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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 Endoscopic harvesting of the radial artery (RA) for coronary bypass surgery, is a well-known technique. However, its effect on graft patency and outcome is still unclear. Previous meta-analysis on the comparison between endoscopic RA harvesting (ERAH) vs open RA harvesting (ORAH) are mostly based on observational unmatched series and, thus, have major methodological limitations. We sought to investigate the impact of harvesting technique on RA graft patency and relevant clinical outcomes using a meta-analytic approach limited to randomized controlled trials and propensity matched studies.

Method A systematic literature search was conducted using PubMed and MEDLINE to identify publications containing comparisons between ERAH and ORAH. Only randomized controlled trials and propensity matched series were included. Data was extracted and analyzed with RevMan. Primary endpoints were wound complications, patency rate, early mortality, and long term 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 difference in graft patency, early and long-term mortality between the two techniques.

Conclusion ERAH significantly reduces wound complications and is associated with similar graft patency, and short and long-term mortality compared to ORAH.

Introduction

The left internal mammary artery (LIMA) has long been reported as the best conduit for coronary artery bypass grafting (CABG)[1]. The radial artery comes in second with comparable results to the saphenous vein in regards to short- and mid-term follow-up[2,3].

Endoscopic radial artery harvesting (ERAH) was recently developed in order to minimize the trauma and improve patient satisfaction. Debate exists as to the better approach for radial artery harvesting. ERAH proponents emphasize the superior cosmetic and perioperative outcomes, whereas skeptics cite the lack of robust safety in clinical data on ERAH, especially in regard to graft patency. Integrity of the endothelium has been reported to be responsible for the normal function of vessels, with any intimal damage leading to conduit failure that could precipitate recurrent angina and need for re-intervention[4].

Our aim in this meta-analysis is to identify all robust and relevant data from the current literature to compare the safety and the efficacy of ERAH versus ORAH for CABG. Our endpoints are wound complications, patency rate, in-hospital, and long term mortality.

Materials and Methods

Data sources and literature search strategy

Literature review was conducted by two independent investigators (MR and MK) 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 (i.e., backward snowballing) to obtain further

studies. For patency rate, we use the search terms “endoscopic radial artery harvesting, patency, outcome” in addition to backward snowballing.

Study selection

Inclusion criteria were: 1) randomized controlled trials or propensity matched studies (PSM); 2) comparing ERAH with ORAH in patients who underwent CABG and included interest outcomes such as wound complications, patency rate, 30 days/in-hospital mortality and long term mortality; 3) published full text manuscript and 4) written in English.

For patency rate, inclusion criteria were 1) studies comparing ERAH with ORAH in CABG patients regardless of study design 2) angiographic follow-up of more than 50% of the overall patient population.

Two investigators (MR and MK) 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 (MG) reviewed the article and an agreement was negotiated. Pertinent articles were then retrieved.

Primary outcomes

Primary outcomes were wound complications, patency rate, early and long-term mortality.

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

Data extraction and Statistical analysis

Microsoft Office Excel 2010 (Microsoft, Redmond, Washington) was used for data extraction. Data extraction of all included studies was performed independently by 2 investigators (MR, MK) and in case

of disagreement a third investigator (MG) was included and an agreement was negotiated. Extracted variables were for matched populations only and included the follows: study name, publication year, study design, number of patients, interventions, age, sex, wound complications, patency rate, 30 days/in-hospital mortality, and long-term mortality.

Review Manager Version 5.3 was used to perform meta-analysis, and the estimated survival data were obtained from the Kaplan–Meier curves[5] using GetData Graph Digitizer software. The data can be synthesized only when the number of studies equals or exceeds two. Measurement data reported as mean ± SD were adopted, and odds ratio (OR) was calculated.

Individual and pooled OR with 95% confidence intervals (CI) were calculated by means of Mantel-Haenszel (M-H) method. Risk difference (RD) was used as a summary estimate in case of 0 event studies. All the statistical results use random-effect models. Heterogeneity was assessed by X^2-test and I^2 and publication bias by 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, USA).

Results

Eligible studies and characteristics of studies

An outline of the systematic review process is shown in Figure 1 and Supplementary Figure 1 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 6 studies (four randomized controlled trials and 2 PSM studies met the inclusion criteria.

Of the 743 patients included 324 (43.6%) underwent ERAH and 419 (56.4%) ORAH. The characteristics of the included studies are shown in Table 1 and 2. Studies included in patency rate analysis are shown Table 3. A total of 827 grafts were assessed by angiogram (458 in ERAH group and 369 in ORAH group) with pooled mean follow-up of 40.9 and 51.5-months in ERAH and ORAH respectively.

Meta-analysis of postoperative outcomes

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 (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, Figure 2A). These results were confirmed in the leave-one-out analysis. (Supplementary figure 2)

Patency rate

No differences were found in the RA patency rate between ERAH and ORAH groups (OR:1.36, CI 0.91–2.04; p=0.14; Figure 2B). This was confirmed in RCT studies subgroup (OR:1.25, CI 0.60–2.60; p=0.55), and in the PSM studies subgroup (OR:1.41, CI 0.87–2.29; p=0.16; Figure 2B). These results were confirmed in the leave-one-out analysis. (Supplementary figure 2)

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; Figure 2C). This was confirmed in 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; Figure 2C).

Similarly, no difference in 5-years mortality was seen between the groups (OR:0.59, CI 0.18-1.93; p=0.87; Figure 2D). No subgroup analyses were done as there was only 2 studies in this variable.

Sensitivity analyses using leave-one-out analyses were done for all outcomes and confirmed our results (Supplementary figure 3)

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

Discussion

The radial (RA) contends with the right internal thoracic artery (RITA) for the role of best second arterial conduit. In a recent meta-analysis of propensity matched trials we found the use of the RITA was associated with a 25% survival benefit compared to the RA at mid-term follow-up[6] . However, as in all meta-analysis of observational studies comparing different surgical techniques, a selection bias based on an unmeasurable surgeon's "eye ball" test (with healthier patients receiving the more invasive bilateral internal thoracic artery (BITA) procedure) cannot be excluded.

On the other hand the recently presented but yet unpublished 10-year results of the RAPCO trial showed better (although not significantly) patency rates and significantly better survival for the RA compared to the RITA[7].

Compared to the second ITA, the RA has the major advantage of not increasing the risk of sternal complications, an event with major clinical and economic implications. In a study by Omran and associates, that included 9000 CABG patients the occurrence of postoperative sternal complications increased operative mortality by 10-fold and incurred additional hospital costs[8]. In a meta-analysis by Dai and coworkers that included 173,000 patients, the rate of deep sternal wound infections was increased by 38% when the second ITA was utilized as a conduit[9].

Also, since the RA can be harvested simultaneously with other conduits, operative time is reduced when compared to the RITA. Overall, operations using the RA are technically easier than using the RITA and probably more friendly for surgeons with limited experience in complex arterial grafting. Together with the excellent long term results reported by RAPCO and us[6,7], along with the above mentioned advantages of the RA and the increasing pressure toward multiple arterial revascularization, it is likely that the RA will experience a resurgence in the near future.

The traditional harvesting of the RA has been open, but several reports have described an endoscopic harvesting technique.

An abundant body of evidence related to harvesting of the saphenous vein testifies to how the endoscopic harvesting is more traumatic and can potentially affect the patency. 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. For these reasons, the concerns regarding vessel damage are even higher for the RA when using the endoscopic approach.

The comparative studies between the two techniques have yielded different results and no consensus about the ideal harvesting method currently exists. In a propensity score matched (PSM) study by Navia and colleagues, found no difference between the two techniques in terms of wound infection and neurological deficits[3]. However, Bisleri and coauthors found that open radial artery harvesting was associated with increased wound infection (7.3% vs 0.0%; p=0.007), poorer wound healing on Hollander scale (3.3 vs 4.7, p<0.001), and increased prevalence of paresthesia at late term follow-up (19.5% vs 3.6%; p<0.001)[10].

So far two meta-analysis have compared endoscopic vs open harvesting techniques for the RA. The first by Wu and colleagues examined 10-studies (8-observational, 2-randomized control trials) and included 2782 patients[11]. Results showed that ERAH was associated with lower incidence of wound infection

(OR:0.31, CI 0.13-0.74; p=0.008) but similar incidence of hematoma formation (OR:0.32, CI 0.07-1.39; p=0.13). Post-operative paresthesia was not examined. In the second study, Cao and coworkers examined 12-studies (1 RCT and the remaining 11 were observational) and included 3314 patients[12]. Their results showed that ERAH had 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).

When examining graft patency and all-cause mortality, Wu and colleagues[11] found that ERAH offered no advantage when compared to ORAH (OR:0.81, CI 0.54-1.21; p=0.3 and OR:1.06, CI 0.26-4.38; p=0.94, respectively). Similarly, Cao and coworkers[12] found that using an endoscopic technique did not improve mortality (0.3% vs 0.5%; p=0.55), incidence of myocardial infarct (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).

However, both studies have major methodological limitations as they included mostly unmatched observational studies[13]. Our meta-analysis focused only on RCT or PSM studies in order to provide a summary of the best available evidence and to avoid the recognized limitations of meta-analysis of observational studies.

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

Conclusion

ERAH significantly reduces wound complications and is associated with similar graft patency, and short and long-term mortality compared to ORAH.

Figure legend

Figure 1. PRISMA flowchart for clinical outcomes.

Figure 2. Forest plot of comparison ERAH vs ORAH: A, Wound complications; B, Patency rate; C, In hospital/30-day mortality; D, Long-term mortality.

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

Supplementary figure 1. PRISMA flowchart for angiographic patency.

Supplementary figure 2. Leave-one-out analysis for: A, Wound complications; B, Patency rate; C, In hospital/30-day mortality; D, Long term mortality.

Authors' contributions

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Critical revision of article: Leonard N Girardi MD

Approval of article: All authors

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Table 1. Overview of included studies

Study	Year	Country	Centers	Study period	Type of study
Bisleri[10]	2016	Poland, Italy	Multicenter	2005-2007	Matched
Burns[14]	2015	Canada	Western University Ontario	2005-2007	RCT
Navia[15]	2011	USA	Cleveland Clinic, Ohio	2002-2004	Matched
Nowicki[16]	2011	Poland	Multicenter	2004-2007	RCT
Rudez[17]	2007	Croatia	Dubrava University Hospital, Zagreb	2002-2004	RCT
Shapira[18]	2006	USA	Boston Medical Center, MA	Till 2005	RCT

RCT, randomized controlled trial

Table 2. Overview of included studies

Study	Age (mean±SD) 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 (%) 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 vs56.8	<40% 15.8 vs 19.8	NR	Wound complications, Mortality
Burns[14]	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[15]	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, Organs failure
Nowicki[16]	<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[17]	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[18]	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 & histologic changes

EF%, ejection fraction; ERAH, Endoscopic Radial Artery Harvesting; DM diabetes mellitus; 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

Table 3. Studies included in patency rates analysis

Study	Year	ERAH No.	ERAH - Patent (%)	ORAH No.	ORAH - Patent (%)	P value*
Burns[14]; RCT	2015	34	31(91.2)	32	28(87.5)	0.63
Nowicki[16]; RCT	2011	100	88(88)	100	86(86)	0.67
Dimitrova[19]	2010	148	124(83.8)	119	94(79)	0.31
Ito[20]	2009	50	48(96)	50	47(94)	0.65
Kim[21]	2007	76	74(97.4)	18	17(94.4)	0.53
Bleiziffer[22]	2007	50	39(78)	50	36(72)	0.49

ERAH, Endoscopic Radial Artery Harvesting; ORAH, Open Radial Artery Harvesting

* calculated using Chi (X^2) square

Table 4. All outcomes of interest

Outcome	Number of studies	Cases	OR/RD	95% CI	Heterogeneity	Test for overall effect	Favors group
Wound complications	5	624	OR=0.33	0.14-0.77	*P*=0.51, I^2=0%	*Z*=2.57, *P*=0.01	ERAH
Patency rate	6	827	OR=1.36	0.91-2.04	*P*=1.00, I^2=0%	*Z*=1.49, *P*=0.14	None
In-hospital/ 30-day mortality	5	543	RD =-0.00	-0.02-0.01	*P*=0.97. I^2=0%	*Z*=0.33, *P*=0.74	None
Long-term mortality	2	240	OR=0.59	0.18-1.93	P=0.87, I^2=0%	*Z*=0.87, *P*=0.39	None

CI, confidence interval; OR, odds ratio; RD, risk difference; ERAH, Endoscopic Radial Artery Harvesting

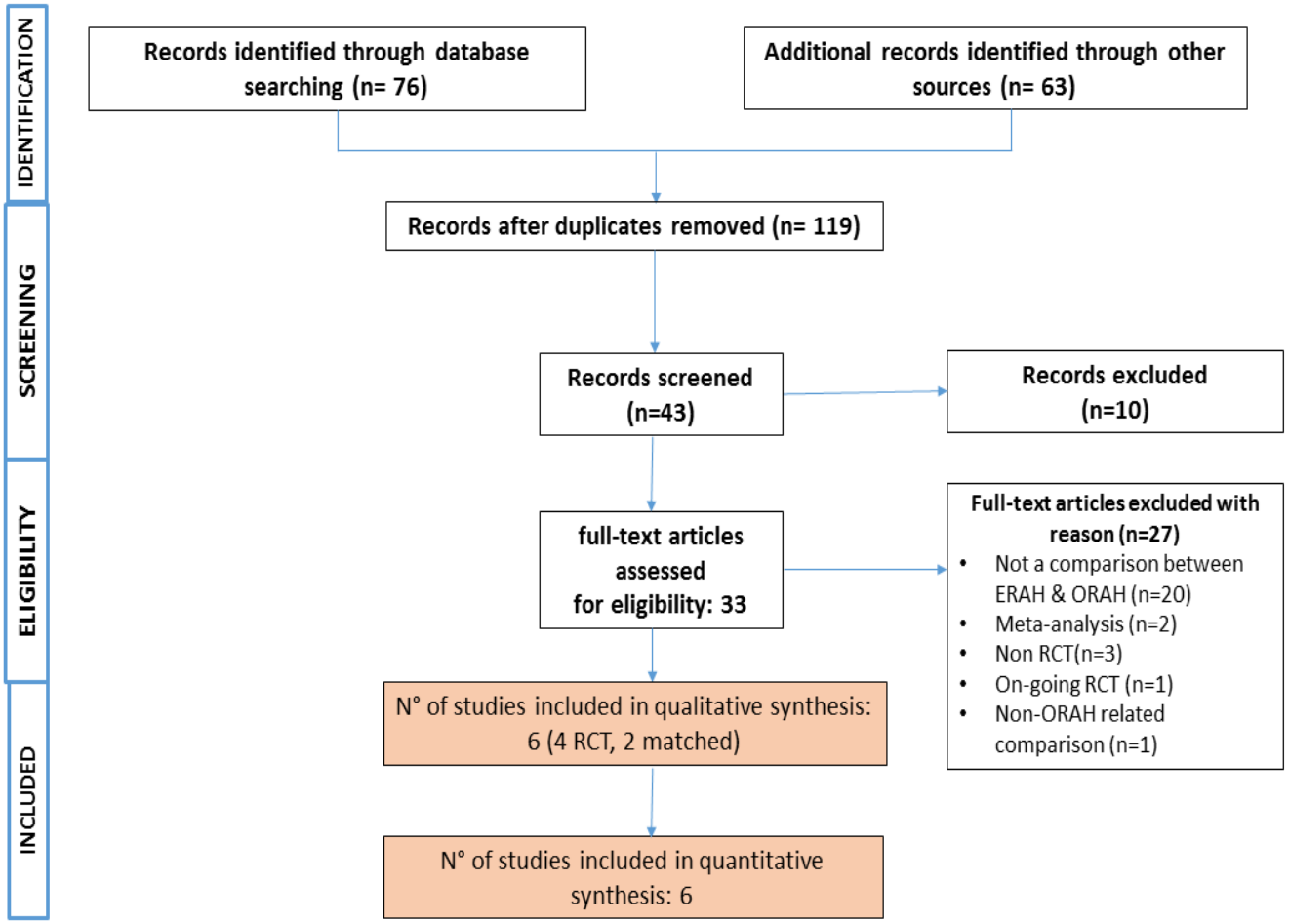
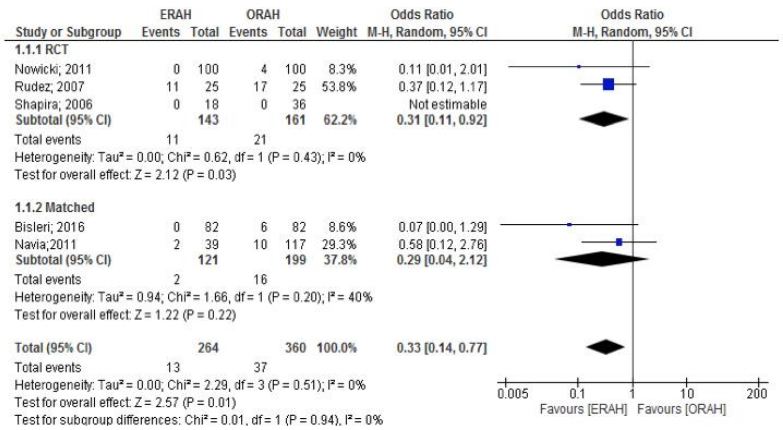
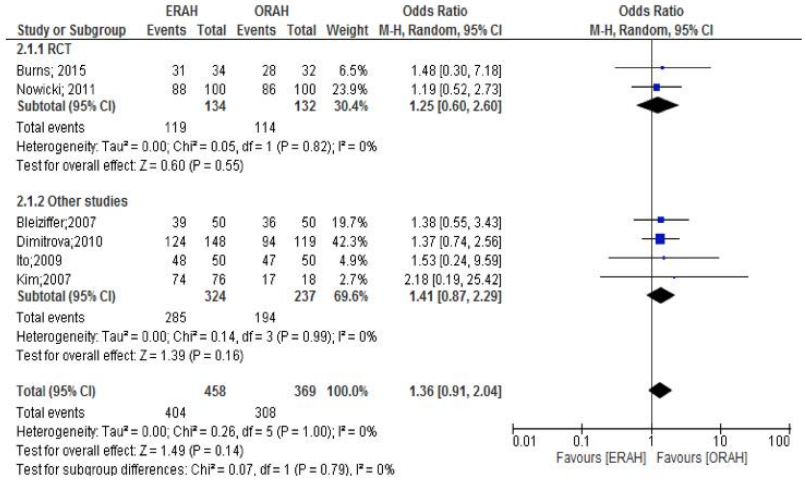

IDENTIFICATION
SCREENING
ELIGIBILITY
INCLUDED
Records identified through database searching (n= 76)
Additional records identified through other sources (n= 63)
Records after duplicates removed (n= 119)
Records screened (n=43)
Records excluded (n=10)
full-text articles assessed for eligibility: 33
Full-text articles excluded with reason (n=27)
• Not a comparison between ERAH & ORAH (n=20)
• Meta-analysis (n=2)
• Non RCT(n=3)
• On-going RCT (n=1)
• Non-ORAH related comparison (n=1)
N° of studies included in qualitative synthesis: 6 (4 RCT, 2 matched)
N° of studies included in quantitative synthesis: 6

Figure 1

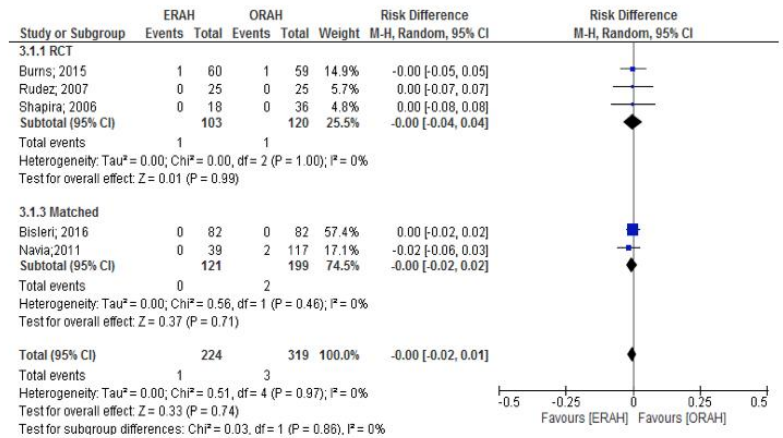
A. Wound complications



B. Patency rate



C. In-hospital/30-day mortality



D. Long-term mortality

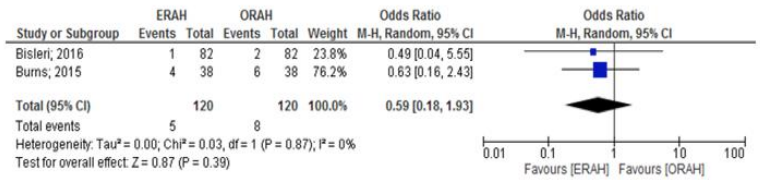


Figure 2

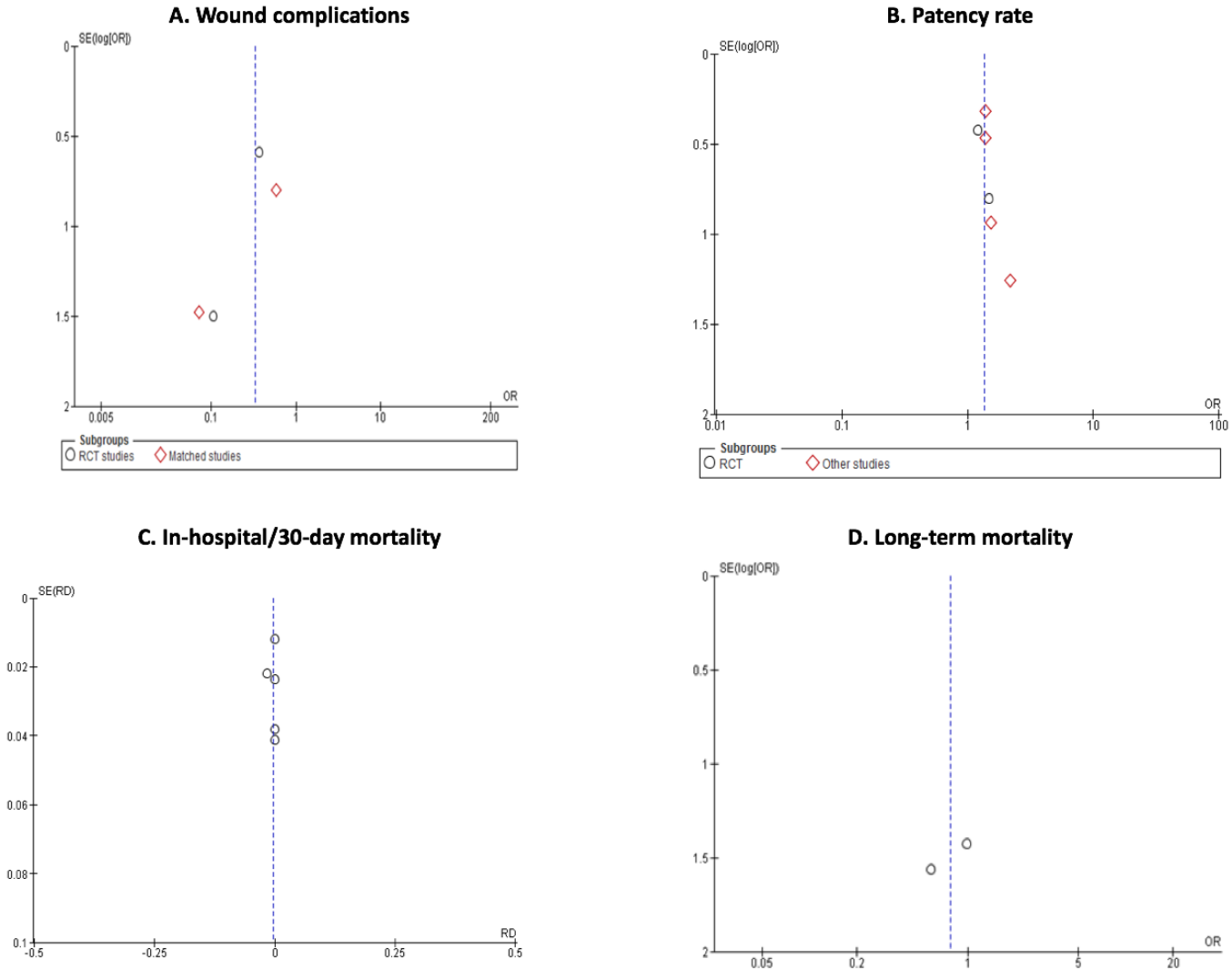
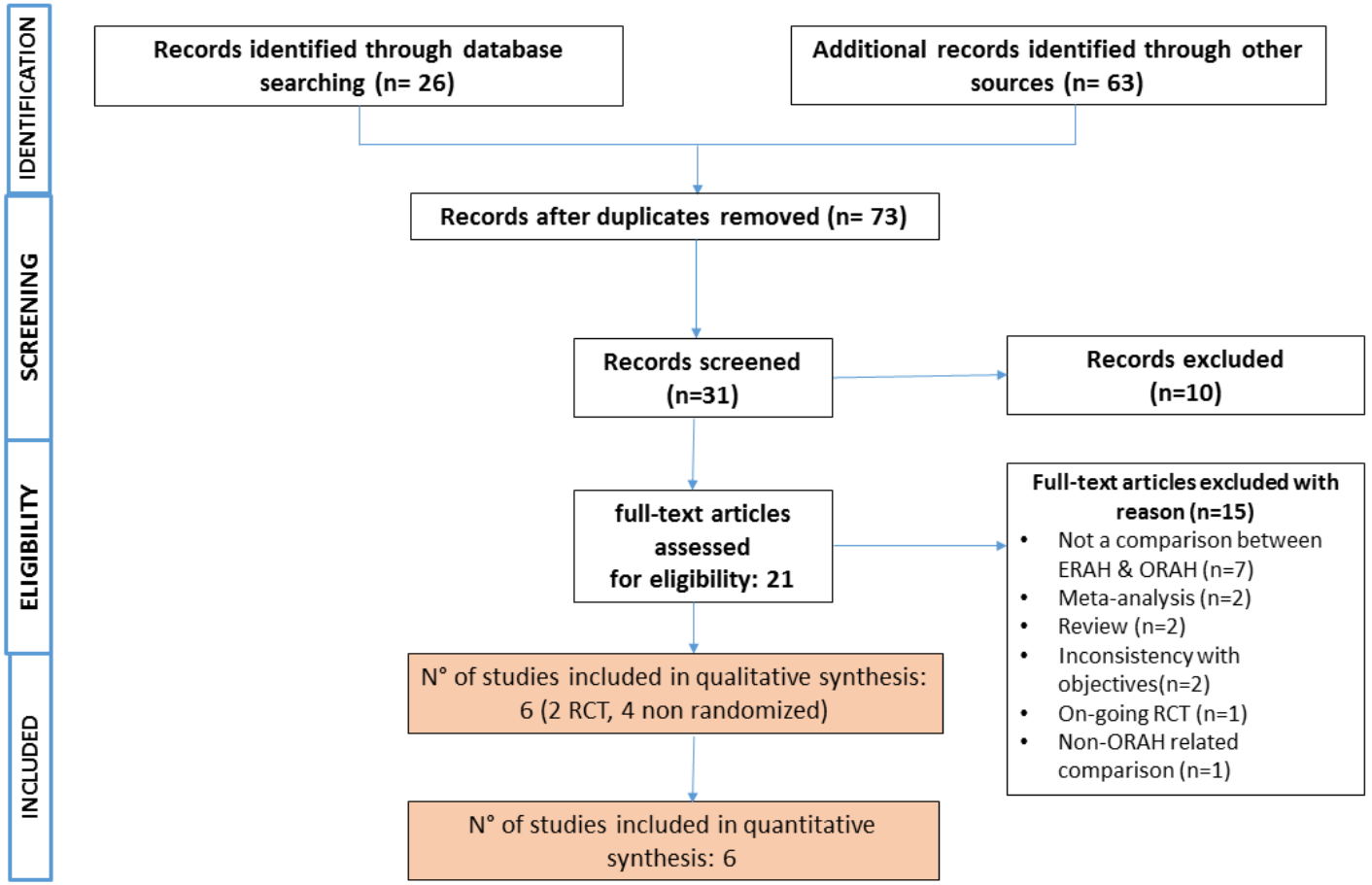

A. Wound complications
SE(log[OR])
0
0.5
1
1.5
2
OR
0.005
0.1
1
10
200
Subgroups
RCT studies
Matched studies
B. Patency rate
SE(log[OR])
0
0.5
1
1.5
2
OR
0.01
0.1
1
10
100
Subgroups
RCT
Other studies
C. In-hospital/30-day mortality
SE(RD)
0
0.02
0.04
0.06
0.08
0.1
RD
-0.5
-0.25
0
0.25
0.5
D. Long-term mortality
SE(log[OR])
0
0.5
1
1.5
2
OR
0.05
0.2
1
5
20

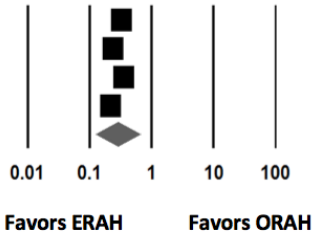
Figure 3



Supplementary figure 1

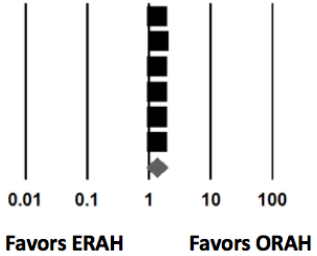
A. Wound complications

Study name	Point	Lower limit	Upper limit	Z-Value	p-Value
Nowicki	0.324	0.136	0.773	-2.539	0.011
Rudez	0.235	0.071	0.777	-2.373	0.018
Bisleri	0.360	0.149	0.868	-2.276	0.023
Navia	0.218	0.083	0.573	-3.091	0.002
	0.286	0.125	0.653	-2.970	0.003



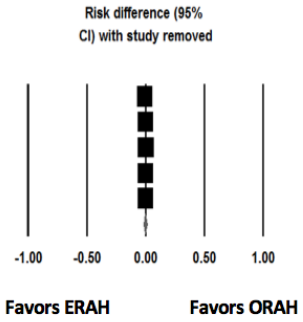
B. Patency rate

Study name	Point	Lower limit	Upper limit	Z-Value	p-Value
Burns	1.352	0.890	2.053	1.414	0.157
Nowicki	1.416	0.891	2.251	1.473	0.141
Bleiziffer	1.355	0.863	2.127	1.321	0.187
Dimitrova	1.349	0.793	2.297	1.103	0.270
Ito	1.351	0.893	2.045	1.425	0.154
Kim	1.342	0.891	2.021	1.408	0.159
	1.360	0.908	2.036	1.491	0.136



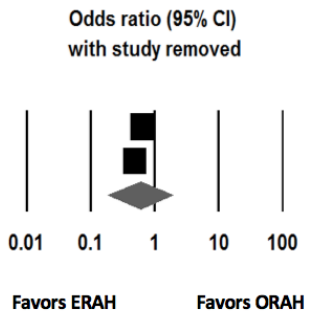
C. In-hospital/30-day mortality

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Bisleri	-0.007	0.014	0.000	-0.034	0.020	-0.499	0.617
Burns	-0.003	0.010	0.000	-0.023	0.016	-0.348	0.728
Navia	-0.000	0.010	0.000	-0.020	0.020	-0.005	0.996
Rudez	-0.003	0.009	0.000	-0.022	0.015	-0.336	0.737
Shapira	-0.003	0.009	0.000	-0.021	0.015	-0.334	0.738
	-0.003	0.009	0.000	-0.021	0.015	-0.326	0.745



D. Long-term mortality

Study name	Point	Lower limit	Upper limit	Z-Value	p-Value
Bisleri	0.631	0.169	2.361	-0.684	0.494
Burns	0.494	0.044	5.555	-0.571	0.568
	0.596	0.187	1.900	-0.874	0.382



Supplementary figure 2