

Efficacy and Safety of Endovascular Fenestrated and Branched Grafts Versus Open Surgery in Thoracoabdominal Aortic Aneurysm Repair

An Updated Systematic Review, Meta-analysis, and Meta-regression

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Objective: To provide an updated systematic review and meta-analysis with meta-regression of efficacy and safety of fenestrated/branched endovascular repair of thoracoabdominal aortic aneurysms (TAAAs) compared with open repair.

Background: Endovascular repair of TAAAs may be a promising alternative to open surgery by reducing invasiveness and expanding the eligible population, but evidence remains limited.

Methods: We applied “Prepared Items for Systematic Reviews and Meta-analysis” guidelines to retrieve, quantitatively pool, and critically evaluate the efficacy and safety (including 30-day mortality, reintervention, spinal cord injury [SCI], and renal injury) of both approaches. Original studies were retrieved from PubMed, Embase, and Cochrane Library until April 20, 2022, excluding papers reporting <10 patients. Pooled proportions and means were determined using a random-effect model. Heterogeneity between studies was evaluated with I^2 statistics.

Results: Sixty-four studies met the predefined inclusion criteria. Endovascular cohort patients were older and had higher rates of comorbidities. Endovascular repair was associated with similar proportions of mortality (0.07, 95% confidence intervals [CI]: 0.06–0.08) compared with open repair (0.09, 95% CI: 0.08–0.12; $P = 0.22$), higher proportions of reintervention (0.19, 95% CI: 0.13–0.26 vs 0.06, 95% CI: 0.04–0.10; $P < 0.01$), similar proportions of transient SCI (0.07, 95% CI: 0.05–0.09 vs 0.06, 95% CI: 0.05–0.08; $P = 0.28$), lower proportions of permanent SCI (0.04, 95% CI: 0.03–0.05 vs 0.06, 95% CI: 0.05–0.07; $P < 0.01$), and renal injury (0.08, 95% CI: 0.06–0.10 vs 0.13, 95% CI: 0.09–0.17; $P = 0.02$). Results were affected by high heterogeneity and potential publication bias.

Conclusions: Despite these limitations and the lack of randomized trials, this meta-analysis suggests that endovascular TAAA repair could be a safer alternative to the open approach.

Key words: endovascular repair, fenestrated and branched grafts, systematic review and meta-analysis, thoracoabdominal aortic aneurysm

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Thoracoabdominal aortic aneurysms (TAAAs) are defined as those aortic aneurysms that involve the renovisceral arteries.^{1,2} Overall, TAAAs account for around 10% of all aortic aneurysms,³ and, despite their rarity, their treatment is burdened by considerable mortality and morbidity.⁴ Since the 1950s, the standard of care has been open surgical repair.^{5,6} In 2001, endovascular repair of the TAAAs was introduced to reduce the invasiveness of treatment, and the technology has been continuously evolving ever since.⁷ While open TAAA repair can only be proposed to patients with acceptable operative risk, potential advantages of endovascular repair include expanding the cohort of patients amenable to treatment^{8,9} and reducing overall costs due to a lower need for intensive care unit (ICU) admission and rehabilitation, and shorter hospitalization.¹⁰

Although previous studies suggest that endovascular TAAA repair could be a promising alternative to the open approach,^{4,11} evidence is still limited due to the variety of endovascular approaches, extent and urgency of TAAA repair, differing patient populations, lack of prospective randomized studies, and minimal medium and long-term follow-up data on the endovascular repair. Further research is needed to assess what clinical, economic, and organizational benefits are driven by each approach.^{9,12} Therefore, the main purpose of this updated systematic review and meta-analysis was to investigate the efficacy and safety of endovascular fenestrated and branched grafts, as compared with open repair in patients with TAAA, accounting for the high heterogeneity of the data available in the literature.

METHODS

We followed the “Prepared Items for Systematic Reviews and Meta-analysis” guidelines^{13,14} and the “Meta-analysis of Observational Studies in Epidemiology” guidelines.¹⁵ A study protocol was developed in advance by the research team and registered in the PROSPERO database (ID number: CRD42021288697), a prospective international registry of systematic reviews funded by the National Institute of Health Research. The research question, search strategy, inclusion and

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TABLE 1. A Priori Defined Inclusion and Exclusion Criteria According to the PICOS Framework

Search strategy	Details
Inclusion criteria	<p>P: adult patients (≥ 18 yr of either sex) affected by a TAAA</p> <p>I: the patient who received an endovascular repair (with off-the-shelf or custom-made F/BEVAR); patient who received open surgical repair (aneurysmectomy and aortic reconstruction with a surgical graft)</p> <p>O: measures of efficacy, effectiveness and safety outcomes of different types of treatment of TAAAs</p> <p>S: both randomized controlled trials and observational studies, reporting original data on at least 10 patients or data from quantitative analysis (both clinical and economic)</p>
Exclusion criteria	<p>P: patients with a juxtarenal or pararenal aortic aneurysm; patients who are pregnant or lactating; patient <18 yr of age</p> <p>I: patients treated with a hybrid (open + endovascular) approach, including open surgical retrograde revascularization of renovisceral arteries, followed by ligation at the ostia of renovisceral arteries aneurysm and final endovascular exclusion with an endograft; patients treated with other endovascular techniques besides fenestrated or branched technology (eg, physician-modified endograft, parallel grafts also described as chimney/snorkel/sandwich techniques)</p> <p>S: studies not published as peer-reviewed, systematic review, meta-analysis, book, book chapter, thesis, protocol, no full-text papers (abstract, conference paper, letter, commentary, erratum, correction, editorial, and note), clinical guidelines and previously published HTA reports, that will be screened to retrieve relevant original studies; studies not reporting original data on TAAAs repair by means of endovascular fenestrated and/or branched (F/BEVAR) grafts; studies reporting on in vitro or animal data</p>
Language filter	English
Time filter	From inception through April 20, 2022
Database	PubMed/Medline, EMBASE, Cochrane Library

F/BEVAR indicates fenestrated/branched endovascular aortic repair; HTA, Health Technology Assessment; PICOS, population, intervention, comparison, outcomes, and study design; TAAA, thoracoabdominal aortic aneurysm.

exclusion criteria, primary outcomes, strategy for data extraction, and data synthesis were determined in the protocol. In particular, our research question was about the efficacy and safety of endovascular fenestrated and branched grafts, as compared with open repair in patients with TAAAs.

Search Methods and Inclusion Criteria

Studies identified by searching the electronic databases PubMed/Medline, Embase, and the Cochrane Library, published up to April 20, 2022, and written in English with available full text, were included. The search strategy was first developed in PubMed/Medline and then adapted for use in the other databases (Table 1). Briefly, we used a combination of free text and exploded MeSH headings, identifying: (1) the concept of “endovascular fenestrated/branched endograft,” (2) “TAAA,” and (3) “open.” Our inclusion criteria were limited to both randomized controlled trials and observational studies, reporting original data on at least 10 patients or data from quantitative analysis (both clinical and economic) and measures of efficacy and safety outcomes of different types of treatment for TAAA. Studies considering off-the-shelf or custom-made fenestrated/branched endovascular TAAA repair and open surgical repair or both of them were included. All studies reporting any of the following in-hospital or 30-day outcomes were included: technical success, mortality, reintervention, hospital length of stay (LoS), ICU LoS, transient spinal cord injury (SCI), permanent SCI, renal injury, respiratory insufficiency, stroke, cardiac complications. We excluded patients treated with a hybrid (open + endovascular) approach or other endovascular techniques besides fenestrated or branched technology and reports of juxta and pararenal abdominal aortic aneurysms. Studies that included thoracic and abdominal aortic aneurysms and TAAAs were included only if TAAA-specific outcomes were reported. We excluded opinion papers (ie, editorials, narrative reviews, commentaries, and letters to the Editor) not providing original data. Systematic reviews were also excluded but screened to retrieve relevant original studies.

Study Selection, Data Extraction, and Quality Appraisal

Identified studies were independently reviewed for eligibility by 2 authors in a 2-step process (G.P.V., A.G., D.B., and S.C.); a first screening was performed based on the title and abstract. Then, full texts were retrieved for a second screening. At both stages, disagreements among reviewers were resolved by consensus and discussed with a fifth author (A.O.). Articles written by the same authors referring to identical study periods and reporting the same number of participants were excluded. Data were independently extracted by 4 authors (G.P.V., A.G., C.B., D.B., and S.C.), supervised by a sixth author (A.O.), using an ad-hoc developed data extraction spreadsheet. The data extraction spreadsheet was piloted on 10 randomly selected papers and modified accordingly. Data extraction included: full reference details, country of study conduction, study design, study period, type of surgical repair, sample size, mean age, number of male patients, and outcomes of interest, including both efficacy and safety variables. Moreover, if available, characteristics of the study population were extracted as the number of events and corresponding relative frequencies, including the number of patients with prior vascular intervention, diabetes mellitus, hypertension, smoking habits, renal insufficiency, chronic obstructive pulmonary disease (COPD), connective tissue disease or Marfan syndrome, coronary artery disease, cerebrovascular disease, dyslipidemia, Crawford classification (type I, II, III, and IV), and urgent repair. Quantitative data were reported as the number of events for each study population characteristic or outcome (for discrete variables) or as the mean, followed by corresponding confidence intervals (CI) and standard deviation (SD) (for continuous variables). Corresponding authors were contacted by email in the event of incomplete available data.

Quality appraisal of included studies was carried out by applying the New Ottawa Scale for cohort or case-control studies, respectively.

Data Pooling and Meta-analysis

We performed descriptive analysis to report and pool the characteristics of the included studies using relative frequencies and weighted means, separately for endovascular and open

repair. With regard to the prespecified outcomes of interest, we would expect variability between studies, for example, by study population; we, therefore, applied random-effect meta-analyses to acquire estimates of the proportion of the selected outcomes rather than to assume a single true value in a fixed-effect approach.¹⁶ Pooled effect sizes (ESs) were calculated as pooled event rates for discrete variables or as pooled means for continuous variables, separately for endovascular and open repair. Heterogeneity was assessed using the I^2 statistic and visual inspection of forest plots. We assessed publication bias with funnel plot visual inspection¹⁷ and the Egger test.¹⁸ A “trim and fill” method was used if publication bias was detected^{19,20} to estimate potential missing studies that contribute to the funnel plot’s asymmetry.²¹ This method assumes that the most extreme ES studies have not been reported, biasing the overall ES estimates.²²

Meta-regression analysis was conducted to investigate sources of heterogeneity and to evaluate the associations between the ES and potential modifier variables, including patients’ characteristics (ie, age, male sex, prior vascular intervention, diabetes, hypertension, smoking habit, and renal insufficiency). Meta-analyses and meta-regressions were conducted using ProMeta3 software (Internovi).

Differences in pooled proportions and means between endovascular versus open repair were calculated using the z test on Stata software version 16.0 (Stata Corporation). Statistical significance was set at $P = 0.05$ for all analyses.

RESULTS

Characteristics of Included Studies

We identified 943 studies by searching the selected databases and listing references of relevant articles. After removing duplicates, 606 records were retrieved. Papers were screened and selected, as illustrated in Figure 1 (477 records were excluded after the title and abstract screening, 6 reports were not retrieved in full text, and 59 were excluded with reasons), resulting in 64 papers meeting our defined inclusion criteria.^{10,23–85} Characteristics of the included studies are reported in Supplemental Table S1 (Supplemental Digital Content 1, <http://links.lww.com/SLA/E987>).

Studies ($n = 64$) were published between 2006 and 2021, with over 15% ($n = 11$, 17.2%) published in the last 3 years.^{29,37,49,51,54,60,65,72,74,81,82} The majority of the studies ($n = 28$, 43.8%) were conducted in Europe (Italy, $n = 12$; Germany, $n = 7$; Netherlands, $n = 3$; Portugal, $n = 1$; France, $n = 3$; United Kingdom, $n = 2$)^{23,26–29,31,43,45–51,54,56–59,64,66,70,72,76,82,84} and in the USA ($n = 27$, 42.2%).^{10,24,25,32,33,35–40,52,53,60–63,65,67,68,71,73,75,77,79,81,85} Five studies were conducted in Japan,^{44,69,78,80,83} two in Brazil,^{41,42} one in Canada,⁷⁴ and one in Serbia.³⁴

All 64 studies had a longitudinal design; their study period ranged from 1 to 39 years, with most of them ($n = 43$, 67.2%) covering <10 years. All studies were retrospective cohort studies, except for one with both retrospective and prospective studies³³ and one with a case-control study design.²⁸ Overall, the sample sizes of included studies ranged from 21⁵¹ to 3619 patients,⁷⁷ with a total sample size of 23,670 patients (mean: 370 patients, median: 112 patients).

Details on included study populations are reported in Supplemental Table S1 (Supplemental Digital Content 1, <http://links.lww.com/SLA/E987>), which reports information on the weighted mean age and sex distribution of the sample patients,

and in Supplemental Table S2 (Supplemental Digital Content 1, <http://links.lww.com/SLA/E987>), which includes details on comorbidities, urgency of treatment, and type of aneurysm addressed according to the Crawford classification.

The included studies’ quality score is also reported in Supplemental Table S1 (Supplemental Digital Content 1, <http://links.lww.com/SLA/E987>). The mean quality score was 7.2/9; 44 studies (68.8%) obtained a score of 7/9, whereas 20 studies (31.2%) obtained a score of 8/9.

Nine studies (14.1%) reported separate data on both endovascular and open TAAA repair, thus resulting in two different data sets each. As a consequence, we included 73 data sets in our review; 40 data sets (54.8%) on endovascular repair and 33 (45.2%) on open repair. ESs were reported in all the included studies (100%) as the number of events and corresponding proportion for technical success, mortality, reintervention, transient and permanent SCI, renal injury, respiratory insufficiency, stroke, and cardiac complications, while as mean days and SD for hospital LoS and ICU LoS. In all the 64 studies (100%), efficacy and safety outcomes were reported as postoperative, that is, as 30-day outcomes, which are shown in Supplemental Table S3 (Supplemental Digital Content 1, <http://links.lww.com/SLA/E987>) and Supplemental Table S4 (Supplemental Digital Content 1, <http://links.lww.com/SLA/E987>).

Endovascular Thoracoabdominal Aortic Aneurysm Repair: Quantitative Reporting, Meta-analysis, and Meta-regression

Quantitative pooling of effect estimates was conducted on the data sets with available data on the considered outcomes, as reported in Table 2; included data sets ranged from 36 for mortality analysis to 6 for ICU LoS analysis. Consequently, included populations differed from 5814 included in the mortality estimates to 512 for ICU LoS. The weighted mean age of the included studies’ populations was 70.4 (95% CI: 66.7–74.2). The weighted mean proportion was 47.1% (95% CI: 37.6%–56.6%) for prior vascular intervention, 82.4% (95% CI: 76.9%–87.8%) for hypertension, 14.5% (95% CI: 12.1%–16.9%) for diabetes, 21.2% (95% CI: 15.8%–26.6%) for renal insufficiency, 32.8% (95% CI: 26.0%–39.5%) for COPD, and 44.6% (95% CI: 37.1%–52.1%) for coronary artery disease.

Of the 40 data sets reporting data on endovascular repair, 23 data sets (57.5%) reported procedural success, with a pooled proportion of technical success across data sets of 0.91 (95% CI: 0.86–0.94, $I^2 = 78.62$, $P < 0.001$). Perioperative mortality was reported in 36 of 40 (90%) of the included data sets. The pooled proportion of perioperative mortality for endovascular TAAA repair was 0.07 (95% CI: 0.06–0.08, $I^2 = 62.28$, $P < 0.001$; Fig. 2A). The estimate for reintervention proportion was determined from 17 of 40 data sets (42.5%) and was 0.19 (95% CI: 0.13–0.26, $I^2 = 89.93$, $P < 0.001$).

Hospital LoS was available from 15 of 40 data sets (37.5%); the pooled mean was 8.67 days (95% CI: 6.85–10.48, $I^2 = 89.85$, $P < 0.001$). Only six data sets out of 40 reported ICU LoS; the pooled mean was 7.18 days (95% CI: 4.16–10.20, $I^2 = 97.43$, $P < 0.001$).

Thirty data sets (75%) reported transient SCI data after endovascular TAAA repair; the overall pooled estimate for the proportion of transient SCI events was 0.07 (95% CI: 0.05–0.09, $I^2 = 75.44$, $P < 0.001$), whereas the overall estimate for permanent SCI was 0.04 (95% CI: 0.03–0.05, $I^2 = 0$, $P < 0.001$) derived from 16 data sets (40%). Estimates of the proportion for postoperative renal injury was 0.08 (95% CI: 0.06–0.10, $I^2 = 85.09$, $P < 0.001$)

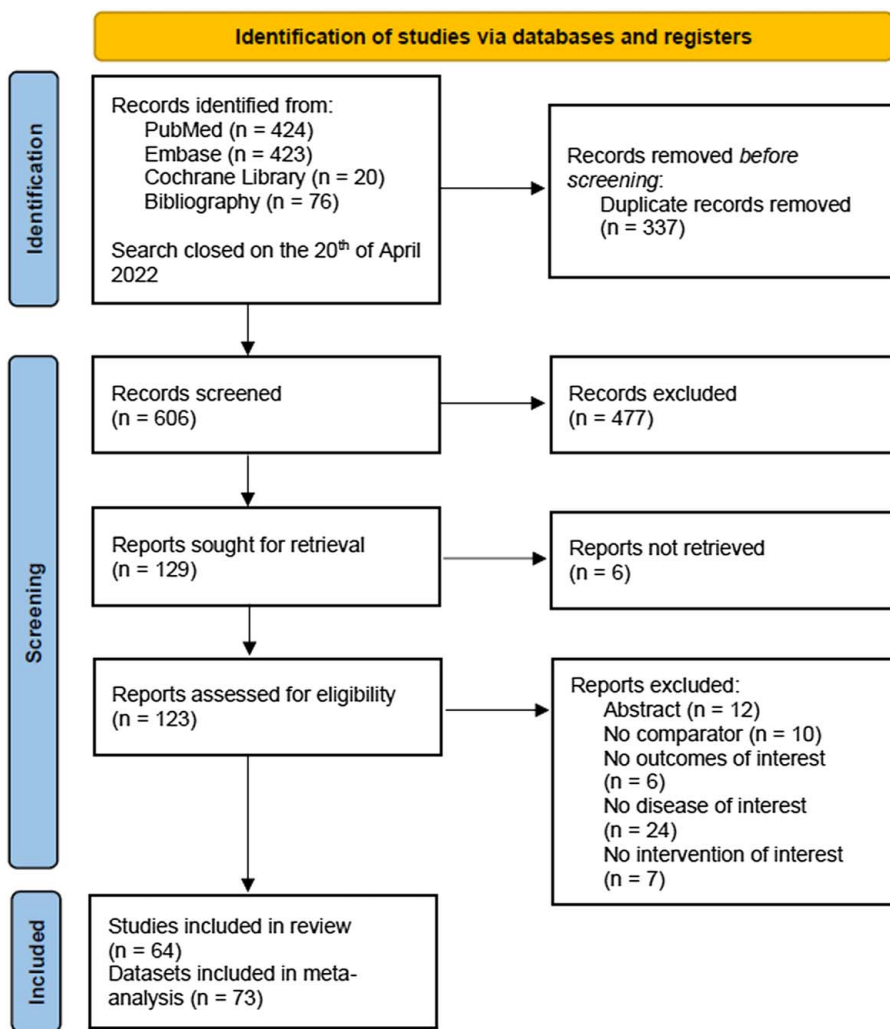


FIGURE 1. Flow diagram of the studies selection process.

available from 25 of 40 data sets (62.5%). Data on respiratory insufficiency were reported in 19 data sets out of 40 (47.5%); the proportion estimate was 0.07 (95% CI: 0.05–0.09, $I^2 = 71.25$, $P < 0.001$). The proportion estimate for stroke was 0.03 (95% CI: 0.03–0.04, $I^2 = 18.53$, $P < 0.001$) derived from 19 data sets (47.5%). The ES for cardiac complications proportion was 0.05 (95% CI: 0.04–0.07, $I^2 = 77.46$, $P < 0.001$) as a pooled estimate from 19 data sets (47.5%).

The funnel plots resulted asymmetric at visual inspection, showing potential publication bias, confirmed by the Egger linear regression test only for mortality (intercept -0.96 , $t = -2.23$, $P = 0.033$; Fig. 2B) and renal injury (intercept -2.24 , $t = -3.50$, $P = 0.002$). However, the ES estimates changed after the trim and fill method, and several data sets were trimmed in the right half of the funnel plot also for ICU LoS, reintervention, transient and permanent SCI, respiratory insufficiency, stroke, and cardiac complications, whereas for technical success some data sets were trimmed on the left of the funnel plot. No unpublished data sets were retrieved for hospital LoS (data not shown).

The results from the random-effect meta-regression used to evaluate the association between the outcomes and selected potential moderators showed a significant association between

age and mortality (slope = -0.06 , $P = 0.019$), renal injury (slope = -0.10 , $P = 0.039$), and transient SCI (slope = -0.13 , $P = 0.022$). Significant associations between hypertension and respiratory insufficiency (slope = 2.92 , $P = 0.027$) and between prior renal insufficiency and stroke (slope = -3.79 , $P = 0.038$) were retrieved. No further significant associations were found (Supplemental Digital Content Table S5, <http://links.lww.com/SLA/E987>).

Open Thoracoabdominal Aortic Aneurysm Repair: Quantitative Reporting, Meta-analysis, and Meta-regression

Quantitative pooling of effect estimates was conducted on the data sets with available data on the considered outcomes, as reported in Table 3; included data sets ranged from 32 for mortality analysis to five for ICU LoS analysis. Consequently, included populations differed from 17,333 included in the mortality estimates to 5875 for ICU LoS. The weighted mean age of the included studies' populations was 65.5 (95% CI: 62.8–68.2). The weighted mean proportion was 21.4% (95% CI: 15.4%–27.4%) for prior vascular intervention, 80.1% (95% CI: 72.4%–87.8%) for hypertension, 9.4% (95% CI: 7.2%–11.5%) for

TABLE 2. Meta-analyses Assessing TAAA Endovascular Repair Outcomes

Type of analysis	No. of included data sets (k)	ES	95% CI, P	No. of participants	χ^2 ; df	<i>I</i> ²	P	Intercept*	<i>t</i> *	<i>P</i> *
Technical success†	23	0.91	0.86–0.94, <0.001	1886	102.92; 22	78.62	<0.001	1.12	1.42	0.169
Mortality†	36	0.07	0.06–0.08, <0.001	5814	92.78; 35	62.28	<0.001	–0.96	–2.23	0.033
Reintervention†	17	0.19	0.13–0.26, <0.001	1886	158.86; 16	89.93	<0.001	–1.34	–0.76	0.458
Hospital LoS‡	15	8.67	6.85–10.48, <0.001	2669	137.91; 14	89.85	<0.001	1.57	1.10	0.291
ICU LoS‡	6	7.18	4.16–10.20, <0.001	512	194.49; 5	97.43	<0.001	7.44	2.30	0.083
Transient SCI†	30	0.07	0.05–0.09, <0.001	3529	118.08; 29	75.44	<0.001	–1.43	–1.82	0.080
Permanent SCI†	16	0.04	0.03–0.05, <0.001	1735	7.20; 15	0.00	0.952	–0.41	–1.13	0.279
Renal injury†	25	0.08	0.06–0.10, <0.001	4711	160.94; 24	85.09	<0.001	–2.24	–3.50	0.002
Respiratory insufficiency†	19	0.07	0.05–0.09, <0.001	4121	62.61; 18	71.25	<0.001	–0.20	–0.24	0.809
Stroke†	19	0.03	0.03–0.04, <0.001	3632	22.09; 18	18.53	0.228	–0.29	–0.65	0.525
Cardiac complications†	19	0.05	0.04–0.07, <0.001	4277	79.86; 18	77.46	<0.001	–0.98	–1.23	0.234

*Egger linear regression test.

†Values are reported as proportions.

‡Values are reported as means (days).

CI indicates confidence intervals; df, degree of freedom; ES, effect size; ICU, intensive care unit; LoS, length of stay; QS, quality score; SCI, spinal cord injury; TAAA, thoracoabdominal aortic aneurysm.

diabetes, 11.2% (95% CI: 5.9%–16.4%) for renal injury, 28.1% (95% CI: 20.3%–35.9%) for COPD, and 32.1% (95% CI: 25.9%–38.3%) for coronary artery disease.

Perioperative mortality for open repair was reported in 32 of 40 (96.9%) of the included data sets. The pooled estimate of the proportion of perioperative mortality of these observational data sets of endovascular TAAA repair was 0.09 (95% CI: 0.08–0.12, *I*² = 93.91, *P* < 0.001; Fig. 3A). The estimate for reintervention proportion was determined from 14 of 33 data sets (42.4%) and was 0.06 (95% CI: 0.04–0.10, *I*² = 95.77, *P* < 0.001) of cases.

Hospital LoS was available from 11 of 33 data sets (33.3%); the pooled mean for hospital LoS was 12.91 days (95% CI: 10.38–15.44, *I*² = 87.61, *P* < 0.001). Only five data sets out of 33 reported ICU LoS; the pooled mean was 10.14 days (95% CI: 6.80–13.48, *I*² = 96.90, *P* < 0.001).

Thirteen data sets (39.4%) reported transient SCI data after open TAAA repair; the overall pooled estimate for the proportion of transient SCI events was 0.06 (95% CI: 0.05–0.08, *I*² = 82.23, *P* < 0.001), whereas the overall estimate for permanent SCI was 0.06 (95% CI: 0.05–0.07, *I*² = 76.73, *P* < 0.001) derived from 21 data sets (63.6%). Estimates of the proportion for postoperative renal injury was 0.13 (95% CI: 0.09–0.17, *I*² = 97.73, *P* < 0.001) available from 24 of 33 data sets (72.7%). Data on respiratory insufficiency were reported in 21 data sets out of 33 (63.6%); proportion estimate was 0.19 (95% CI: 0.14–0.25, *I*² = 98.37, *P* < 0.001). The proportion estimate for stroke was 0.05 (95% CI: 0.04–0.06, *I*² = 82.13, *P* < 0.001) derived from 22 data sets (66.7%). The ES for cardiac complications proportion was 0.06 (95% CI: 0.04–0.09, *I*² = 97.97, *P* < 0.001) as a pooled estimate from 18 data sets (54.5%).

The funnel plots resulted asymmetric at visual inspection, showing potential publication bias, confirmed by the Egger linear regression test only for mortality (intercept: –2.59, *t* = –2.64, *P* = 0.013; Fig. 3B), renal injury (intercept: –4.15, *t* = –2.33, *P* = 0.030), and cardiac complications (intercept: –5.25, *t* = –2.85, *P* = 0.011). However, the ES estimates changed after the trim and fill method, and several data sets were trimmed in the right half of the funnel plot also for hospital LoS, ICU LoS, reintervention, permanent SCI, respiratory insufficiency, and stroke, while no data sets were trimmed for transient SCI (data not shown).

The results from the random-effect meta-regression used to evaluate the association between the open repair outcomes and selected potential moderators showed a significant association between hypertension and both mortality (slope = –3.78, *P* = 0.010) and renal injury (slope = –6.93, *P* = 0.004). Moreover, smoking habit was significantly associated with reintervention (slope = –2.80, *P* = 0.020) and stroke (slope = 2.59, *P* = 0.018), whereas male sex was related to transient SCI (slope = 3.82, *P* = 0.020). No further significant associations were found (Supplemental Digital Content Table S6, <http://links.lww.com/SLA/E987>).

Endovascular Versus Open Thoracoabdominal Aortic Aneurysm Repair

A summary of the study outcomes is presented in Table 4. There was no difference in the pooled proportion of perioperative mortality between the two techniques (*P* = 0.22). Patients in the endovascular data set experienced a higher incidence of reinterventions compared with patients treated with open surgery (*P* < 0.01). Pooled mean for hospital LoS was statistically

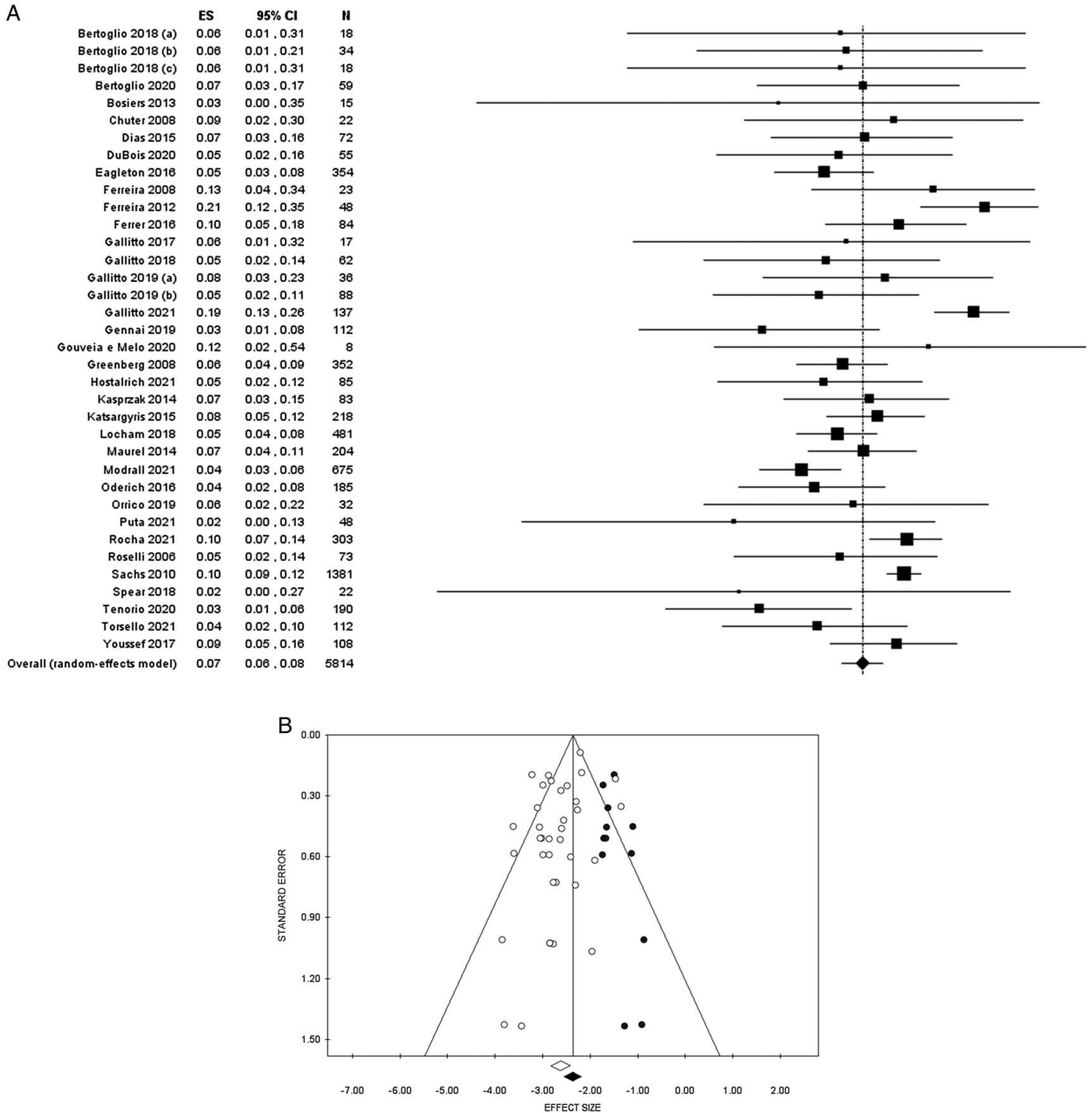


FIGURE 2. Forest plot (A) and funnel plot (B), after trim and fill method, of the meta-analysis assessing the pooled proportion of in-hospital mortality in TAAA endovascular repair data sets.

lower for endovascular treatments ($P < 0.01$), whereas no statistically significant difference was retrieved for ICU LoS.

Permanent SCI ($P < 0.01$), renal injury ($P = 0.02$), respiratory insufficiency ($P < 0.01$), and stroke ($P < 0.01$) occurred more frequently after open TAAA repair. No significant differences were reported for cardiac complications and transient SCI, whereas in the latter case, there was a trend toward higher incidence among endovascular TAAA-treated patients.

DISCUSSION

This study summarizes the updated best-available literature reporting 30-day outcomes after either endovascular or open TAAA repair and discusses their efficacy and safety. The analysis included 73 data sets (from 64 studies), of which 40 and 33 reported outcomes after endovascular and open TAAA repair, respectively. Endovascular-treated patients were older and had higher rates of prior vascular interventions,

TABLE 3. Meta-analyses Assessing TAAA Open Repair Outcomes

Type of analysis	No. of included data sets (k)	ES	95% CI, P	No. of participants	χ^2 ; df	I ²	P	Intercept*	r*	P*
Mortality†	32	0.09	0.08–0.12; <0.001	17333	509.08; 31	93.91	<0.001	-2.59	-2.64	0.013
Reintervention†	14	0.06	0.04–0.10; <0.001	7846	307.61; 13	95.77	<0.001	-1.39	-0.62	0.547
Hospital LoS‡	11	12.91	10.38–15.44; <0.001	7134	80.71; 10	87.61	<0.001	0.65	0.45	0.663
ICU LoS‡	5	10.14	6.80–13.48; <0.001	5875	129.07; 4	96.90	<0.001	1.70	0.33	0.766
Transient SCI†	13	0.06	0.05–0.08; <0.001	7458	67.51; 12	82.23	<0.001	1.48	1.31	0.218
Permanent SCI†	21	0.06	0.05–0.07; <0.001	8516	85.96; 20	76.73	<0.001	-0.40	-0.56	0.580
Renal injury†	24	0.13	0.09–0.17; <0.001	14995	1013.62; 23	97.73	<0.001	-4.15	-2.33	0.030
Respiratory insufficiency†	21	0.19	0.14–0.25; <0.001	14735	1229.82; 20	98.37	<0.001	-2.23	-0.83	0.417
Stroke†	22	0.05	0.04–0.06; <0.001	13509	117.49; 21	82.13	<0.001	-0.11	-0.13	0.901
Cardiac complications†	18	0.06	0.04–0.09; <0.001	12738	836.26; 17	97.97	<0.001	-5.25	-2.85	0.011

*Egger linear regression test.

†Values are reported as proportions.

‡Values are reported as means (days).

CI indicates confidence intervals; df, degree of freedom; ES, effect size; ICU, intensive care unit; LoS, length of stay; QS, quality score; SCI, spinal cord injury; TAAA, thoracoabdominal aortic aneurysm.

hypertension, diabetes, renal insufficiency, COPD, and coronary artery disease. Pooling data from nearly 6000 patients for endovascular TAAA repair and more than 17,000 for open surgery, we reported among endovascular-treated patients significantly lower rates of permanent SCI, renal injury, respiratory insufficiency, stroke, higher rates of reintervention, and shorter hospital LoS. Similar rates emerged between both endovascular and open repair with reference to mortality, cardiac complications, and ICU LoS, even if trends were in favor of the endovascular approach. Higher rates of transient SCI were reported among patients treated with endovascular grafts, but the difference was not significant.

A comparison of the main outcomes between studies suggests that endovascular TAAA repair is associated with higher rates of reintervention but generally lower proportions of major adverse events and no difference in mortality. These findings are in line with those of previous meta-analyses conducted on both comparative studies of endovascular versus open TAAA⁴ and studies reporting contemporary early outcomes after endovascular and open repair.^{11,86} In detail, the comparative studies meta-analysis⁴ and a further meta-analysis on thoracic aortic aneurysms repair⁸⁷ retrieved a survival benefit for endovascular over open surgery, which was not observed in our results and those by Rocha et al.¹¹ Concerning safety outcomes, we reported higher rates of transient SCI among endovascular-treated patients, by Rocha et al,¹¹ whereas other postoperative injuries had consistently lower rates in the available literature, especially for renal injury and permanent SCI.⁸⁷ The lower rates of disabling adverse events, such as postoperative stroke and permanent SCI in the endovascular cohort, is both a key point in the definition of clinical success² and a proxy for better late survival and quality of life.^{88–90} Finally, we retrieved a shorter hospital LoS for endovascular repair, as confirmed by Rocha et al¹¹ and Alsawas et al.⁸⁷

Across reported studies, the incidence of comorbidities, such as hypertension, diabetes, renal insufficiency, COPD, and coronary disease, in patients undergoing repair of TAAA is high. The burden of associated diseases might complicate the perioperative course of a patient and may influence clinicians' choices of treatment. Based on our results and previous systematic reviews,^{4,11,87} given the perception that endovascular TAAA repair reduces perioperative complications, patients undergoing endovascular repair were typically older and had more comorbidities. These different baseline risks make it difficult to directly compare complication rates between techniques. Results of the meta-regression analyses strengthen preoperative patients' characteristics role highlighting the significant association of age and comorbidities with selected outcomes. In this setting, sex may drive significant outcome differences that need to be further explored, as we could not perform differentiated analyses due to the absence of stratified data.^{91–93}

Even though endovascular repair seemed to be the more efficacious and safer technique in TAAA repair, we need to be cautious in interpreting the results because of the variations we reported in terms of definitions, techniques, and populations, resulting in the high heterogeneity we retrieved in the pooled analyses. Moreover, some clinical outcomes of interest were reported in a minority of patients (such as early reintervention and permanent SCI available only for 40% of the endovascular cohort); this must be a stimulus for researchers for a thorough data reporting in further publications in which sustained technical success, clinical success, and long-term quality of life should be compared between the two treatment modalities. Finally, endovascular TAAA repair with branched and fenestrated endograft is certainly less invasive, with the potential to

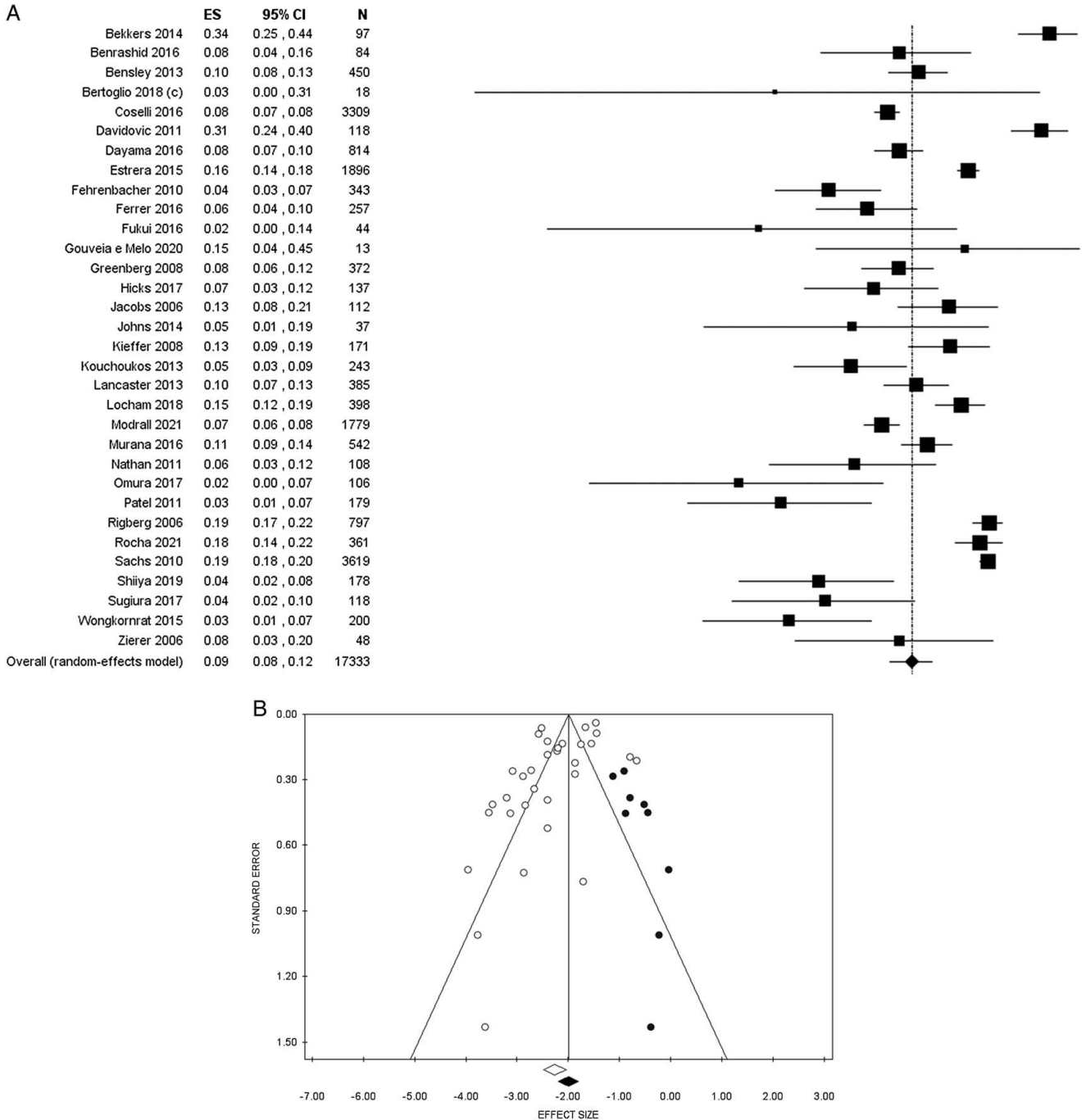


FIGURE 3. Forest plot (A) and funnel plot (B), after trim and fill method, of the meta-analysis assessing the pooled proportion of in-hospital mortality in TAAA open repair data sets.

significantly decrease the morbidity and mortality associated with open aneurysm repair in the short-term, nevertheless, this strategy still carries a significant risk of perioperative mortality and complications. Most reports focus on perioperative outcomes while the outcomes of endovascular TAAA have not been deeply investigated in the long run. These risks must be carefully weighed against the natural history of TAAAs when recommending repair, regardless of technique.

Open repair has been assessed as the gold standard technique for decades and can be considered a standardized procedure. In contrast, endovascular approaches are being recommended to an increasingly wide population of patients and are still evolving. They greatly vary among and within centres concerning staging, devices used, bridging stents, and spinal cord protection protocols, reinforcing the need for comparative data. With advancing standardization of endovascular repair and the progression of the

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TABLE 4. TAAA Endovascular Versus Open Repair Outcomes

Outcomes	Endovascular TAAA repair	Open TAAA repair	P
Mortality†	0.07 (0.06–0.08); N1 = 36; N2 = 5814	0.09 (0.08–0.12); N1 = 32; N2 = 17,333	0.22
Reintervention†	0.19 (0.13–0.26); N1 = 17; N2 = 1886	0.06 (0.04–0.10); N1 = 14; N2 = 7846	< 0.01*
Hospital stay length‡	8.67 (6.85–10.48); N1 = 15; N2 = 2669	12.91 (10.38–15.44); N1 = 11; N2 = 7134	< 0.01*
ICU stay length‡	7.18 (4.16–10.20); N1 = 6; N2 = 512	10.14 (6.80–13.48); N1 = 5; N2 = 5875	0.08
Transient SCI†	0.07 (0.05–0.09); N1 = 30; N2 = 3529	0.06 (0.05–0.08); N1 = 13; N2 = 7458	0.28
Permanent SCI†	0.04 (0.03–0.05); N1 = 16; N2 = 1735	0.06 (0.05–0.07); N1 = 21; N2 = 8516	< 0.01*
Renal injury†	0.08 (0.06–0.10); N1 = 25; N2 = 4711	0.13 (0.09–0.17); N1 = 24; N2 = 14,995	0.02*
Respiratory insufficiency†	0.07 (0.05–0.09); N1 = 19; N2 = 4121	0.19 (0.14–0.25); N1 = 21; N2 = 14,735	< 0.01*
Stroke†	0.03 (0.03–0.04); N1 = 19; N2 = 3632	0.05 (0.04–0.06); N1 = 22; N2 = 13,509	< 0.01*
Cardiac complications†	0.05 (0.04–0.07); N1 = 19; N2 = 4277	0.06 (0.04–0.09); N1 = 18; N2 = 12,738	0.44

N1 = number of included data sets; N2 = number of participants.

*Statistically significant ($P < 0.05$).

†Values are reported as proportions (95% CI).

‡Values are reported as means (95% CI). ICU indicates intensive care unit; SCI, spinal cord injury; TAAA, thoracoabdominal aneurysm.

learning curve of clinicians (a possible source of bias for many included studies), an improvement in outcome might be possible, even if the rigorous inspection of funnel plots and the use of the Egger test highlighted a relevant publication bias that might affect previous, ours and future results. We consistently retrieved an abundance of studies supporting endovascular repair superiority and a relative lack of studies in favor of open surgery, which, anyway has been performed for 70 years and has seen several improvements, especially in the fields of renovisceral perfusion strategies and spinal cord protection.^{94–98}

Therefore, before interpreting our findings further, we must consider some limitations and strengths. The first limitation is the high degree of heterogeneity of our analyses due to the observational nature of the included studies (no randomized trials were retrieved), carried out with different study designs, over different time periods, in various centres, and using uniform inclusion criteria, which might limit the generalizability of pooled effect estimates. Furthermore, our results should be analyzed in light of the differences exhibited in patients' baseline characteristics between groups (older and sicker patients among endovascular-treated) and of the lack of information on several of these characteristics, which are not reported uniformly in all studies. Meta-analyses included only unadjusted data and the lack of long-term outcomes for TAAA repair did not allow us to provide evidence on the long-run efficacy of the studied techniques. Lastly, several included studies had small sample sizes with poor precision but detailed clinical data, whereas most of the included patients came from routinely collected population-based administrative health databases, which might have brought limits to outcomes assessment, as well as the impossibility of conducting an individual-level data meta-analysis.

Despite these limitations, to the best of our knowledge, this systematic review and meta-analysis is the most updated and comprehensive summary of the available evidence on endovascular and open TAAA repair outcomes. The large number of studies analyzed ($n = 64$), the use of rigorous methodology and definitions, and strict adherence to Prepared Items for Systematic Reviews and Meta-analysis guidelines (for duplicate citation review and data extraction) are additional relevant strengths of this paper. A comprehensive literature review was carried out, using a wide range of databases and search terms through a combination of MeSH and free text words, to maximize the number of studies retrieved and minimize the chance of publication bias. Besides, further studies were retrieved from the reference listing of relevant articles. Moreover, to overcome high heterogeneity and investigate the role of potential sources of bias, we performed meta-regression

analyses, taking into account the impact of selected variables. Such a comprehensive and rigorous summary of the available evidence offers several meaningful insights, valuable to plan, implement, and evaluate clinical pathways, as well as future avenues of research, highlighting the paucity of higher quality evidence in terms of adjusted estimates or randomization.

CONCLUSIONS

Our updated review and meta-analysis suggest that endovascular TAAA repair could be a safer alternative to the open approach. These results, cautiously in line with previous studies, could provide a solid base to guide clinical choices and inform future guidelines and recommendations from scientific societies. A multidisciplinary approach could also be a game-changer, taking into account in-hospital costs and organizational adaptations and, thus enabling a multidimensional evaluation of new techniques, as suggested by new Health Technology Assessment (HTA) models. Yet, with reference to future pathways of research, given the lack of randomization in available studies and of consistency and standardization for definitions and reporting of disease characteristics (including aneurysm size and status of procedure) and postoperative adverse events, there is a strong need to establish uniform standards to be applied in randomized trials. These efforts could be greatly repaid by the accurate evaluation of the independent efficacy and safety of the two TAAA repair approaches, purging future results from the confounding effect of patients' comorbidities and complications that may affect final outcomes. Therefore, until further extended studies are carried out, any definitive conclusion about the incidence, degree, and duration of the outcomes of TAAA surgical repair must still be interpreted with caution and, for now, only systematic assessment of the literature could provide the best-available quantitative synthesis clinicians seek for.

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