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Endoscopic versus open radial artery harvesting: A meta-analysis of randomized controlled and propensity matched studies

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Abstract

Background: We sought to investigate the impact of radial artery harvesting techniques on clinical outcomes using a meta-analytic approach limited to randomized controlled trials and propensity-matched studies for clinical outcomes, in which graft patency was analyzed.

Methods: A systematic literature review was conducted using PubMed and MEDLINE to identify publications containing comparisons between endoscopic radial artery harvesting (ERAH) and open harvesting (ORAH). Only randomized controlled trials and propensity-matched series were included. Data were extracted and analyzed with RevMan. The primary endpoint was wound complication rate, while secondary endpoints were patency rate, early mortality, and long-term cardiac mortality.

Results: Six studies comprising 743 patients were included in the meta-analysis. Of them 324 (43.6%) underwent ERAH and 419 (56.4%) ORAH. ERAH was associated with a lower incidence of wound complications (odds ratio: 0.33, confidence interval 0.14-0.77; p = 0.01). There were no differences in graft patency, and early and long-term cardiac mortality between the two techniques.

Conclusion: ERAH reduces wound complications and does not affect graft patency, or short- and long-term mortality compared to ORAH.

KEYWORDS

coronary artery surgery, endoscopic radial artery harvesting, meta-analysis, patency rate, radial artery harvesting, wound complication

1 | INTRODUCTION

Endoscopic radial artery harvesting (ERAH) was recently developed in order to minimize surgical trauma and improve cosmesis.[1,2] ERAH proponents emphasize the superior cosmetic and perioperative outcomes. However, the possibility that ERAH can lead to increased endothelial damage and graft failure has been proposed.[3]

Previous meta-analyses comparing ERAH and the open harvesting (ORAH) were based on observational unmatched series and angiographic series with very low rates of angiographic reassessment.

We sought to investigate the impact of the harvesting technique on radial artery (RA) graft patency and relevant clinical outcomes using a meta-analysis limited to randomized controlled trials (RCT) and propensity-matched (PSM) studies and those angiographic series with >50% rate of angiographic reassessment. We hypothesize that ERAH is associated with a lower wound complication rate but equivalent patency rate, and early and long-term cardiac mortality compared to ORAH.

2 | MATERIALS AND METHODS

This work was designed as a systemic review and meta-analysis, with reporting following the Preferred Reporting Items for Systemic Reviews and Meta-Analysis statement (PRISMA) (Supplementary Table S1).[4,5]

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2.1 | Data sources and literature search strategy

A literature review was conducted using PubMed by two independent investigators (M.R. and M.K.) through PubMed online data sources (up to November 2016), using the search terms "endoscopic radial artery harvesting." In addition, upon identifying other meta-analyses, systematic reviews, or RCTs, references were scanned for relevant articles and pertinent reviews (ie, backward snowballing) to obtain further studies. For patency rate, we used the search terms "endoscopic radial artery harvesting, patency, outcome" in addition to backward snowballing.

2.2 | Study selection

Inclusion criteria for the clinical outcome studies were as follows: 1) RCTs or PSM; 2) comparing ERAH with ORAH in patients who underwent coronary artery bypass grafting (CABG) and included outcomes such as wound complications, patency rate, 30 days/in-hospital mortality, and long-term cardiac mortality; 3) published full text manuscript; and 4) written in English.

The inclusion criteria for studies evaluating graft patency were as follows: 1) matched, unmatched, and RCT studies comparing ERAH with ORAH in CABG patients; 2) angiographic follow-up of more than 50% of the overall patient population.

Two investigators (M.R. and M.K.) independently reviewed the search results at the title and abstract level to determine whether the study met our inclusion criteria. In case of disagreement a third investigator (M.G.) reviewed the article and an agreement was negotiated. Pertinent articles were then retrieved.

2.3 | Primary outcomes

Primary outcomes were wound complications, while secondary outcomes were patency rate, and early and long-term cardiac mortality. Patency was determined by either invasive angiography or by computer tomography angiogram.

Due to differing definitions used in each study several outcome parameters were combined. In particular, hematoma, infection, as well as motor and sensory nerve deficits (hand pain and paresthesia) were combined in the definition of wound complications and in-hospital 30-day mortality in the definition of early mortality.

2.4 | Data extraction and statistical analysis

Microsoft Office Excel 2010 (Microsoft, Redmond, WA) was used for data extraction. Data extraction of all included studies was performed independently by two investigators (M.R. and M.K.) and in case of disagreement a third investigator (M.G.) was included and an agreement was negotiated. Extracted variables for PSM studies were taken from among the matched population and for RCTs the entire cohort was used. Variables included the following: study name, publication year, study design, number of patients, interventions, age, sex, wound complications, patency rate, in-hospital 30-day mortality, and long-term cardiac mortality. Included variables for studies examining graft patency included: study name, publication year, number of patients, intervention, and graft patency.

Review Manager Version 5.3 (The Cochrane Collaboration, the Nordic Cochrane Centre and Copenhagen, Denmark) was used to perform the meta-analysis, and the estimated survival data were obtained from the Kaplan-Meier curves according to a previously described method.[6] The data can be synthesized only when the number of studies equals or exceeds two. Measurement data reported as mean ± standard deviation were adopted; odds ratios (ORs) with standard error for the PSM and RCT studies were calculated and aggregated on the log scale. Individual and pooled OR with 95% confidence intervals (CI) were calculated by means of the DerSimonian-Laird (inverse variance) method.[7] Risk difference (RD) was used as a summary estimate in case of zero event studies. Hypothesis testing for statistical homogeneity was set at the two-tailed 0.10 level and was based on the Cochran Q test, with I2 values of 25%, 50%, and 75% representing mild, moderate, and severe heterogeneity, respectively. Random-effect model was used if I2 >25%, otherwise fixed effect model was used. Publication bias was graphically assessed using the funnel plots. The subgroup analysis was performed based on the study design (whether RCT or matched). Leave one out analysis was performed by Comprehensive Meta-Analysis software, version 2 (Biostat, Englewood, NJ). The quality of the included studies was assessed by the Newcastle-Ottawa Scale.[8] Only high-quality studies, defined as those achieving seven or more stars, were included in this review.

3 | RESULTS

3.1 | Eligible studies and characteristics of studies

An outline of the systematic review process is shown in Fig. 1 and Supplementary Fig. S1, respectively. For clinical outcomes 139 studies were identified. After removal of duplicates 119 studies were screened. Thirty-three full-text articles were assessed for eligibility. Among them six studies (four RCT and two PSM studies) met the inclusion criteria.

Table 1 shows that the overall quality of the studies was high with only one study with a score of 7/9.

Of the 743 patients included 324 (43.6%) underwent ERAH and 419 (56.4%) ORAH. The characteristics of the included studies are shown in Tables 1 and 2. Average harvest time for each technique showed that ERAH was on average longer (50.9 ± 19.1 min vs 41.2 ± 1.26 min, p = 0.35).

Studies which included patency rates are shown Table 3. A total of 466 grafts were assessed by angiogram (234 in ERAH group and 232 in ORAH group) with pooled mean follow-up of 42.6 and 42.2 months in ERAH and ORAH, respectively.

3.2 | Meta-analysis of postoperative outcomes

3.2.1 | Wound complications

Overall ERAH was associated with a significantly lower risk of wound complication in comparison to ORAH (OR: 0.33, CI 0.14-0.77; p = 0.01). This difference was confirmed in the RCT studies subgroup

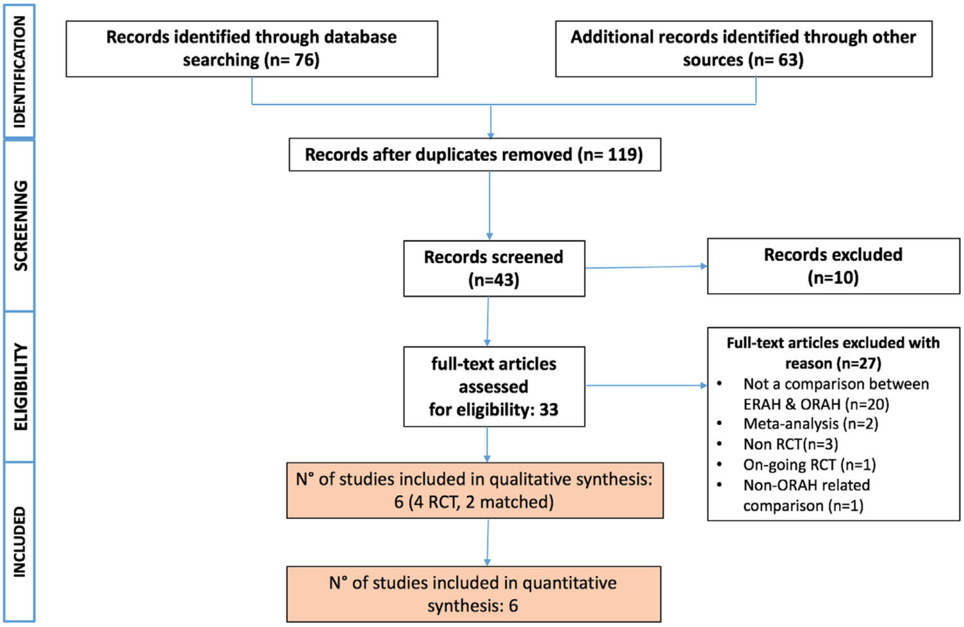

FIGURE 1 PRISMA flowchart for clinical outcomes

(OR 0.31, CI 0.11-0.92; p = 0.03), but not in the PSM studies subgroup (OR: 0.29, CI 0.04-2.12; p = 0.21, Fig. 2A). SPSS independent sample t-test was used to calculate standard deviation and p value for the mean. The mean incidence of neuro-sensory complications were 14.8% ± 18.8 in the ERAH group and 26.5% ± 27.4% in the ORAH group (p = 0.58). Mean length harvested was 16.0 ± 2.2 cm ERAH vs 15.1 ± 2.2 cm ORAH (p > 0.05).

3.2.2 | Patency rate

No differences were found in the RA patency rate between ERAH and ORAH groups (OR: 1.32, CI 0.76-2.27; p = 0.32; Fig. 2B). This was confirmed both in the RCT studies subgroup (OR: 1.25, CI 0.60-2.60; p = 0.55), and in the PSM studies subgroup (OR: 1.41, CI 0.62-3.18; p = 0.41; Fig. 2B).

3.2.3 | Early and long-term survival outcome

There was no statistical difference in early mortality between both groups (OR: 0.78, CI 0.10-6.11; p = 0.81; Fig. 2C). This was confirmed both in the RCT studies subgroup (RD = −0.00, CI = −0.04-0.04, p = 1.00), and in the PSM studies subgroup (RD = −0.00, CI = −0.02-0.02, p = 1.00; Fig. 2C).

No difference in 5-year cardiac-related mortality was seen between the groups (OR: 0.67, CI 0.11-4.17; p = 0.66; Fig. 2D). No subgroup analyses were done as there were only two studies for this outcome.

Sensitivity analyses using leave-one-out analyses confirmed those results (Supplementary Fig. S2)

Table 4 summarizes the main findings of the analysis. Funnel plots of individual outcomes are shown in Fig. 3.

4 | DISCUSSION

The traditional harvesting of the RA has been open, but several reports have described an endoscopic harvesting technique.[9] The RA is more fragile than the saphenous vein and endothelial integrity is of particularly importance in the RA which has a recognized early spastic tendency.

TABLE 1 Overview of included studies

Study	Year	Country	Centers	Study period	Type of study	Newcastle-Ottawa scale
Bisleri[10]	2016	Poland, Italy	Multicenter	2005-2007	Matched	8/9
Burns[20]	2015	Canada	Western University Ontario	2005-2007	RCT	8/9
Navia[2]	2011	USA	Cleveland Clinic, Ohio	2002-2004	Matched	7/9
Nowicki[18]	2011	Poland	Multicenter	2004-2007	RCT	8/9
Rudez[21]	2007	Croatia	Dubrava University Hospital, Zagreb	2002-2004	RCT	8/9
Shapira[14]	2006	USA	Boston Medical Center, MA	Until 2005	RCT	8/9

RCT, randomized controlled trial.

TABLE 2 Overview of included studies

Study	Age[a] ERAH vs ORAH	Median follow-up	Males (%) ERAH vs ORAH	DM (%) ERAH vs ORAH	HTN (%) ERAH vs ORAH	2-VD (%) ERAH vs ORAH	3-VD (%) ERAH vs ORAH	PVD (%) ERAH vs ORAH	Dyslipidemia (%) ERAH vs ORAH	EF[a] ERAH vs ORAH	Urgent operation (%) ERAH vs ORAH	Outcomes
Bisleri[10]	62.1 ± 10.2 vs 70.5 ± 8.3	NR	74.7 vs 74.1	23.1 vs 34.6	73.1 vs 67.9	36.5 vs 39	63.4 vs 61.7	26.8 vs 34.6	63.4 vs 56.8	<40% 15.8 vs 19.8	NR	Wound complications, mortality
Burns[20]	57.8 vs 57.9	79.2 ± 8.6 months	90 vs 93.2	25.1 vs 20.4	NR	NR	NR	0 vs 3.4	NR	NR	48.3 vs 54.2	Mortality, patency, QoL
Navia[2]	60 ± 9.9 vs 62 ± 9.1	NR	90 vs 95	18 vs 19	77 vs 79	NR	NR	41 vs 43	NR	50 ± 13 vs 47 ± 13	NR	Wound complications, mortality, organ failure
Nowicki[18]	<70 years in both	3 years	88 vs 91	20 vs 18	NR	NR	NR	NR	NR	NR	NR	Wound complications, mortality, patency, endothelial integrity
Rudez[21]	60.5 ± 9.2 vs 61.2 ± 9.8	37 ± 7 months	64 vs 72	32 vs 24	56 vs 60	NR	NR	NR	76 vs 68	NR	NR	Wound complications, mortality
Shapira[14]	60 ± 10 vs 62 ± 12	NR	66.7 vs 72.2	41.7 vs 44	72 vs 80.6	NR	NR	22.2 vs 22	88.9 vs 94	54 ± 11 vs 53 ± 13	NR	Wound complications, mortality, histological changes, adhesion molecule expression, and histologic changes

DM, diabetes mellitus; EF%, ejection fraction; ERAH, endoscopic radial artery harvesting; HTN, hypertension; NR, not reported; ORAH, open radial artery harvesting; PVD, peripheral vascular disease; QoL, quality of life; 2-VD, 2-vessel disease; 3-VD, 3-vessel disease.
[a]Expressed as mean ± standard deviation.

TABLE 3 Studies included in patency rates analysis

Study	Year	Angiographic reassessment (%)	ERAH No.	ERAH-patent (%)	ORAH No.	ORAH-patent (%)	P value[a]	Newcastle-Ottoawa scale
Burns[20]; RCT	2015	55	34	31 (91.2)	32	28 (87.5)	0.63	8/9
Nowicki[18]; RCT	2011	100	100	88 (88)	100	86 (86)	0.67	8/9
Ito[22]	2009	100	50	48 (96)	50	47 (94)	0.65	8/9
Bleiziffer[23]	2007	100	50	39 (78)	50	36 (72)	0.49	8/9

ERAH, endoscopic radial artery harvesting; ORAH, open radial artery harvesting; RCT, randomized controlled trial.
[a]Calculated using Chi (χ^2) square.

The comparative studies between the two techniques have yielded different results and no consensus about the ideal harvesting method currently exists. In a PSM study by Navia et al[2] no difference was found between the two techniques in terms of wound infection and neurological deficits. However, Bisleri and coauthors found that open RA harvesting was associated with increased wound infection (7.3% vs 0.0%; p = 0.007), poorer wound healing using the Hollander scale (3.3 vs 4.7, p < 0.001), and increased prevalence of paresthesia at long term follow-up (19.5% vs 3.6%; p < 0.001).[10]

Two meta-analyses have compared endoscopic vs open harvesting techniques for the RA. The first by Wu et al[11] examined 10 studies (eight observational, two randomized control trials) and included 2782 patients. The results showed that ERAH was associated with a lower incidence of wound infection (OR:0.31, CI 0.13-0.74; p = 0.008) and a similar incidence of hematoma formation (OR:0.32, CI 0.07-1.39; p = 0.13) with no difference in graft patency and all-cause mortality (OR:0.81, CI 0.54-1.21; p = 0.3 and OR:1.06, CI 0.26-4.38; p = 0.94, respectively). Cao and coworkers examined 12-studies (1 RCT and 11 observational) and included 3314 patients.[12] They concluded that ERAH had a significantly lower incidence of wound infections (RR:0.36, CI 0.16-0.82; p = 0.01), hematoma formation (RR:0.45; CI 0.26-0.77; p = 0.004), and paresthesia (RR:0.77, CI 0.61-0.99; p = 0.04). Operative mortality (0.3% vs 0.5%; p = 0.55), incidence of myocardial infarction (0.8% vs 1.0%; p = 0.62), and graft patency (2-studies, 88.7% vs 85.5%; p = 0.24 and 2-studies, 75.9% vs 78.1%; p = 0.97) were similar between the two techniques.

Both studies included a large number of unmatched observational studies.[13] In addition most of the series included in the angiographic analysis had a very low rate of angiographic reassessment so that the quoted patency rates do not necessarily reflect the real patency in the entire cohort.

Our meta-analysis focused only on RCT or PSM studies and on angiographic series with >50% re-assessment rate in order to provide a summary of the best available evidence.

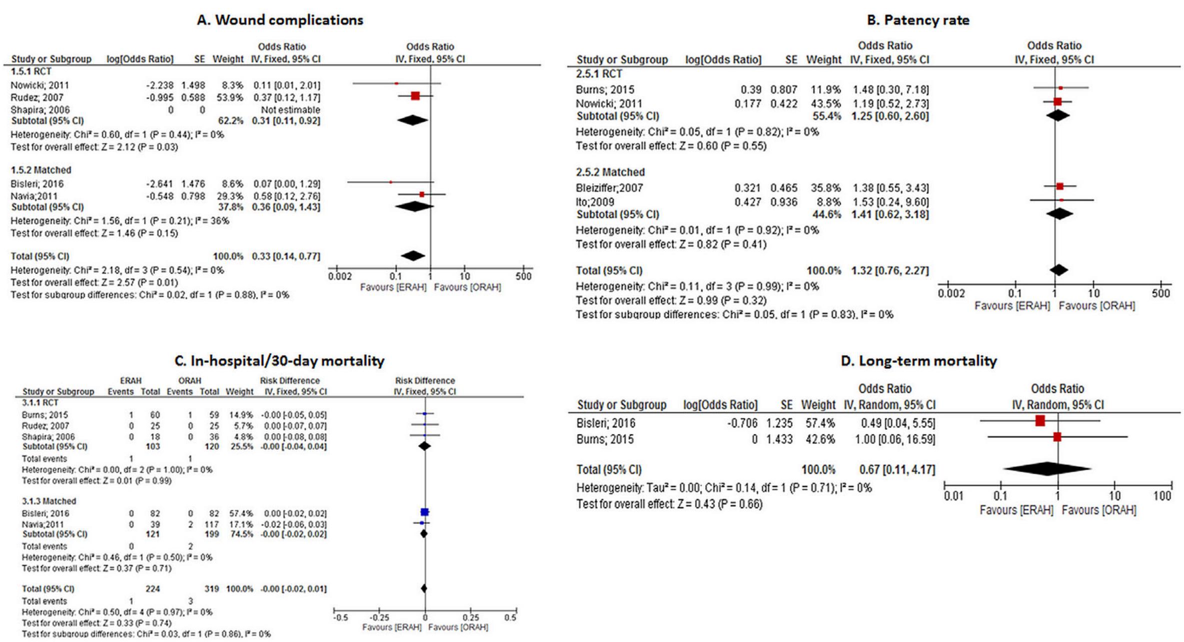

FIGURE 2 Forest plot of comparison ERAH versus ORAH: A, Wound complications; B, Patency rate; C, In hospital/30-day mortality; D, Long-term cardiac mortality. ERAH, endoscopic radial artery harvesting; ORAH, open radial artery harvesting

TABLE 4 All outcomes of interest

Outcome	Studies	Cases	Effect estimate	OR/RD	95%CI	Heterogeneity	Test for overall effect	Favors group
Wound complications	5	624	0.33 [0.14, 0.77]	OR = 0.33	0.14-0.77	P = 0.54, I^2 = 0%	Z = 2.57, P = 0.01	ERAH
Patency rate	4	466	1.32 [0.76, 2.27]	OR = 1.32	0.76-2.27	P = 0.99, I^2 = 0%	Z = 0.99, P = 0.32	None
In-hospital/30-day mortality	5	543	−0.00 [−0.02, 0.01]	RD = −0.00	−0.02-0.01	P = 0.97, I^2 = 0%	Z = 0.33, P = 0.74	None
Cardiac related long-term mortality	2	240	0.67 [0.11, 4.17]	OR = 0.67	0.11, 4.17	P = 0.71, I^2 = 0%	Z = 0.43, P = 0.66	None

CI, confidence interval; ERAH, endoscopic radial artery harvesting; OR, odds ratio; RD, risk difference.

Our results showed a significantly lower incidence of wound complications in the ERAH series with no difference in graft patency rate, and short- and long-term mortality.

Several other factors should be considered when comparing these two techniques. First, in an era of increasing hospital expenditures, procedural cost is of concern. While Navia et al[2] did not give a dollar amount they did mention that the endoscopic technique uses more equipment which suggests a higher cost expenditure. Shapira and coauthors reported that ERAH was more expensive quoting a 500.00 US dollar price tag for the endoscopic harvesting kit.[14] Second, our data showed that ERAH took longer to perform than ORAH (50.9 min vs 41.2 min). This is in line with previous studies[15] and must be taken into account when planning operations on high-risk patients. Third, endoscopic harvesting is a more complex procedure and the subsequent learning curve is steeper. Navia et al[2] suggested that physicians should first learn vein harvesting before moving to the more complex RA. Two other studies reported a significant learning curve, indicated by a reduction in the operative time after 10 cases[15] in one study, and 20 in the other.[16] In an earlier study, Shapira and coauthors reported a significant learning curve (75 min for the first 20 cases and 63 min for the last 50 cases). Average RA harvest time was 66 minutes with a range of 25-120 minutes.[16] Another report by Simek and coauthors confirmed a significant learning curve.[15] A significant drop in overall harvesting time (56.2 ± 18.6 vs. 38.6 ± 8.6 min, p < 0.001) and forearm ischemia time (41.8 ± 12.7

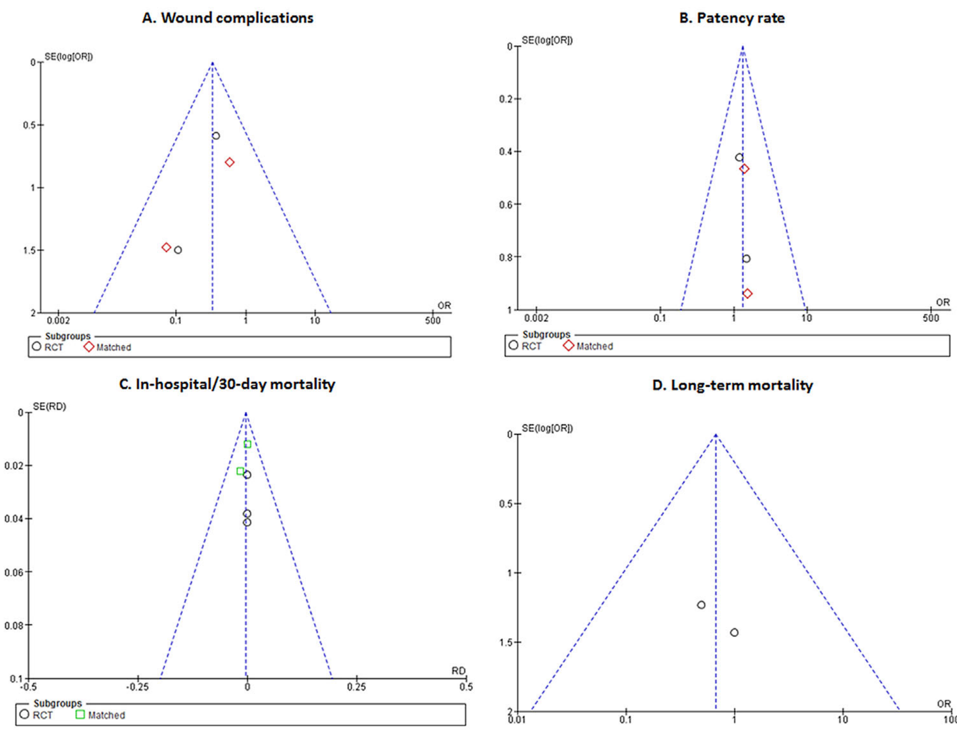

FIGURE 3 Funnel plot for publication bias: A, Wound complications; B, Patency rate; C, In hospital/30-day mortality; D, Long-term cardiac mortality

vs 24.2 ± 3.2 min, $p < 0.001$) was found over this period and the authors concluded that around 10 cases are needed to become proficient with the technique. The number of grafts damaged and thus not used for grafting is of concern. Shapira and coauthors in a 2004 paper describing their initial experience with endoscopic harvesting found that 1.3% of grafts were damaged by the harmonic scalpel.[16] A similar study by Burris and coauthors found that intimal trauma of any kind ($p < 0.001$) and minor ostial intimal tears (luminal tears occurring at branch points) ($p = 0.003$) were more frequently in the ERAH group.[17] Finally, as conduit length is of concern during grafting, the amount of artery harvested is a consideration. In one study included in our analysis length harvested for ERAH was 16 and 15.1 cm for ORAH.[18]

The present analysis has several limitations. Ideally meta-analysis should be conducted only on RCT data.

The meta-analytic approach based on PSM studies can be relied on as evidence when RCTs are not possible or not available,[19] but it is not as methodologically robust as the one based on RCT. In addition, all the included studies have a follow-up limited to the first 5-7 years after surgery. In this time frame, the number of clinical events and of arterial graft failure is low such that this meta-analysis can be underpowered to detect moderate differences. Most of the events that we pooled together in the combined endpoint of wound complications are minor changes and are unlikely to impact patient outcome and quality of life. The use of antispasmodic agents were not described and were unable to be included in our analysis.

5 | CONCLUSION

In conclusion, with the limitations of the present meta-analysis, we found that ERAH reduces wound complications and does not affect graft patency and short- and long-term mortality compared to ORAH. The wound complications reported with both techniques appear to be minor. ERAH takes longer to harvest the conduit and adds additional cost to the procedure. Its main advantage appears to be cosmetic. Our meta-analysis shows that ERAH can improve cosmesis without affecting graft patency or short- or long-term cardiac mortality.

CONFLICTS OF INTEREST

None.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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