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Open Versus Endovascular Stent Graft Repair of Abdominal Aortic Aneurysms

A Meta-Analysis of Randomized Trials

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Objectives This study sought to evaluate the short-, intermediate-, and longer-term outcomes after endovascular versus open repair of abdominal aortic aneurysms (AAA), including both AAA-related and all-cause mortality.

Background Endovascular stent graft placement for AAA has gained broad acceptance as an alternative to open surgical repair due to a lower perioperative morbidity and mortality. The intermediate- and long-term all-cause and aneurysm-related mortality vary among studies. Thus, we sought to perform a meta-analysis of open versus endovascular repair for treating AAA.

Methods Electronic databases were queried for identification of prospective, randomized trials of open surgery versus endovascular stent graft repair of AAA. A total of 10 published papers reporting on 6 studies at different follow-up intervals were identified; they involved 2,899 patients with AAA repair procedures, of whom, 1,470 underwent endovascular stent graft AAA exclusion and 1,429 were treated by open AAA repair.

Results At 30 days, the pooled relative risk of all-cause mortality was lower in the endovascular group (relative risk [RR]: 0.35, 95% confidence interval [CI]: 0.19 to 0.64) than in the open surgery group. At intermediate follow-up, the all-cause mortality had a nonsignificant difference (RR: 0.78, 95% CI: 0.57 to 1.08), the AAA-related mortality was significantly lower (RR: 0.46, 95% CI: 0.28 to 0.74) and reintervention rates were higher (RR: 1.48, 95% CI: 1.06 to 2.08) in the endovascular group than in the open surgery group. At long-term follow-up, there was no significant difference in all-cause mortality (RR: 0.99, 95% CI: 0.85 to 1.15) or AAA-related mortality (RR: 1.58, 95% CI: 0.20 to 12.74), whereas the significant difference in the rate of reinterventions persisted (RR: 2.54, 95% CI: 1.58 to 4.08).

Conclusions In patients randomized to open or endovascular AAA repair, all-cause perioperative mortality, as well as AAA-related mortality at short- and intermediate-term follow-up are lower in patients undergoing endovascular stent graft placement. This was associated with greater reintervention in the endovascular group noted at intermediate follow-up. Long-term survival appears to converge between the 2 groups. (J Am Coll Cardiol Intv 2012;5:1071–80) © 2012 by the American College of Cardiology Foundation

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Elective repair of abdominal aortic aneurysms (AAA) with a diameter of at least 5.0 to 5.5 cm is indicated to prevent risk of rupture and death: women are considered candidates for elective repair at AAA of 5.0 cm, and men at 5.5 cm (1). Open surgical repair (OSR) by means of laparotomy or retroperitoneal approach, and replacement of the aneurysmal aortic segment with a synthetic graft had been the mainstay of therapy for over 40 years. Given its long-term durability, open repair has traditionally been offered to patients with a moderate life expectancy. The major disadvantage of open repair has been an associated 30-day mortality rate of 4% to 5% and even up to 8.2% in some series (2–4). Advanced age, cardiovascular disease, and other major medical comorbidities may place certain patients with AAA at prohibitive operative risk (1).

A less invasive procedure to treat AAA, introduced in 1991 (5), was developed with the intent to avoid the procedural morbidity and mortality of OSR and the secondary benefit of decreasing the length of hospital stay and rehabilitation (6). Performed by introducing a stent endograft via bilateral femoral arterial access and AAA exclusion by proximal and distal fixation at the healthy arterial segments, endovascular aneurysm repair (EVAR) has revolutionized the approach and treatment of this condition (7). In the beginning, EVAR was offered only to patients at high operative risk. With evolution in device technology and technique, the application of EVAR has been broadened and is currently offered to patients with longer life expectancies (8). The safety and efficacy of endovascular repair was established early with retrospective cohort studies and prospective registries. Two large European registries—the RETA (United Kingdom Registry for Endovascular Treatment of Aneurysms) and the EUROSTAR (European Collaborators on Stent-graft Techniques for Abdominal Aortic Aneurysm Repair) registry—established 30-day mortality rates after EVAR at 2.9% and 3.1%, respectively (9,10). Although the 30-day mortality rates were lower for EVAR than for OSR in such historical cohorts, selection bias was a potential factor.

Abbreviations and Acronyms

AAA = abdominal aortic aneurysm(s)
CI = confidence intervals
EVAR = endovascular aneurysm repair
OSR = open surgical repair
RCT = randomized control trial(s)
RR = relative risk

Multiple prospective randomized controlled trials have been implemented to help determine the comparative morbidity and mortality and the need for reintervention in patients undergoing EVAR versus OSR (11–20). Lower 30-day mortality rates as well as decreased lengths of stay have been associated with EVAR in these studies; however, the longer-term results of these randomized trials vary. We conducted a meta-analysis of the currently available randomized prospective clinical trials comparing open versus endovascular repair of asymptomatic infrarenal AAA to determine whether EVAR improves morbidity and mortality, and we assessed the need for reintervention in both intermediate- and long-term follow-up periods.

Methods

The primary aim of the present meta-analysis was to compare the outcomes of EVAR versus open repair for AAA in prospective randomized control trials. The outcomes of interest are all-cause mortality, aneurysm-related mortality, and rates of reintervention; all defined according to the study protocols as provided in the Online Appendix.

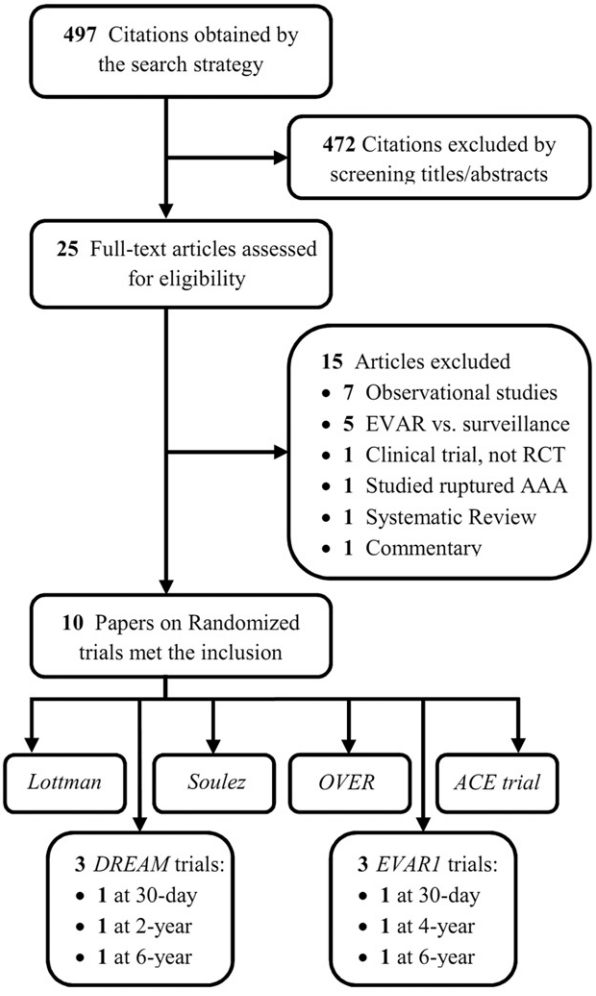

Figure 1. Flow Chart of the Study

AAA = abdominal aortic aneurysm(s); ACE = ACE Anevrysme de l'aorte abdominale: Chirurgie versus Endoprothese [Carotid Endarterectomy] trial; DREAM = Dutch Randomized Endovascular Aneurysm Management trial; EVAR = endovascular aneurysm repair; EVAR-1 = United Kingdom Endovascular Aneurysm Repair 1 trial; OVER = Open Versus Endovascular Repair trial; RCT = randomized controlled trial(s).

Information sources and search methods. A comprehensive literature search was conducted with the electronic databases MEDLINE, EMBASE, and the CENTRAL (Cochrane Central Register of Controlled Trials) for abstracts using various combinations of the terms "aortic aneurysm," "abdominal," "endovascular," "operative procedures," and "surgery" in the abstract or title. Two reviewers (G.D., B.F.) identified articles eligible for further review by performing a screen of abstracts and titles. If a study was deemed relevant, the paper was obtained and reviewed. In addition, bibliographic references of identified randomized clinical trials and review articles, to find randomized clinical trials not identified by the electronic searches, were reviewed. The proceedings of international conferences on AAA were also screened to identify upcoming clinical trials, although none was identified beyond those published.

Study identification. Previously described data sources were searched for possible studies irrespective for dates of publications. The search was not limited to the English-language literature. The final search identified 10 original papers that fulfilled the criteria for inclusion (Fig. 1).

Risk of bias assessment. Methodological quality was defined as the control of bias assessed through the reported methods in each individual trial using the Cochrane risk of bias tool (21). Two reviewers (G.D., B.F.) independently assessed trial quality by examining 2 components: generation of allocation sequence (classified as adequate if based on computer-generated random numbers, tables of random numbers, or similar), concealment of allocation (classified as adequate if based on central randomization, sealed envelopes, or similar), outcome blinding, incomplete outcome data, selective outcome reporting, and any other potential source of bias. Disagreements between the reviewers were resolved by discussion or arbitrated with a third coauthor (P.F.).

Data collection and extraction. Pre-specified data elements were extracted from each trial, including patient demographics, baseline characteristics, study design, sample size, procedure type, outcome measures and primary endpoints at different periods of follow-up, and other study characteristics (Tables 1 and 2). The number of events in each trial was extracted, when available, based on the intention-to-treat approach. All outcomes were defined according to the protocol definitions, which are provided in the Online Appendix. When a study reported follow-up at different periods, outcomes for these periods were also extracted.

Statistical analysis and data synthesis. From the abstracted data, we calculated the relative risk (RR) using the inverse variance method for each study outcome to allow for pooling of similar outcomes.

The average effects for the outcomes and 95% confidence intervals (CI) were obtained using a random effects model, as described by DerSimonian and Kacker (22). We chose the random effects method as the primary analysis because of its conservative summary estimate and incorporation between and within study variance. The analysis was repeated with the fixed-effect method. To assess heterogeneity of treatment effect among trials, we used the I^2 statistic. The I^2 statistic represents the proportion of heterogeneity of treatment effect across trials that were not attributable to chance or random error. Hence, a value of 50% reflects significant heterogeneity that is due to real differences in study populations, protocols, interventions, and outcomes (23).

Statistics of funnel plots were used to assess the presence of publication and other reporting biases by plotting the precision (inverse of the standard error) against the log risk ratio. Using the Begg-Mazumdar rank correlation (24) and the Egger linear regression (25,26) method, we examined the association between the study size and estimated treatment effects; a p value ≤ 0.1 was considered significant.

Sensitivity analyses were performed to assess the effects of selected measures of study quality and clinical factors on mortality and reintervention. The influence of each study was estimated by deleting each in turn from the analysis and noting the degree to which the effect size and significance of the treatment effect changed. This analysis was performed for each study outcome. We considered a study influential if the exclusion of it changed our conclusion or the effect estimate by at least 20%.

Table 1. Trial Description and Quality Assessment

Trial (Ref. #)	Year	Study Location	Institutions, n	Subjects Randomized, N	Study Period	Max Follow-Up Time, yrs	Mean/Median Follow-Up Time, yrs	Adequate Sequence Generation	Clear Inclusion/ Exclusion Criteria
ACE (12)	2011	France	25	306	2003–2009	4.80	3.00	Yes	Clear
DREAM (13,14,19)	2004, 2005, 2010	Netherlands	25	351	2000–2009	8.20	6.40	Yes	Clear
EVAR-1 (11,15,16)	2004, 2005, 2010	United Kingdom	37	1,252	1999–2009	10.00	6.00	Yes	Clear
OVER (17)	2009	United States	42	881	2002–2008	2.00	1.80	Yes	Clear
Soulez et al. (20)	2005	Canada	1	40	1998–2002	4.00	2.30	Yes	Clear
Lottman et al. (18)	2004	Netherlands	2	76	1996–1999	0.25	0.25	Yes	Clear

ACE = ACE [Carotid Endarterectomy] trial; DREAM = Dutch Randomized Endovascular Aneurysm Management trial; EVAR-1 = United Kingdom Endovascular Aneurysm Repair 1 trial; OVER = Open Versus Endovascular Repair trial.

Table 2. Baseline Characteristics of Trials' Arms

	EVAR							Open Repair						
Study/First Author (Ref. #)	ACE (12)	DREAM (14)	EVAR-1 (16)	OVER (17)	Soulez et al. (20)	Lottman et al. (18)	Total*	ACE (12)	DREAM (14)	EVAR-1 (16)	OVER (17)	Soulez et al. (20)	Lottman et al. (18)	Total*
Patients, N	150	173	626	444	20	57	1,470	149	178	626	437	20	19	1,429
Aneurysm diameter, cm	55.2 ± 8.1	6.06 ± 0.9	6.4 ± 0.9	5.7 ± 0.8	5.3 ± 0.48	5.2 (4.0–6.1)	—	55.6 ± 6.6	6.0 ± 0.85	6.5 ± 1.0	5.7 ± 1.0	5.1 ± 1.61	5.6 (5.2–8.4)	—
Age, yrs	68.9 ± 7.7	69.6 ± 6.8	74.1 ± 6.1	69.6 ± 7.8	70.3 ± 6.4	68 (52–81)	—	70 ± 7.1	70.7 ± 6.6	74.0 ± 6.1	70.5 ± 7.8	71.2 ± 7.6	69 (52–82)	—
Male	151 (100)	161 (93.1)	565 (90.3)	441 (99.3)	19 (95)	54 (94.7)	1,391 (94.6)	146 (98)	161 (90.4)	570 (91.1)	435 (99.5)	20 (100)	16 (84.2)	1,348 (94.3)
Smoking	73 (48.7)	111 (64.2)	553 (88.3)	428 (96.4)	19 (95)	—	1,184 (83.8)	74 (49.7)	98 (55.1)	580 (92.6)	413 (94.5)	16 (80)	—	1,181 (83.8)
Coronary heart disease	49 (32.3)	71 (41)	269 (43.0)	174 (39.2)	13 (65)	—	576 (40.8)	65 (43.6)	83 (46.6)	261 (41.8)	185 (42.3)	14 (60)	—	608 (43.1)
Diabetes	20 (13.3)	18 (10.4)	61 (9.8)	100 (22.5)	1 (5)	—	200 (14.2)	29 (19.5)	17 (9.6)	68 (11)	100 (22.9)	5 (25)	—	219 (15.5)
HTN	99 (66)	101 (58.4)	—	347 (78.2)	8 (40)	—	555 (70.5)	95 (63.8)	97 (54.5)	—	330 (75.5)	10 (50)	—	532 (67.9)
Pulmonary	29 (19.3)	47 (27.7)†	—	126 (28.4)	6 (30)	—	208 (26.4)	42 (28.2)	15 (8.4)†	—	133 (30.4)	3 (15)	—	193 (24.6)
HL	103 (68.7)	81 (47)	—	—	13 (65)	—	197 (57.4)	98 (65.8)	94 (52.6)	—	—	9 (45)	—	201 (57.9)
Renal	21 (14)	13 (7.5)	—	—	1 (5)	—	35 (10.2)	15 (10.1)	15 (8.4)	—	—	5 (25)	—	35 (10.1)
ASA classes 2 and 3	135 (90.0)	136 (75.3)	—	—	—	57 (100)	328 (86.3)	137 (91.9)	134 (78.6)	—	—	—	19 (100)	290 (83.8)
Cerebral or carotid artery disease	12 (8.0)‡	25 (14.5)‡	—	67 (15.1)	—	—	104 (13.6)	12 (8.1)‡	27 (15.2)‡	—	70 (16.0)	—	—	109 (14.3)
Aspirin	—	70 (40.5)	338 (54)	244 (55)†	—	—	652 (52.5)	—	72 (40.4)	325 (51.9)	277 (63.4)†	—	—	674 (54.3)
Beta-blockers	—	76 (43.9)	—	282 (63.5)	—	—	358 (58.0)	—	92 (51.7)	—	282 (64.5)	—	—	374 (60.8)
Statin	—	63 (37.3)	216 (34.9)	—	—	—	279 (34.9)	—	72 (41.9)	224 (36.0)	—	—	—	296 (36.8)
PAD	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Values are n (%), mean ± SD, or median (range). *Percentages are calculated only out of reported numbers. †p Value <0.05 for EVAR versus open repair comparisons; p Values for all other values are >0.05. ‡Carotid artery disease.

— = data not available; ASA = American Society of Anesthesiologists; EVAR = endovascular aneurysm repair; HL = hyperlipidemia; HTN = hypertension; PAD = peripheral artery disease; IV = inverse variance; other abbreviations as in Table 1.

The p value threshold for statistical significance was set at 0.05 for effect sizes. Analyses were conducted using features on RevMan (version 5.0, The Nordic Cochrane Center, Copenhagen, Denmark) and StatsDirect (version 2.7.8, Cheshire, England). The study was performed in accordance with the recommendations set forth by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) work groups (27).

Results

A total of 497 abstracts were identified by the screening electronic search strategy, of which 25 full-text articles met the eligibility for assessment. A total of 10 papers (reporting on 6 studies at different follow-up points) met the inclusion criteria of prospective randomized control trials (RCT) evaluating OSR versus EVAR. Figure 1 depicts the results of the search strategy, and Table 1 summarizes the included studies.

The DREAM (Dutch Randomized Endovascular Aneurysm Management) Trial Group published 3 papers on the same randomized patient groups at 30-day, 2-year, and 6-year (median) follow-up; EVAR-1 (United Kingdom Endovascular Aneurysm Repair-1) Trial Investigators also published 3 papers, at 30-day, 2-year, and 4-year (median) follow-up; these 2 trials were the first large randomized trials reporting on outcomes of OSR versus EVAR, besides having the longest follow-up periods among included RCT. A total of 2,899 patients with AAA repair procedures, 1,470 treated with EVAR and 1,429 undergoing OSR, were analyzed. All included studies have available results at different points; therefore, we opted to analyze them at short-term (30-day), intermediate-term (up to 2 years), and long-term (3 years or longer) follow-up.

The baseline characteristics between the 2 groups were similar in weighted analysis among all studies (Table 2). In general, the baseline characteristics were well matched between the 2 groups in all studies; only imbalances were: 1) more instances of pulmonary comorbidity in the EVAR group in 1 study (10); and 2) more pre-operative aspirin use in the OSR group in another (13).

Procedure-related variables and acute events are summarized in Table 3. There were no differences in crossover and immediate conversion (both rates very low). Length of hospitalization and intensive care unit stay were significantly shorter with EVAR, whereas general anesthesia was more frequent with the OSR group. There were no differences in reported acute cerebrovascular complications, cardiac complications, and renal complications.

Survival analysis. The 30-day all-cause mortality was lower with EVAR (RR: 0.35, 95% CI: 0.19 to 0.64); all such mortality is considered procedure-related (and therefore AAA-related). At intermediate-term follow-up (cumulative results up to 2 years following procedure), the survival

Table 3. Procedure-Related Variables and Complications

Study/First Author (Ref. #)	EVAR						Open Repair						
	ACE (12)	DREAM (14)	EVAR-1 (16)	OVER (17)	Soulez et al. (20)	Lottman et al. (18)	Total*	ACE (12)	DREAM (14)	EVAR-1 (16)	OVER (17)	Soulez et al. (20)	Lottman et al. (18)	Total*
Patients, N	150	173	543	444	20	57	1,387	149	178	539	437	20	19	1,342
Crossover (before or after start)	4 (2.7)	4 (2.3)	4 (0.7)	12 (0.3)	0 (0)	1 (1.8)	25 (1.8)	17 (1.13)	4 (2.25)	17 (3.15)	13 (3.0)	0 (0)	0 (0)	51 (3.8)
Immediate conversion	0 (0)	3 (1.7)	4 (0.7)	1 (0.2)	0 (0)	1 (1.8)	9 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hospital stay, days	5.8 ± 5.5†	4 (3–6)†	—	3.0 (2.0–5.0)†	4.5 ± 2.4†	5 (2–21)†	—	10.4 ± 8.3†	10 (8–15)†	—	7.0 (6.0–10.0)†	11.5 ± 8.1†	11 (8–50)†	—
ICU stay, h	—	3 (0–20)†	—	24 (24–48)†	3.4 ± 11.3†	19 (8–90)	—	—	23 (21–47)†	—	96 (72–144)†	38.5 ± 33†	21 (16–360)	—
Type of anesthesia used														
General	141 (94.6)	94 (54.9)†	—	—	18 (90)	—	253 (74.4)	150 (100)	171 (98.3)†	—	—	20 (100)	—	341 (99.1)*
Local	4 (2.7)	68 (39.8)	—	—	1 (5)	—	73 (21.5)	0 (0)	2 (1.1)‡	—	—	0 (0)	—	2 (0.6)*
Regional	4 (2.7)	9 (5.3)	—	—	1 (5)	—	14 (4.1)	0 (0)	1 (0.6)‡	—	—	0 (0)	—	1 (0.3)*
Cerebrovascular complications§	1	1	—	7	—	—	10 (1.3)	1	2	—	4	—	—	5 (0.7)*
Cardiac complications§	6	3	—	6	—	—	17 (2.2)	4	2	—	12	—	—	21 (2.7)*
Renal complications§	3	2	—	5	—	—	8 (1.3)	1	2	—	3	—	—	4 (0.7)

Values are n (%), mean ± SD, or median (range). *Percentages are calculated only out of reported numbers. †p Values <0.05; no p values provided in other 2 studies. ‡Values reflect patients who crossed over from open to endovascular repair. §Complications are defined as cerebrovascular = stroke; cardiac = myocardial infarction, renal = renal failure; except in DREAM, wherein variables are not specified.
— = data not available; ICU = intensive care unit; other abbreviations as in Tables 1 and 2.

benefit was concordant but of marginal significance (RR: 0.78, 95% CI: 0.57 to 1.08); at long-term follow-up (cumulative results beyond 2 years), there was no difference (RR: 0.99, 95% CI: 0.85 to 1.15) (Fig. 2).

Analysis of AAA-related mortality at intermediate-term follow-up revealed a significantly lower rate with EVAR (RR: 0.46, 95% CI: 0.28 to 0.74); there was no significant difference at long-term follow-up (RR: 1.57, 95% CI: 0.20 to 12.35) (Fig. 3).

Secondary interventions related to the original AAA repair were consistently higher in the EVAR group at both intermediate-term (RR: 1.48, 95% CI: 1.06 to 2.08) and at long-term follow-up (RR: 2.53, 95% CI: 1.58 to 4.05) (Fig. 4).

Risk of bias assessment. We qualitatively assessed the risk of bias for all studies. The qualitative assessment was performed by evaluating various indicators of individual study using the Cochrane risk of bias tool (21). By visual inspection, most studies were classified as low risk of bias across all domains of study quality (Figs. 5A and 5B). Both the allocation concealment and the outcome blinding are not well addressed across the studies; this could be acceptable in similar trials that compare surgical procedures.

Sensitivity analysis. The overall effect calculated by either a random or fixed effects model yielded similar overall estimates for each of the endpoints. The influence of each study was estimated by sequentially deleting 1 study from the analysis and noting the degree to which the pooled estimate or the conclusions might be changed. We considered a study influential if its exclusion changed the estimation of the effect estimate by at least 20% among included trials. When omitting the ACE (ACE [Carotid Endarterectomy]) trial (12), or OVER (Open Versus Endovascular Repair) (17), all findings remained unchanged.

Omission of EVAR-1 (the largest trial in the series) (16), led to a change in our findings, making reintervention rate at intermediate follow-up no longer affected by randomiza-

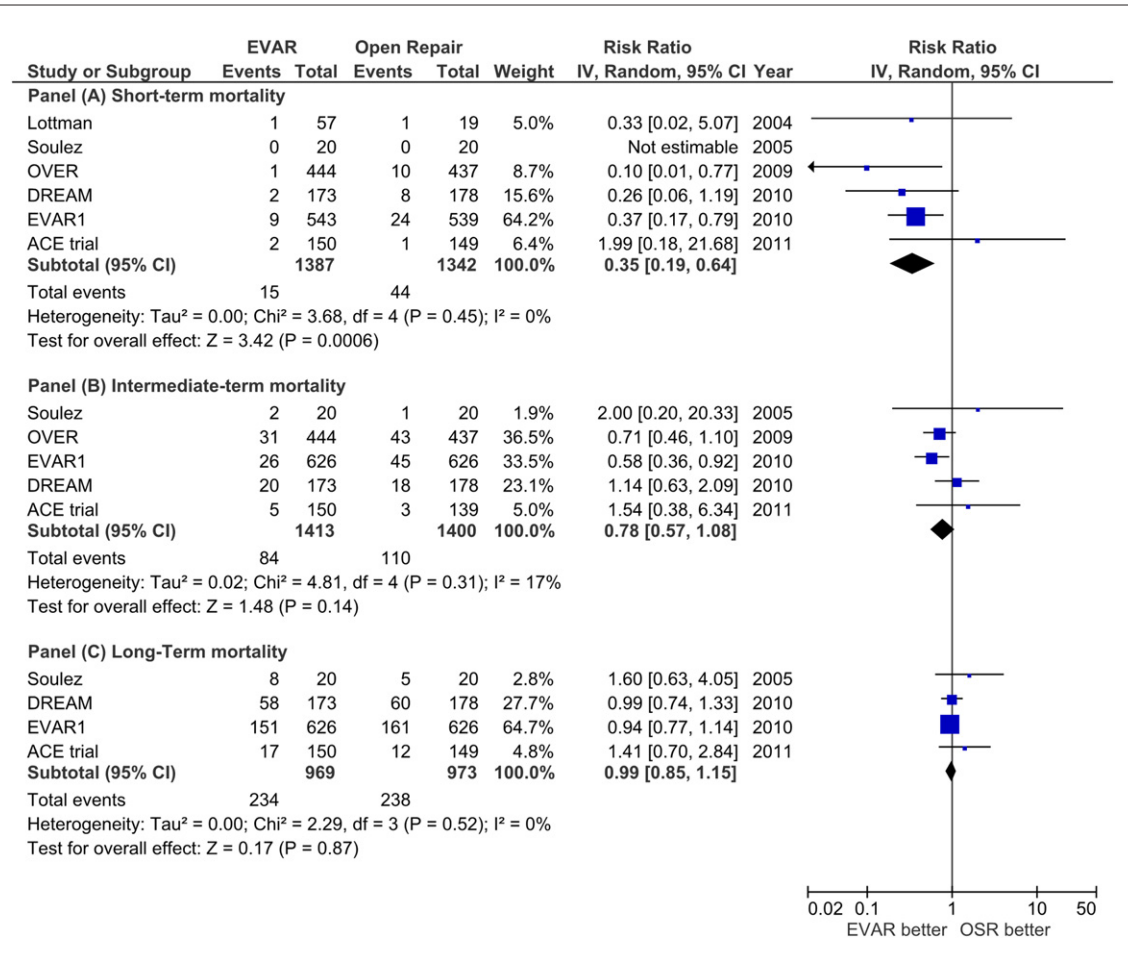

Figure 2. All-Cause Mortality

(A) Pooled mortality rates reported at 30-day post-procedure follow-up. **(B)** Cumulative outcomes reported at intermediate follow-up (up to 2 years after procedure). **(C)** Cumulative outcomes reported at follow-up of at least 3 years after procedure. CI = confidence interval(s); IV = intravenous; OSR = open surgical repair; other abbreviations as in Figure 1.

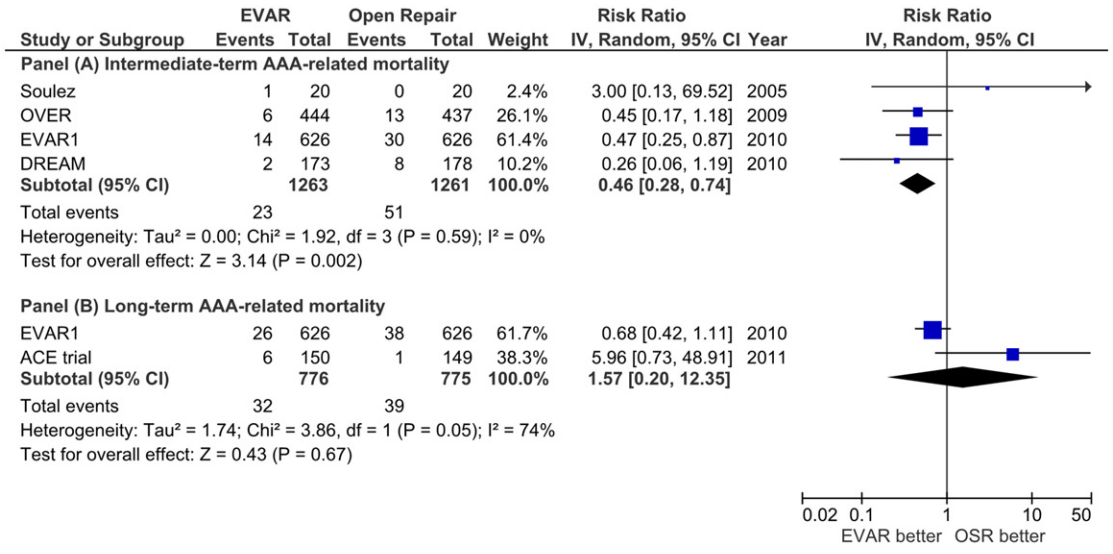

Figure 3. Aneurysm-Related Mortality

(A) Cumulative outcomes reported at intermediate follow-up (up to 2 years after procedure). **(B)** Cumulative outcomes reported at follow-up of at least 3 years after procedure. Abbreviations as in Figures 1 and 2.

tion to EVAR versus OSR, being that the RR = 1.81 (95% CI: 0.94 to 3.45), but otherwise yielded concordant results.

Omission of the DREAM trial, which has the longest period of follow-up time (14), led to a change in the results of intermediate-term follow-up analysis in favor of EVAR in both all-cause mortality (new values: RR: 0.69, 95% CI: 0.50 to 0.94, indicating survival advantage with EVAR) and reintervention rate (RR: 1.32, 95% CI: 0.99 to 1.75,

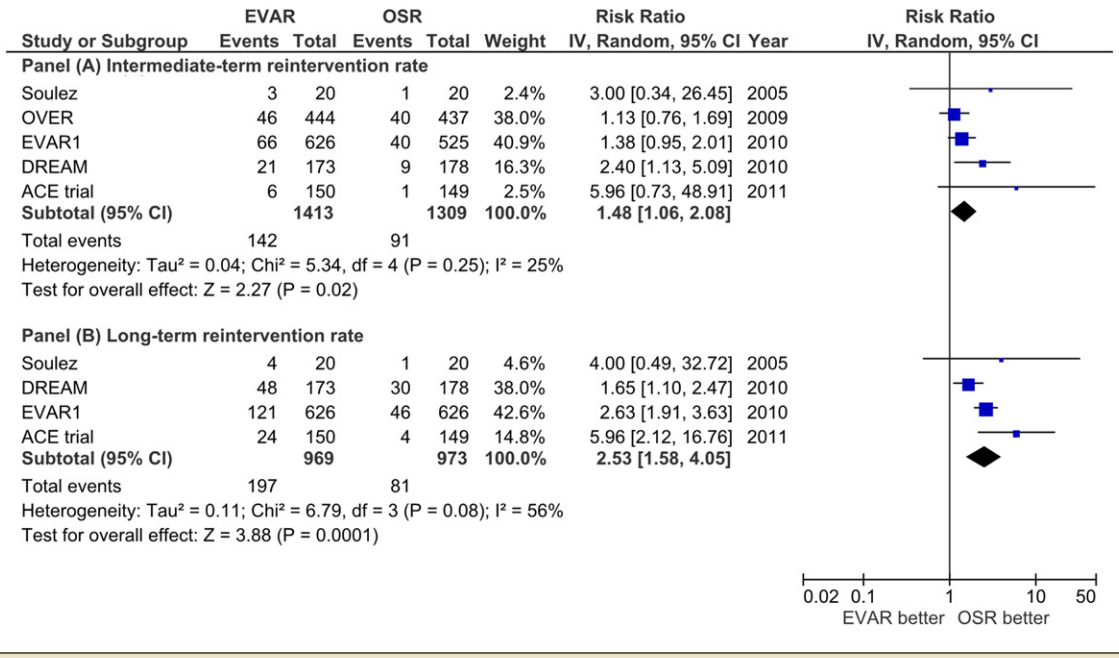

Figure 4. Reintervention Rates

(A) Cumulative outcomes reported at intermediate follow-up (up to 2 years after procedure). **(B)** Cumulative outcomes reported at follow-up of at least 3 years after procedure. Abbreviations as in Figures 1 and 2.

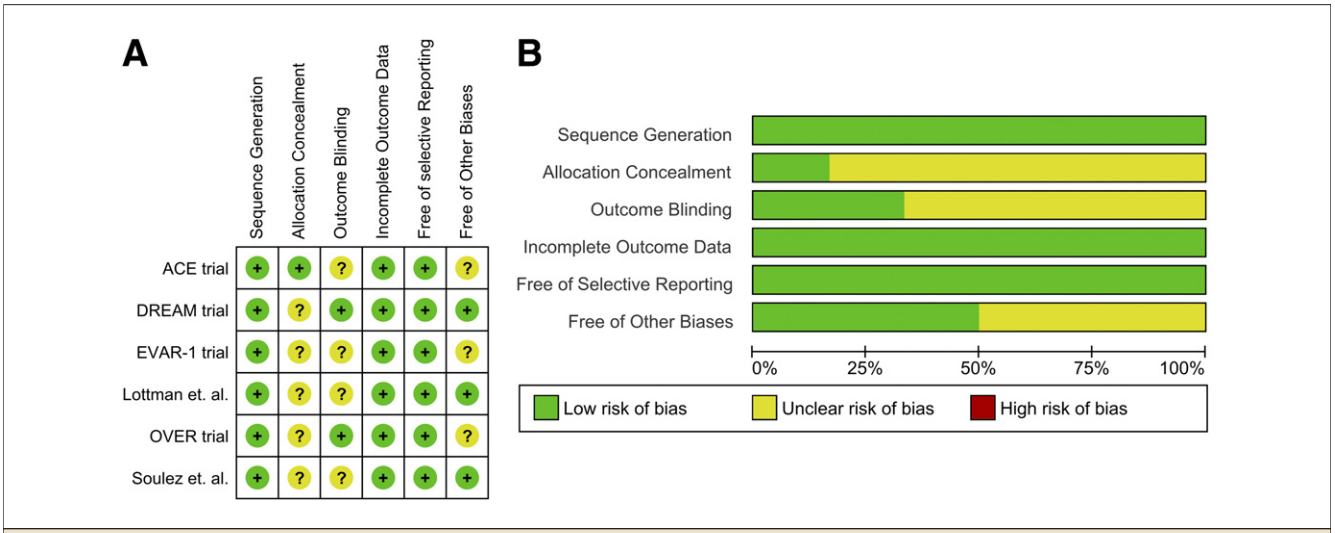

Figure 5. Risk of Bias

(A) Review authors' judgments about each risk of bias item for each included study. **(B)** Review authors' judgments about each risk of bias item presented as percentages across all included studies. Abbreviations as in Figure 1.

indicating absence of significant difference between the groups); other results remained qualitatively unchanged.

When evaluating for publication bias, Begg-Mazumdar and Egger bias indicators were calculated and did not reveal a statistically significant risk of publication bias for all-cause mortality, aneurysm-related mortality, or reintervention rates (Table 4), except for all-cause mortality at more than 3-year follow-up time. This asymmetry in the funnel plot was due to the 2 small trials by ACE (12) and Soulez et al. (20), both of which have wide confidence intervals and point estimates nonsignificantly in favor of OSR. Nevertheless, imputation of a small positive trial to achieve symmetry in the funnel plot for long-term mortality would not be expected to significantly alter the summary estimates in a meaningful way. The relative risk of 0.99 for long-term mortality was the result of the significantly larger DREAM and EVAR-1 trials.

Table 4. Begg-Mazumdar and Egger p Values for Publication Bias (Funnel Plot)

	30 Days	≤2 Years	≥3 Years
All-cause mortality			
Begg-Mazumdar	0.8167	0.8167	0.0833
Egger	0.9958	0.1743	0.0035
AAA-related mortality			
Begg-Mazumdar	—	0.8167	0.75
Egger	—	0.9958	0.611
Reintervention			
Begg-Mazumdar	—	0.8167	0.75
Egger	—	0.084	0.5245

Discussion

This meta-analysis of prospective randomized control trials comparing endovascular to open surgical AAA repair provides an aggregate analysis of the currently available body of evidence. An early survival advantage of endovascular repair within the first 30 days after the procedure has been demonstrated. The present study extends this advantage by documenting a statistically significant reduction in intermediate-term AAA-related mortality with EVAR versus OSR. No differences at long-term mortality were found by the analysis of the limited number of studies with available clinical data beyond 2 years after the procedure. The survival benefit with EVAR at early and intermediate-term follow-up was accompanied by a higher rate of reintervention in the EVAR group. According to early surgical series, the mortality was mainly due to myocardial infarction, stroke, and cardiovascular death late (28), and the AAA presence has been considered as a degenerative condition of the aortic wall (29).

Of the studies included, none was designed to determine whether the reinterventions could have in any way contributed to the enhanced durability of endograft technique or might have led to further complications. Therefore, we can offer no definitive guidance on how to distinguish between these 2 possibilities from this report. Its association with lower intermediate AAA-related mortality might make one believe that the reinterventions were not in vain; however, this statement would need verification with patient-level data analysis, which was not available. Another confounding factor in relation to reintervention is the fact that EVAR routinely requires imaging follow-up (preferably with com-

puterized tomography or ultrasound), whereas OSR requires limited or no imaging follow-up (30).

Several important factors common to these trials help establish a fair comparison between the 2 treatment modalities. The suitability of the patients to undergo either an open or endovascular repair has allowed comparison of patients with similar aneurysm anatomy and overall health status. The randomized, prospective nature of these studies and the very low crossover and conversion rates have minimized the potential for selection bias. At present, these trials have reported results at a wide range of post-procedure periods (0.5 to 10 years); thus an analysis of results according to clinically meaningful follow-up periods (perioperative short term, intermediate term, long term) was adopted in an attempt to appropriately maximize the utilization of available data and to afford sufficient power to perform clinically meaningful comparisons. In previous reviews (31–33), EVAR was associated with lower operative mortality and similar mid-term mortality as OSR. We extended these observations in documenting significantly lower AAA-related mortality with EVAR at the intermediate term and similar long-term mortality with both technical approaches. We believe that our paper has the largest number of included RCT and the most updated data on this specific topic.

These results, however, cannot be generalized to all patients with AAA. A key patient-selection criterion of these studies was a low or intermediate surgical risk. Excluding high-risk patients should have altered mortality outcomes and complication rates in both treatment groups. The requirement for aortic anatomy amenable to either open or endovascular repair can also potentially improve outcomes in both treatment arms, as mortality rates were generally lower in the randomized trials than in retrospective cohort studies (1–15).

Study limitations. An inherent limitation of this meta-analysis is the inclusion of the EVAR procedure across time in the different trials. Endovascular devices and EVAR technique have undergone significant refinements and improvements since the first-generation devices. Physician experience and their criteria for determining the appropriateness for endovascular repair have also changed with time. These improvements have the potential to decrease complications requiring reintervention and also to increase long-term survival after EVAR. Hospital systems have also improved significantly over time, as is evident from the rather long average length of in-hospital stay after EVAR in all the trials included in our analysis, compared with the current clinical practice (largely targeting a single-day hospital stay with no need for intensive care unit admission for routine cases). Hence, we judged that the data available would not be generalizable to contemporary practice even if an economic analysis might have been feasible. We planned to test by means of meta-regression the impact of device type and minimum sheath size for a given device on the results of the meta-analysis, but unfortunately, controlling for those modifiers was not reachable.

Conclusions

The medical therapy for cardiovascular disease has improved significantly (e.g., statins, hypertension treatment, smoking-cessation measures, antiplatelet agent, and so on) and allows greater efficacy in preventing cardiovascular morbidity and mortality over time. This would likely suppress the longer-term events and tend to equalize the long-term survival after either type of procedure. The appropriate utilization of medical therapy variables in an AAA-treatment meta-analysis would necessitate the knowledge of patient-level data of medical therapy prescription and adherence, not only in-hospital (during index procedure), but also during the long-term follow-up. Such data were not available in any of the studies included in the present analysis. Patients included in randomized trials are usually followed much more aggressively than in routine practice; this means that reintervention rates in the real world for EVAR are likely to be lower than the RCT-based estimates.

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Key Words: abdominal aortic aneurysm ■ aortic aneurysm ■ endovascular procedure ■ general surgery ■ vascular disease ■ vascular surgical procedures.

APPENDIX

For definitions of outcomes of interest and protocol, please see the online version of this paper.