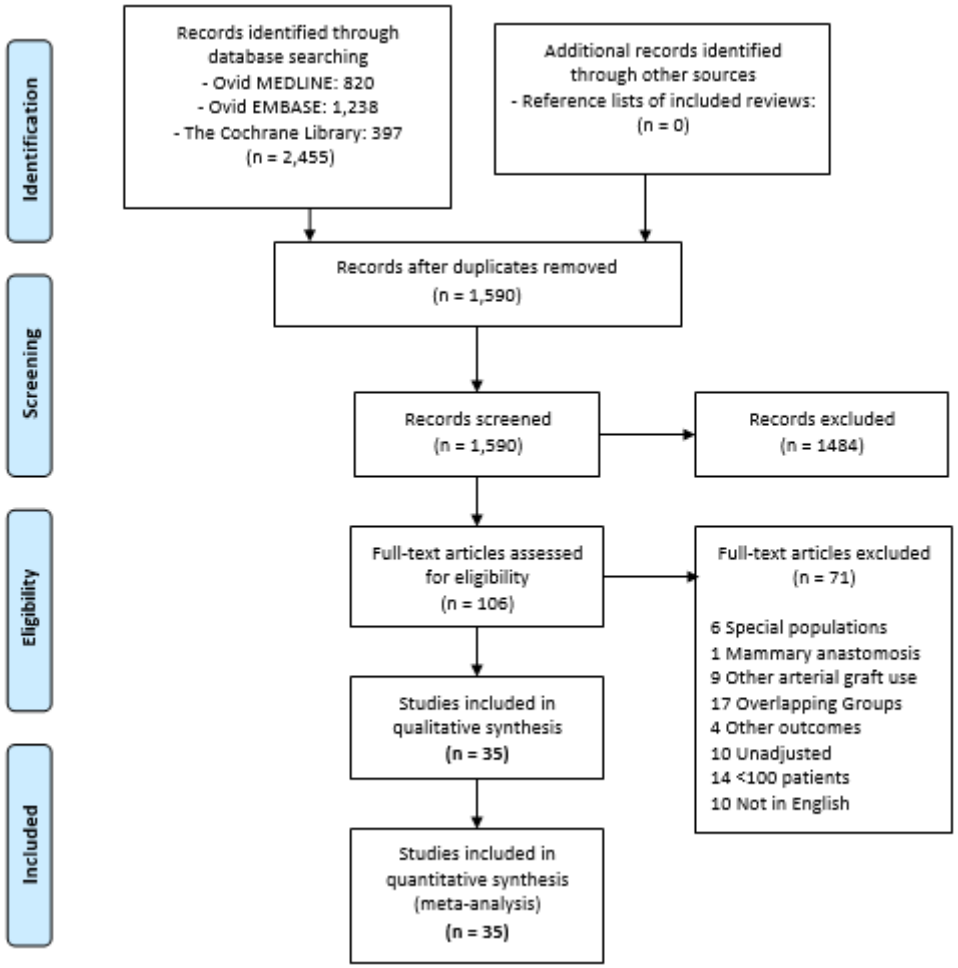


Figure S2. A: Forest plot showing subgroup differences for skeletonization on deep sternal wound infection (DSWI) in RITA vs RA/SVG pairwise comparisons (Subgroup difference P-value=0.1933); B: Forest plot showing subgroup differences for skeletonization on deep sternal wound infection (DSWI) in RITA vs SVG pairwise comparisons (Subgroup difference P-value=0.4194); C: Forest plot showing subgroup differences for skeletonization on deep sternal wound infection (DSWI) in RITA vs RA pairwise comparisons (Subgroup difference P-value=0.2786). RA, radial artery; RITA, right internal artery; SV, saphenous vein.

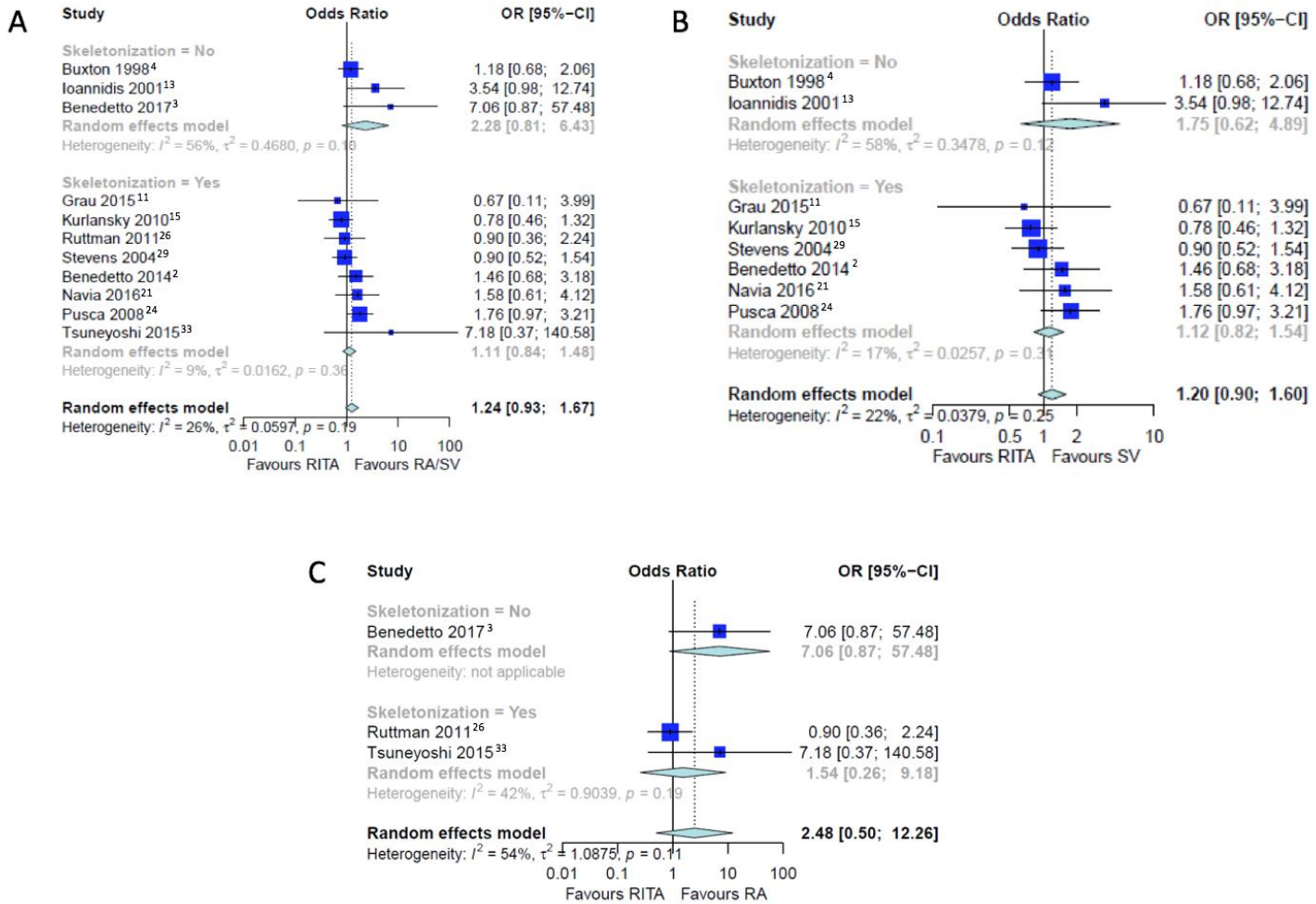


Figure S3. Long-term mortality for arterial grafts (RA/RITA) vs SV in RCT vs non-RCT trials (Subgroup difference P value=0.4897).
ART; All arterial grafts, RA; radial artery, RITA; right internal thoracic artery, SV; saphenous vein.

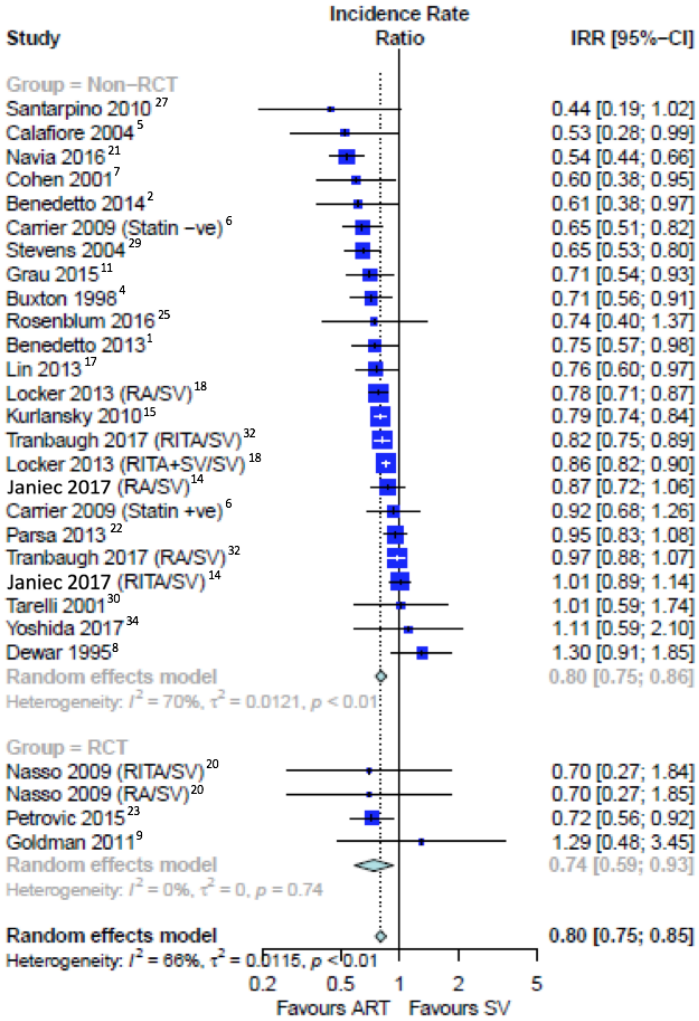


Figure S4. Leave one out (A) and Funnel plot (B) for the primary analysis. RA, radial artery; RITA, right internal artery; SV, saphenous vein.

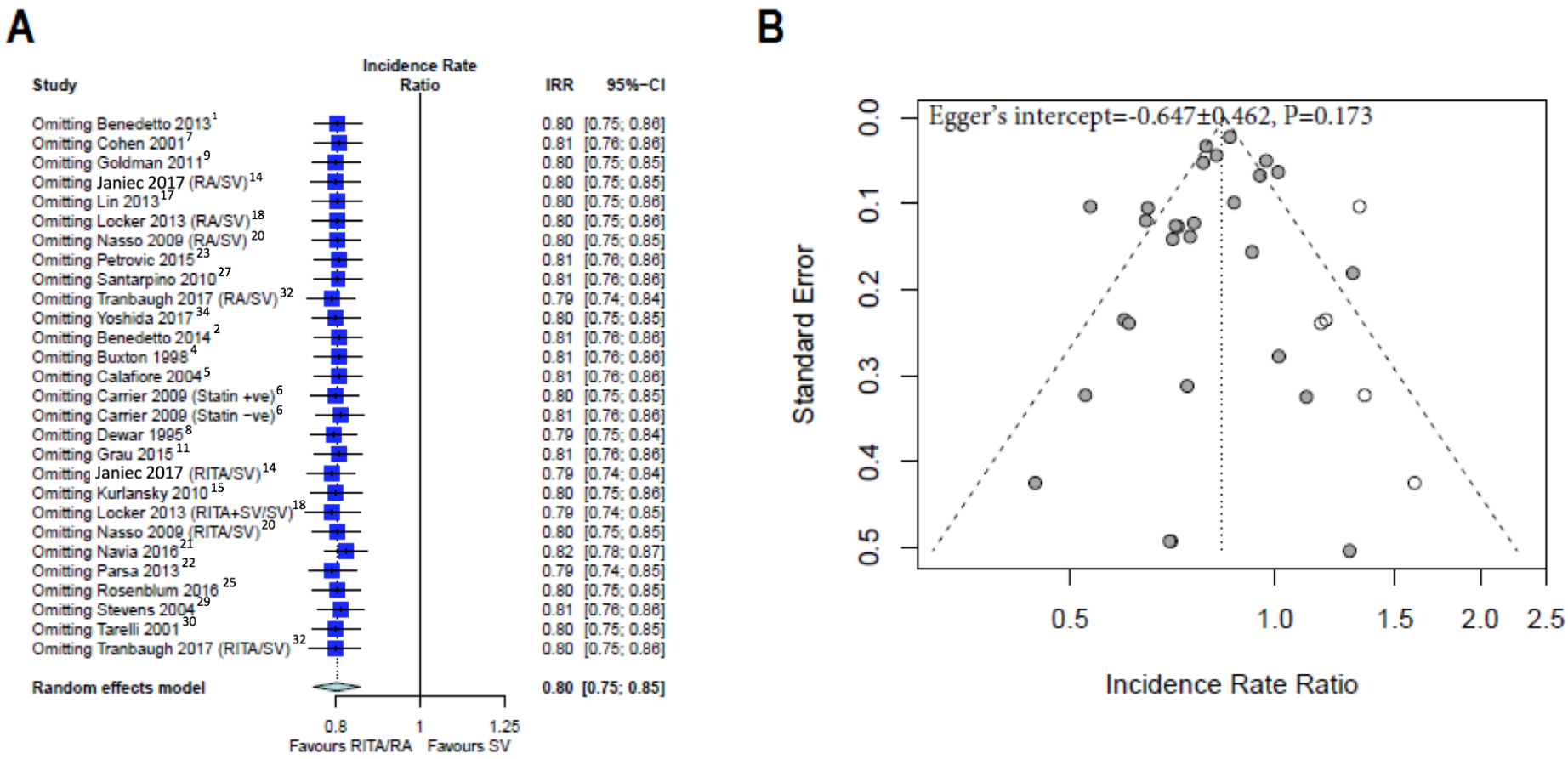
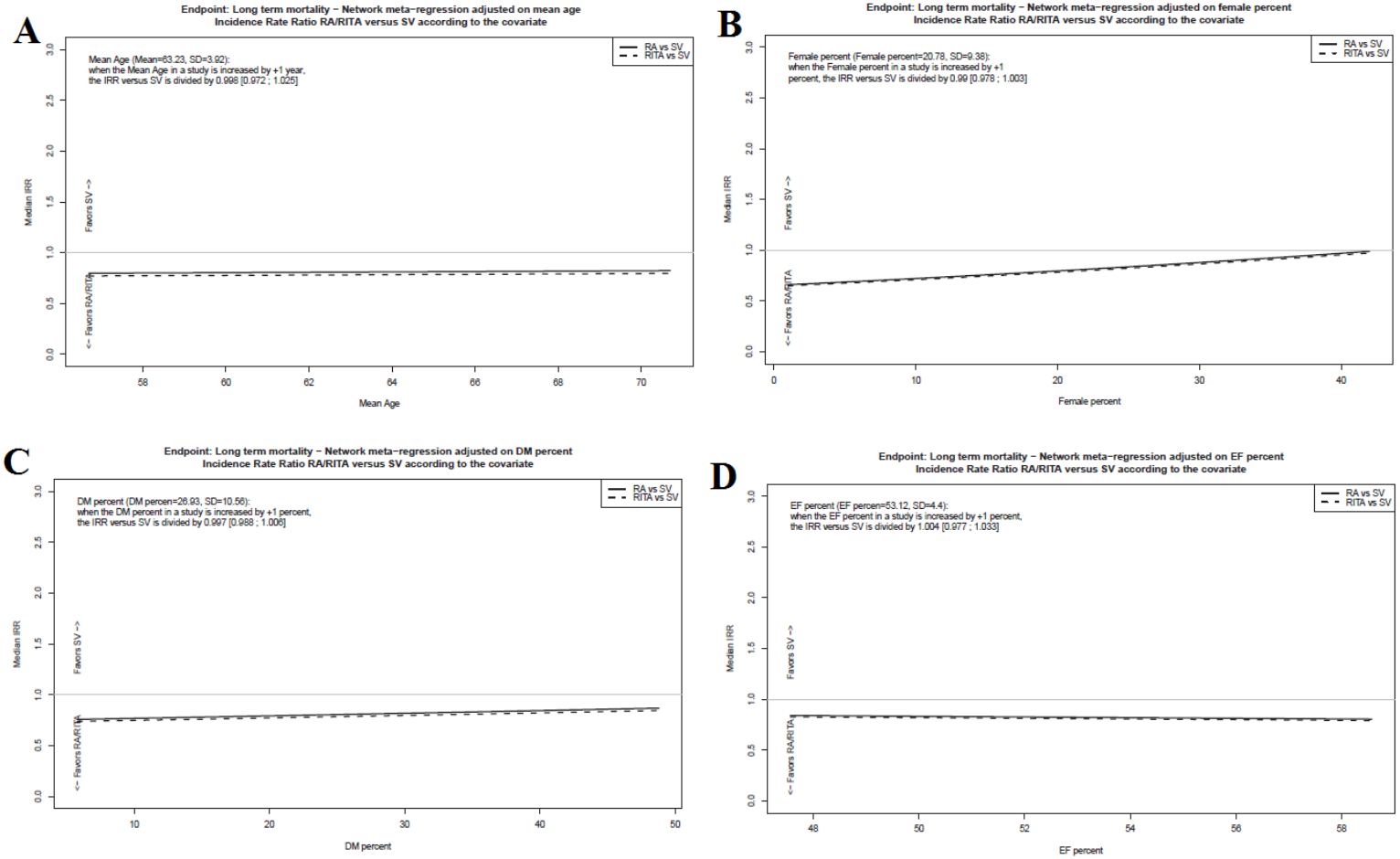


Figure S5. Network meta-regression for long term mortality. A: Mean age; B: Female percent; C: Diabetes mellitus percent; D: Ejection fraction (EF) percent.



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