Effectiveness of surgical interventions for thoracic aortic aneurysms: A systematic review and meta-analysis

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ABSTRACT

Objective: A systematic review and meta-analysis was conducted to evaluate the effectiveness of thoracic endovascular aortic repair (TEVAR) and open repair in patients with descending thoracic aortic aneurysms (TAAs).

Methods: PubMed, Ovid MEDLINE, Ovid Embase, EBSCO Cumulative Index to Nursing and Allied Health Literature, and Scopus were searched from each database's inception to January 29, 2016. We selected studies that compared the two approaches in adults with TAAs and reported 30-day mortality or procedure complications. Two reviewers independently extracted data, and conflicts were resolved by consensus. Random-effects meta-analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). The main outcomes and measures were all-cause 30-day mortality, 30-day paraplegia or spinal cord ischemia, stroke, pulmonary complications, and length of hospital and intensive care unit (ICU) stay.

Results: Twenty-seven studies of moderate methodologic quality were included. TEVAR was associated with lower 30-day mortality in ruptured (OR, 0.58; 95% CI, 0.38-0.88) and intact (OR, 0.6; 95% CI, 0.36-0.99) aneurysms. Paraplegia or spinal cord ischemia (OR, 0.35; 95% CI, 0.2-0.61) and pulmonary complications (OR, 0.41; 95% CI, 0.37-0.46) were reduced in patients undergoing TEVAR, whereas a reduction in stroke risk was not statistically significant (OR, 0.89; 95% CI, 0.76-1.03). Pooled mean difference in length of hospital and ICU stay was lower for TEVAR by −5.17 days (95% CI, −7.77 to −2.57) and −5.89 days (95% CI, −9.65 to −2.12), respectively. Three studies showed that compared with open repair, a hybrid approach reduced hospital stay (pooled mean difference, −8.83 days; 95% CI, −14.37 to −3.29) and ICU stay (pooled mean difference, −3.17 days (95% CI, −5.54 to −0.97), with minimal evidence on other outcomes studied.

Conclusions: Observational evidence at high risk of confounding suggests that compared with open repair for TAA, TEVAR reduced risk of mortality, paraplegia, spinal cord ischemia, and pulmonary complications within 30 days of intervention. Patients undergoing TEVAR also had shorter length of hospital and ICU stay compared with patients undergoing open repair. (J Vasc Surg 2017;66:1258-68.)

The thoracic aorta anatomically includes the ascending aorta, the aortic arch, and the descending thoracic aorta. Aortic disease, including the ascending and abdominal aorta, is among the 20 leading causes of death in the United States.[1] Thoracic aortic aneurysms (TAAs) are located in the descending thoracic aorta (35%), ascending aorta (40%), aortic arch (15%), and thoracoabdominal aorta (10%).[2] For the purposes of this review, the management of aneurysms of the descending thoracic aorta is the focus, including some studies that examine the thoracoabdominal aorta as well as the distal aortic arch. Defining aortic diameters in patients with TAAs is critical and typically performed by cross-sectional imaging, including computed tomography angiography, as diameter is the strongest predictor of rupture, with a reported mean aortic diameter of ruptured thoracoabdominal aortic aneurysms (TAAAs) of 6.1 cm.[3] Therefore, repair of TAAs is often recommended once these aneurysms have reached 5.5 to 6.0 cm. TAAs have an approximate overall incidence rate of 10.4 per 100,000 person-years.[4] Most patients with TAAs have no symptoms attributable to their disease at the time of diagnosis,[2] and therefore the diagnosis is often made when the patient is being evaluated for unrelated conditions. Yet, whereas most patients with TAAs are asymptomatic, most aneurysms will become symptomatic before they rupture.[5] Given its silent nature, the true incidence of TAA is therefore likely higher.[6] Current practice guidelines recommend early treatment of asymptomatic TAA once it is detected and a certain size diameter, usually 6 cm, has been reached.[7]

Originally performed with a standard "clamp and sew" technique,[8] open TAA repair has evolved with improved outcomes through the use of cardiopulmonary bypass and spinal fluid drainage.[2] Centers of excellence in this

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procedure report elective mortality and paraplegia rates as low as 4.8% and 4.6% for open TAA repair, respectively.[9] In contrast, national mortality rates before the introduction of endovascular technology were 22%.[10] Mortality rates after surgical treatment of ruptured TAAs are even higher, even though rates as low as 26% have been reported.[11] Data from multiple sources including single centers, industry-sponsored trials, and large national databases suggest that thoracic endovascular aortic repair (TEVAR) of isolated descending TAAs is a safe alternative to open surgery. TEVAR was first described as an alternative treatment in 1994,[12] and since then, multiple studies have compared open TAA repair with TEVAR. Regardless, multiple studies have suggested an improvement in early outcomes with TEVAR, whereas others have not.

Other studies have suggested a hybrid repair (a combination of open and endovascular approaches) in distal aortic arch aneurysms and TAAAs as a method by which to treat these complex aneurysms. The most common clinical scenario for this is when there is an inadequate landing zone for a stent graft in the proximal descending thoracic aorta. Therefore, a surgical procedure is performed first, most often with a left common carotid artery to left subclavian artery bypass or a left subclavian artery transposition.[13] Others have described extending the landing zone distally for stent grafts by performing bypasses to the visceral and renal arteries followed by stent grafting.[14] Still others have described performing a staged hybrid approach by performing the thoracic portion of the TAAA repair endovascularly and the abdominal portion with open surgery.[15] Although purely endovascular solutions are available in Europe, they are not currently available in the United States outside of the clinical trial. Clearly, the considerable variation in the management of these complex aneurysms suggests that no single approach has an absolute advantage over a different approach.

To evaluate the effectiveness of the different management paradigms in patients with TAAs, a systematic review and meta-analysis was performed comparing open and endovascular approaches as well as hybrid approaches on important perioperative outcomes, including mortality, paraplegia, pulmonary complications, and hospital and intensive care unit (ICU) length of stay.

METHODS

This systematic review and meta-analysis follows a priori determined inclusion criteria and is reported in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[16]

Eligibility criteria. Eligible studies were published in English and comparative (ie, compared any two interventions, including TEVAR, open repair, and hybrid surgery) in adult patients with TAA or TAAA. Aneurysms (or true aneurysms) were defined by current practice guidelines as permanent localized dilation of an artery, having at least a 50% increase in diameter compared with the expected normal diameter of the artery.[7] Only nondissected aneurysms were included in this systematic review, including degenerative or atherosclerotic and congenital aneurysms. Both ruptured and not ruptured aneurysms were included. Studies with other thoracic aortic diseases, such as acute or chronic aortic dissections, intramural hematoma, penetrating atherosclerotic ulcer, acute traumatic aortic injury, and pseudoaneurysms, were excluded unless a subgroup of outcomes for patients with aneurysms only was reported. Crawford (type IV) TAAAs, because they are limited to the abdominal aorta below the diaphragm, were also excluded.

Information sources. A comprehensive search of several databases from each database's inception to January 29, 2016, in any language, was conducted. The databases included Ovid Medline In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. The search strategy was designed and conducted by an experienced librarian with input from the study's principal investigator. Controlled vocabulary supplemented with keywords was used to search for studies of management of TAAs. The actual strategy is available as an Appendix (online only).

Study selection and data collection. Two reviewers independently reviewed titles and abstracts of candidate studies. Disagreement on abstracts led to inclusion of the citation for full-text review. Included studies from this level were reviewed in full version by two reviewers independently. Any conflicts about the eligibility of the studies were solved by consensus of all reviewers. Data from included studies were abstracted in duplicate by two independent reviewers using a standardized form that was created using a web-based program (DistillerSR; Evidence Partners, Ottawa, Canada). Disagreement on data extraction was resolved by consensus of the two reviewers.

Outcomes. The primary outcome was 30-day mortality. Secondary outcomes were 30-day paraplegia, stroke, and pulmonary complications in addition to ICU and hospital length of stay. Data about iliac artery complications, need for tracheostomy, and estimated blood loss were collected when available; however, the data were inadequate to be included.

Risk of bias. Two reviewers independently assessed the risk of bias in the included studies using a standardized form based on the Newcastle-Ottawa Scale tool.[17] The assessment considered three main domains (patient

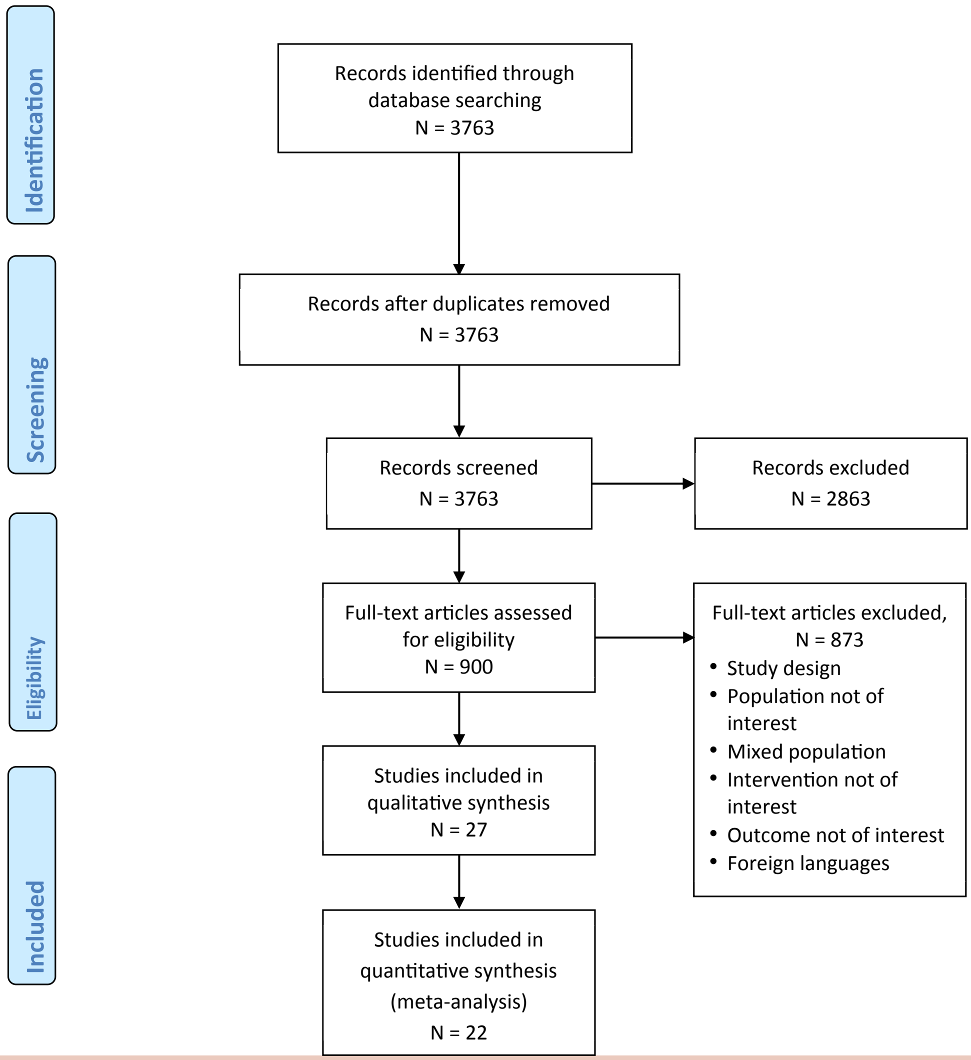

Fig 1. Study selection.

selection, comparability between the two study arms, outcomes assessment). To assess for publication bias in reporting the main outcome of 30-day mortality, funnel plots for asymmetry were examined.

Quality of evidence. To assess quality of evidence in each outcome, a Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was applied. Criteria used to evaluate quality of evidence were risk of bias, indirectness (surrogate outcomes), imprecision (wide confidence intervals [CIs]), inconsistency (heterogeneity), and publication bias.[18]

Data synthesis. A random-effects model meta-analysis was used to estimate pooled odds ratios (ORs) and 95% CIs for 30-day mortality, paralysis or spinal cord ischemia, stroke, and pulmonary complications. We similarly pooled the mean difference and 95% CI for hospital length of stay and estimated between-trial inconsistency not due to chance using the I^2 statistic.

To explore the effects of rupture on 30-day mortality, a subgroup analysis was also conducted. We explored publication bias by evaluating funnel plots. These plots can reveal a small study effect (ie, smaller studies demonstrate different results from larger studies, which can indicate publication bias because theoretically study size should not affect the estimated outcome measure). Open Meta software[19] and Stata 14 (StataCorp LP, College Station, Tex) were used to conduct analyses.

RESULTS

Study selection

The initial database search identified 3763 records, of which 27 studies were eventually included (Fig 1). The agreement among reviewers on study selection was 97% with κ of 0.74. Many studies were excluded because of reporting on mixed populations (mixing dissected and nondissected aneurysms; thoracoabdominal aneurysms type IV with other types; abdominal and thoracic

Table I. Characteristics of the studies, thoracic endovascular aortic repair (*TEVAR*) vs open repair

First author, year	Data source	Study period	Country	Aneurysm type	Aneurysm location				TEVAR, No.	Open repair, No.
					Asc	Arch	Des	TA		
Michel,[20] 2015	Window's trial database for TEVAR, national hospital discharge database for open	2009-2012	France	Intact				X	42	71
Von Allmen,[21] 2014	Hospital Episode Statistics	2006-2011	United Kingdom	Mixed			X		451	308
Yuri,[22] 2012	Single center	2006-2009	Japan	Mixed	X	X	X		30	32
Desai,[23] 2012	Single center	1999-2007	United States	Mixed			X		106	45
Jonker,[24] 2011	Multicenter	1995-2009	United States, Italy, The Netherlands	Ruptured			X		92	69
Andrassy,[25] 2011	Single center	1992-2008	Germany	Mixed			X		53	24
Glade,[26] 2005	Multicenter	1997-2003	Netherlands	Intact			X		42	53
Ehrlich,[27] 1998	Single center	1989-1997	Austria	Mixed			X		10	58
Andrassy,[28] 2006	Single center	1997-2000	Germany	Mixed			X		9	6
Patel,[29] 2008	Single center	1993-2007	United States	Mixed			X		45	32
Kim,[30] 2015	Single center	1992-2013	United States	Intact			X	X	63	78
Najibi,[31] 2002	Single center	1996-1998	United States	Intact			X		19	10
Doss,[32] 2003	Single center	1999-2002	Germany	Ruptured			X		13	11
Patel,[33] 2013	Medicare Provider Analysis and Review data set	2004-2007	United States	Intact			X		3517	3554
Brooke,[34] 2013	Medicare Provider Analysis and Review database	2000-2007	United States	Intact	X	X	X		1914	7850
Conrad,[35] 2010	Medicare Provider Analysis and Review data set	2004-2007	United States	Ruptured	X	X	X		368	665
Hughes,[36] 2014	Nationwide Inpatient Sample	1998-2007	United States	Intact	X	X	X		712	8255
Gopaldas,[37] 2011	Nationwide Inpatient Sample	2006-2008	United States	Ruptured			X		364	559
Bhamidipati,[38] 2011	Nationwide Inpatient Sample	2005-2007	United States	Mixed	X	X	X	X	7644	32,948
Gopaldas,[39] 2010	Nationwide Inpatient Sample	2006-2007	United States	Intact			X		2563	9106
Bavaria,[40] 2007 Makaroun,[41] 2008 Dillavou,[42] 2008	Multicenter (TAG trial patients)	1999-2001	United States	Intact			X		140	94

Asc, Ascending; *Des*, descending; *TA*, thoracoabdominal.

aneurysms, including primarily the ascending aorta or the arch).

Study characteristics

Of the 27 included studies, 23 compared TEVAR with open repair (Table I). Three studies compared a hybrid approach (a mix of TEVAR and open repair) with an open approach (Supplementary Table I, online only), and one study compared medical treatment with open surgery (Supplementary Table II, online only). Thirteen of the included studies were done in single centers. Many studies used national databases; four of them used the Nationwide Inpatient Sample (NIS) and three used the Medicare Provider Analysis and Review database. Three studies used data from the Gore TAG trial.[43] To prevent overlap and to reduce the chances of not having unique patients in analysis, only two of the four studies that used NIS were included in meta-analysis (Gopaldas et al[37,39]). The study of Hughes et al[36] included patients from 1998 to 2007 but used only two

Table II. Risk of bias

First author, year	Selection	Comparability	Outcome assessment	Risk of bias
Michel,[20] 2015	High	High	Low	High
Von Allmen,[21] 2014	Moderate	Moderate	Low	Moderate
Yuri,[22] 2012	High	Low	Low	High
Desai,[23] 2012	High	High	Low	High
Jonker,[24] 2011	Low	High	Low	High
Andrassy,[25] 2011	High	High	Low	High
Glade,[26] 2005	Low	High	Low	High
Ehrlich,[27] 1998	High	Moderate	Low	High
Andrassy,[28] 2006	Moderate	Moderate	Low	Moderate
Patel,[29] 2008	High	High	Low	High
Kim,[30] 2015	High	Low	Low	High
Najibi,[31] 2002	High	High	Low	High
Doss,[32] 2003	High	High	Low	High
Patel,[33] 2013	Low	Moderate	Low	Moderate
Brooke,[34] 2013	Low	High	Low	High
Conrad,[35] 2010	Low	Low	Low	Low
Hughes,[36] 2014	High	High	Low	High
Gopaldas,[37] 2011	Moderate	High	Low	High
Bhamidipati,[38] 2011	Moderate	High	Low	High
Gopaldas,[39] 2010	Moderate	High	Low	High
Bavaria,[40] 2007 Makaroun,[41] 2008 Dillavou,[42] 2008	High	High	Low	High
Kurazumi,[44] 2014	High	High	Low	High
Iba,[45] 2014	Low	Low	Low	Low
Usui,[46] 2001	High	Low	Low	High
Murphy,[47] 2009	Moderate	Moderate	Low	Moderate

International Classification of Diseases, Ninth Revision codes to identify patients (39.73, Endovascular implantation of graft in thoracic aorta; and 38.45, Resection of vessel with replacement, thoracic aorta). Gopaldas et al, on the other hand, included both codes in addition to 441.1 (Thoracic aneurysm, ruptured) and 441.2 (Thoracic aneurysm without mention of rupture). Bhamidipati et al reported both TAA and TAAA, and their main outcome was in-hospital mortality (not 30-day mortality)[38]; hence, this study was excluded from mortality analysis. This study was included in the 30-day stroke analysis because it was the only NIS study that reported this outcome. Studies reporting data from the Gore TAG clinical trial were considered as one study in meta-analysis. Similarly, we included only two of the three studies using Medicare data. We excluded the study of Brooke et al[34] because years of enrollment were overlapping with the study by Patel et al.[33]

Most included studies had high risk of bias (Table II); the most common concern in these studies was the comparability between the groups. Patients who had TEVAR, for example, were often older than patients undergoing open TAAA repair.

Meta-analysis

TEVAR vs open repair.

Thirty-day all-cause mortality. Eighteen studies including 22,702 patients reported 30-day mortality. TEVAR reduced the risk of 30-day mortality (OR, 0.56; 95% CI, 0.4-0.74). Inconsistency among these studies was moderate ($I^2 = 69\%$; Fig 2). Funnel plot examination showed asymmetry suggesting publication bias (Supplementary Fig 1, online only). The quality of evidence in this analysis was very low (Supplementary Table III, online only).

Subgroup analysis was done to compare 30-day mortality risk between intact (19,985 patients) and ruptured (2282 patients) aneurysms. In each subgroup, TEVAR reduced the risk of 30-day mortality in intact aneurysms (nine studies; OR, 0.6; 95% CI, 0.36-0.99; $I^2 = 77\%$) and in ruptured aneurysms (five studies; OR, 0.58; 95% CI, 0.38-0.88; $I^2 = 65\%$). No statistically significant interaction was reported between the two subgroups (Fig 3). Only one study compared 30-day mortality[20] for patients with supradiaphragmatic TAAAs. The difference between the TEVAR and open repair groups was not statistically significant (OR, 0.55; 95% CI, 0.18-1.66).

Studies	Estimate (95% C.I.)	Ev/Trt	Ev/Ctrl
Ehrlich 1998	0.247 (0.029, 2.098)	1/10	18/58
Najibi 2002	0.500 (0.028, 8.952)	1/19	1/10
Glade 2005	0.392 (0.075, 2.049)	2/42	6/53
Andrassy 06 2006	0.684 (0.012, 39.072)	0/9	0/6
Bavaria 2007	0.165 (0.045, 0.610)	3/140	11/94
Patel 08 2008	0.202 (0.038, 1.074)	2/45	6/32
Gopaldas10 2010	1.003 (0.749, 1.344)	59/2563	209/9106
Conrad 2010	0.381 (0.287, 0.507)	87/368	298/665
Gopaldas 11 2011	0.760 (0.560, 1.030)	85/364	160/559
Jonker 2011	0.644 (0.299, 1.389)	16/92	17/69
Andrassy 11 2011	0.180 (0.041, 0.796)	3/53	6/24
Yuri 2012	1.066 (0.020, 55.393)	0/30	0/32
Desai 2012	0.408 (0.079, 2.102)	3/106	3/45
Patel 13 2013	0.402 (0.336, 0.481)	183/3517	427/3554
Von Allmen 2014	0.985 (0.627, 1.547)	52/451	36/308
Michel 2015	0.550 (0.183, 1.656)	5/42	14/71
Bum Kim 2015	1.695 (0.365, 7.869)	4/63	3/78
Doss 2003	0.375 (0.029, 4.809)	1/13	2/11
Overall (I^2=69% , P< 0.001)	0.546 (0.402, 0.743)	507/7927	1217/14775

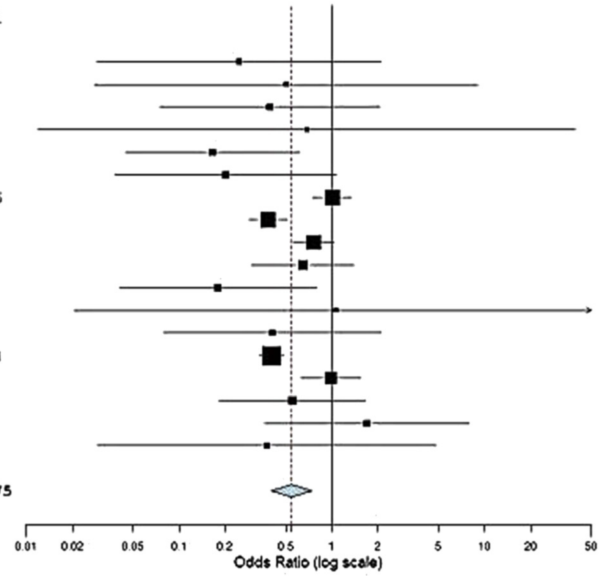

Fig 2. The 30-day mortality, thoracic endovascular aortic repair (TEVAR) vs open repair. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.

Thirty-day paraplegia or spinal cord ischemia. Six studies including 771 patients reported 30-day paraplegia or spinal cord ischemia. TEVAR reduced paraplegia or spinal cord ischemia (OR, 0.35; 95% CI, 0.2-0.61). Inconsistency among these studies was minimal ($I^2 = 0\%$; Fig 4). The quality of evidence in this analysis was very low (Supplementary Table III, online only).

Thirty-day stroke. Eight studies including 41,401 patients reported 30-day stroke rates. The reduction in risk with TEVAR was not statistically significant (OR, 0.89; 95% CI, 0.76-1.03). Inconsistency among these studies was minimal ($I^2 = 0\%$; Supplementary Fig 2, online only). The quality of evidence in this analysis was very low (Supplementary Table III, online only). Sensitivity analysis excluding one study, in which NIS[38] data were used without specification about whether type IV aneurysm was included, revealed similar conclusions (Supplementary Fig 3, online only).

Thirty-day pulmonary complications. Four studies including 18,996 patients reported 30-day pulmonary complications. TEVAR was associated with a reduction in risk (OR, 0.41; 95% CI, 0.37-0.46). Inconsistency among these studies was minimal ($I^2 = 0\%$; Supplementary Fig 4, online only). The quality of evidence in this analysis was very low (Supplementary Table III, online only).

Length of ICU stay. Four studies including 346 patients reported ICU length of stay. TEVAR was associated with shorter stay (pooled mean difference, −5.89 days; 95% CI, −9.65 to −2.12). Heterogeneity between these studies was moderate ($I^2 = 65\%$; Fig 5). The quality of evidence in this analysis was very low (Supplementary Table III, online only).

Length of hospital stay. Six studies including 1331 patients reported hospital length of stay. TEVAR was associated with shorter stay (pooled mean difference, −5.17 days; 95% CI, −7.77 to −2.57). Heterogeneity between these studies was high ($I^2 = 91\%$; Fig 6). The quality of evidence in this analysis was very low (Supplementary Table III, online only).

Hybrid approach vs open repair.

Thirty-day all-cause mortality. Three studies including 249 patients compared 30-day mortality between a hybrid approach and purely open TAA repair, and the difference was not statistically significant (OR, 0.44; 95% CI, 0.1-1.95). Inconsistency among these studies was minimal ($I^2 = 0\%$; Fig 7). The quality of evidence in this analysis was very low (Supplementary Table IV, online only).

Thirty-day paraplegia or spinal cord ischemia. Three studies including 249 patients evaluated paraplegia or spinal cord ischemia. The difference was not statistically significant (OR, 1.13; 95% CI, 0.15-8.35). Inconsistency among these studies was minimal ($I^2 = 0\%$; Supplementary Fig 5, online only). The quality of evidence in this analysis was very low (Supplementary Table IV, online only).

Length of ICU stay. Three studies including 249 patients reported ICU length of stay. The hybrid approach was associated with shorter stay (pooled mean difference, −3.17 days; 95% CI, −5.54 to −0.97). Heterogeneity between these studies was moderate ($I^2 = 68\%$; Fig 8). The quality of evidence in this analysis was very low (Supplementary Table IV, online only).

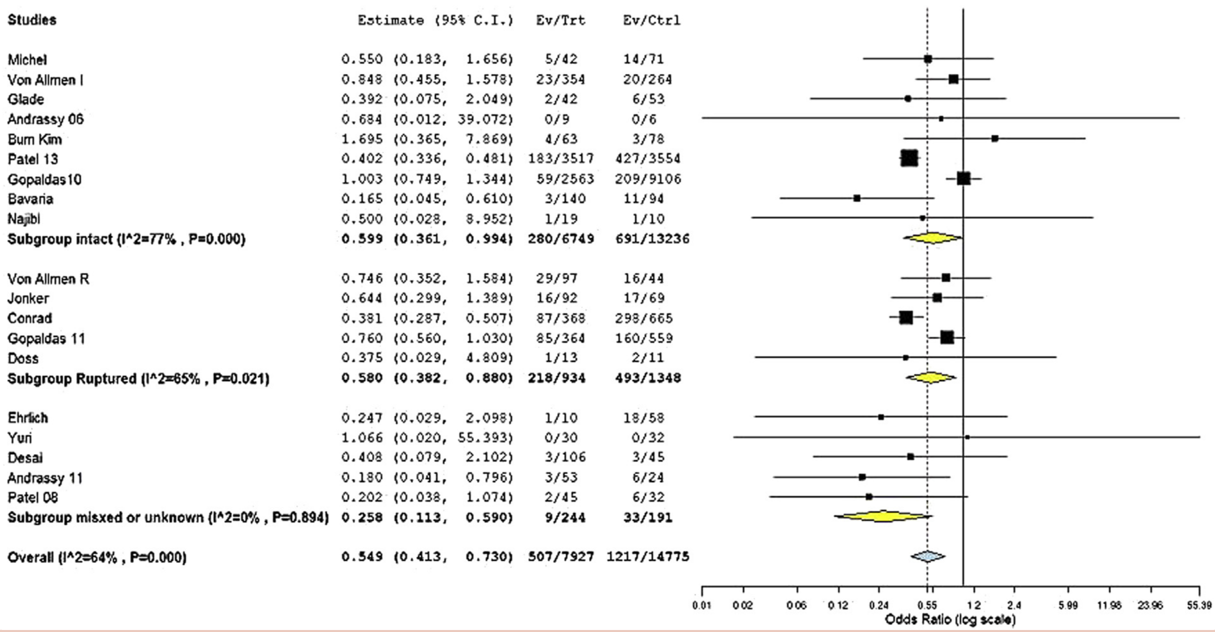

Fig 3. Subgroup analysis for 30-day mortality, thoracic endovascular aortic repair (TEVAR) vs open repair in intact vs ruptured vs unknown or mixed aneurysms. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.

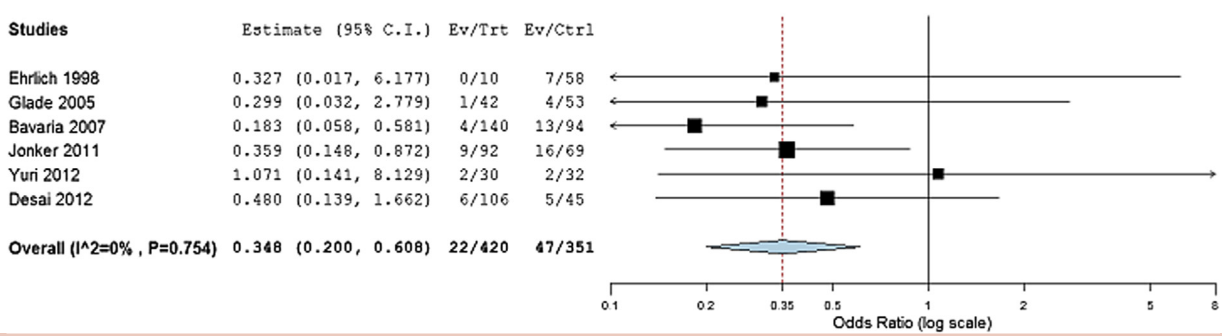

Fig 4. The 30-day paraplegia or spinal cord ischemia, thoracic endovascular aortic repair (TEVAR) vs open repair. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.

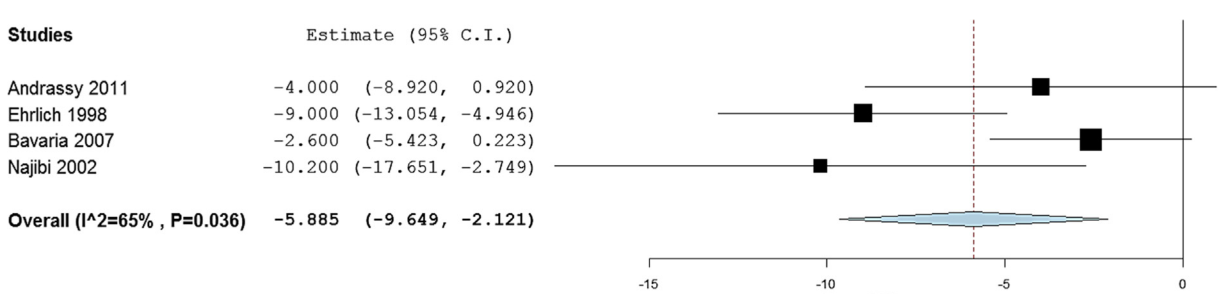

Fig 5. Length of intensive care unit (ICU) stay, thoracic endovascular aortic repair (TEVAR) vs open repair. *CI,* Confidence interval.

Length of hospital stay. Three studies including 249 patients reported length of hospital stay. The hybrid approach was associated with shorter hospital stay (pooled mean difference, −8.83 days; 95% CI, −14.37 to −3.29). Heterogeneity between these studies was minimal (I^2 = 0%; Fig 9). The quality of evidence in this analysis was very low (Supplementary Table IV, online only).

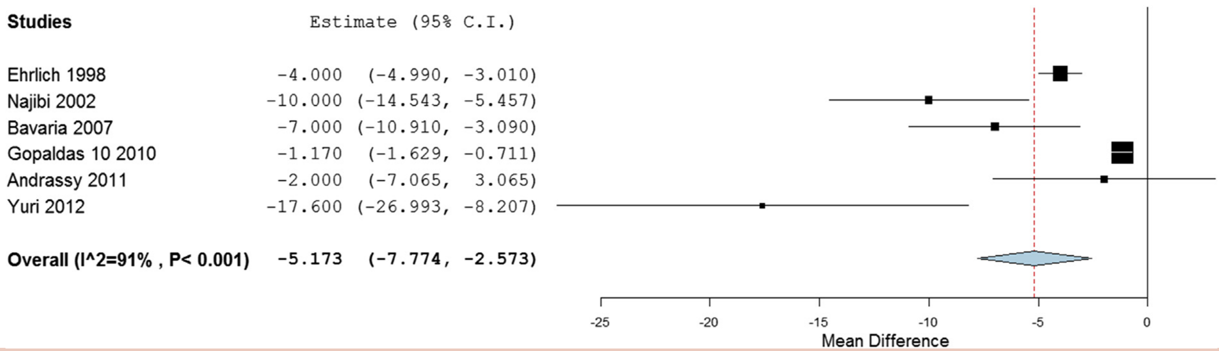

Fig 6. Length of hospital stay, thoracic endovascular aortic repair (TEVAR) vs open repair. *CI*, Confidence interval.

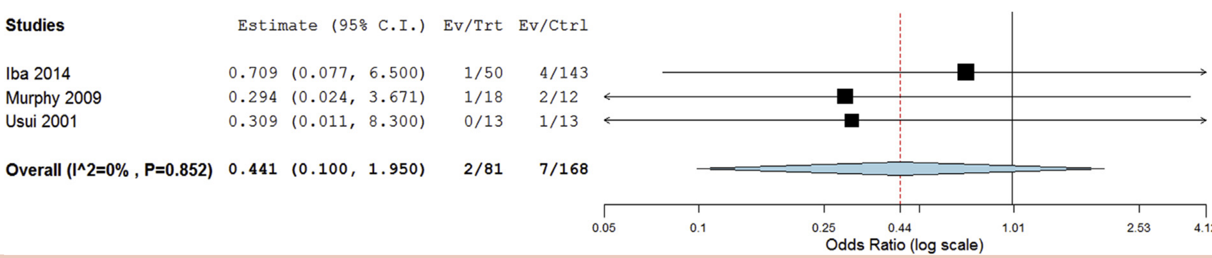

Fig 7. The 30-day mortality odds ratio (OR), hybrid vs open repair. *CI*, Confidence interval; *Ev/Trt*, observed number of events in the treatment group; *Ev/Ctrl*, observed number of events in the control group.

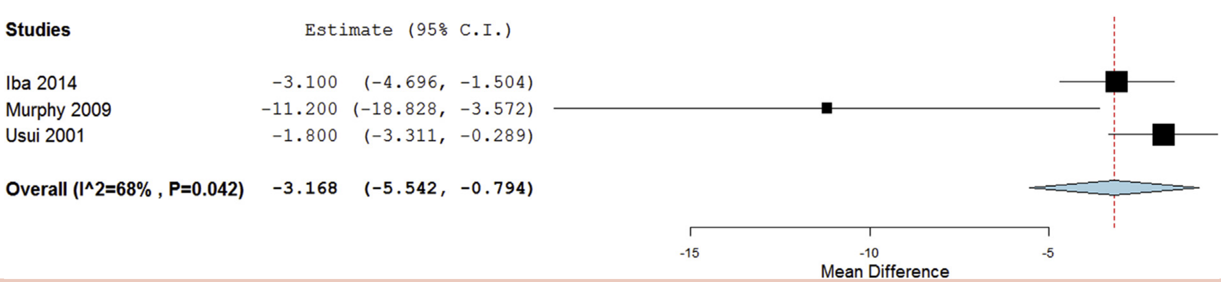

Fig 8. Length of intensive care unit (ICU) stay, hybrid vs open repair. *CI*, Confidence interval.

DISCUSSION

This systematic review and meta-analysis demonstrated that compared with open TAA repair, TEVAR reduces the risk of mortality, paraplegia or spinal cord ischemia, and pulmonary complication within 30 days of intervention. Patients undergoing TEVAR also had a shorter hospital and ICU length of stay. The effect on stroke was imprecise and unclear, probably because these results were at least partially contaminated by the use of TEVAR in combination with open procedures (ie, hybrid) to proximally extend the landing zone for endovascular aneurysm repair. It has been well documented that coverage of the left subclavian artery may be associated with a higher stroke rate.[13] The authors of the Society for Vascular Surgery guidelines, in terms of revascularization of the left subclavian artery in association with TEVAR, suggested the following: (1) in patients who need elective TEVAR where achievement of a proximal seal necessitates coverage of the left subclavian artery, we suggest routine preoperative revascularization, despite the very low-quality evidence (GRADE 2, level C); (2) in selected patients who have an anatomy that compromises perfusion to critical organs, routine preoperative left subclavian artery revascularization is strongly recommended, despite the very low-quality evidence (GRADE 1, level C); and (3) in patients who need urgent TEVAR for life-threatening acute aortic syndromes where achievement of a proximal seal necessitates coverage of the left subclavian artery, we suggest that revascularization should be individualized and addressed expectantly on the basis of anatomy, urgency, and availability of surgical expertise (GRADE 2, level C). Whereas there are myriad reasons this might be true, including its impact on the left vertebral artery when the left vertebral artery

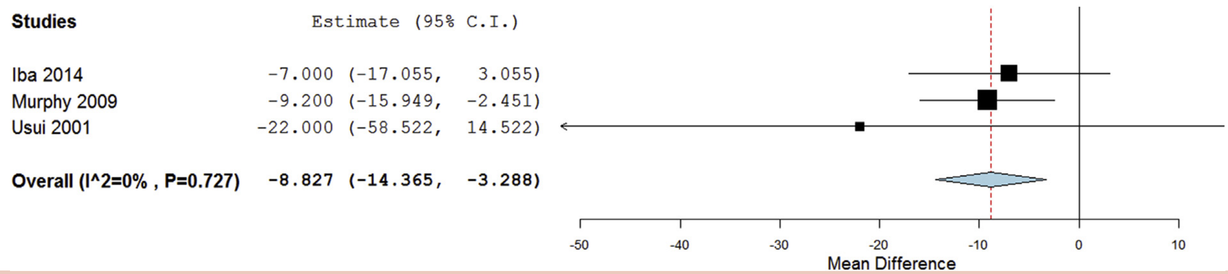

Fig 9. Length of hospital stay, hybrid vs open repair. *CI,* Confidence interval.

ends in a posterior communicating artery, coverage of the left subclavian artery also likely is a marker for more aggressive manipulation of the endograft in the aortic arch, which is believed to be a risk factor for stroke. Patients who had a hybrid treatment had shorter hospital length of stay compared with patients who had open TAA repair, with unclear and imprecise effects on other patient-important outcomes. The certainty in evidence (quality of evidence) is low to very low because of high likelihood of confounding in all analyses.

In a subgroup analysis for 30-day mortality, TEVAR was found to be superior to open repair in intact and ruptured aneurysms. These results are consistent with two previous systematic reviews by Jonker et al[48] and Walsh et al.[49] Jonker et al included ruptured descending TAAs only in noncomparative studies and found that 30-day mortality was 19% for patients treated with TEVAR for ruptured descending TAA compared with 33% for patients treated with open repair with an OR of 2.15 (95% CI, 1.15-4.01). Walsh et al included only three studies, with studies reporting aneurysms due to dissection with an OR of 0.25 (95% CI, 0.09-0.66).

Whereas the present study suggests that TEVAR reduces the risk of short-term complications compared with open TAA repair, its long-term effectiveness is still unclear. We found only three studies that reported long-term follow-up. In the study of Makaroun et al,[41] patients were followed up from the Gore TAG trial and compared with historical controls. Two-year survival rates were similar between the two groups. Andrassy et al[25] found a significantly improved long-term survival after TEVAR in symptomatic patients compared with those receiving open surgery. In the study of Desai et al,[23] overall survival at 10 years was similar between groups; however, TEVAR patients were older and had significantly more comorbidities, which placed them at a higher risk of mortality compared with open repair patients.

Limitations of this systematic review relate to the likelihood of loss of data from studies with mixed populations. These studies likely included eligible patients who fulfill the criteria for inclusion in this analysis. Whereas an attempt was made to analyze multiple other variables, we were unable to adequately determine differences in iliac artery complications, the need for tracheostomy, and blood loss. The quality of evidence (certainty in the evidence) clearly limits inferences and lowers confidence in the meta-analytic estimates. Finally, there is clearly a potential selection bias during the period included in this meta-analysis as more endovascular devices are available, more people are trained to perform TEVAR, and fewer institutions were likely to be actually performing open TAA repair at the end of the study period compared with the beginning of the study period.

CONCLUSIONS

Patients who undergo TEVAR have reduced risk of mortality, paraplegia, and pulmonary complications within 30 days of intervention compared with patients who undergo open TAA repair, even though the quality of evidence is very low. Patients undergoing TEVAR also had a shorter hospital and ICU length of stay. Clearly, more high-quality studies with long-term follow-up comparing TEVAR and open repair directly are needed but will probably never be performed for multiple reasons. Data are clear from large national databases that a paradigm shift has occurred across the United States in the treatment of TAAs. The present data confirm for the most part what has been shown by multiple large single-center studies, industry-sponsored trials, and national databases, namely, that mortality and paraplegia are reduced in TEVAR compared with open TAA repair. In addition, fewer hospitals and training programs adequately train surgeons to perform open TAA repair.[50] Given these observations and the likelihood that industry will likely develop more globally available and purely endovascular approaches to the ascending aorta, aortic arch, and thoracoabdominal aorta, a randomized, clinical trial addressing the effects of TEVAR vs open TAAA repair will likely never be performed.

We would like to thank Dr Ahmed T. Ahmed for help in screening studies for inclusion.

AUTHOR CONTRIBUTIONS

Conception and design: MA, GU, MM
Analysis and interpretation: MA
Data collection: MA, FZ, LLM, JA, PE
Writing the article: MA, GU, MM
Critical revision of the article: MA, FZ, LLM, JA, PE, GU, MM
Final approval of the article: MA, FZ, LLM, JA, PE, GU, MM

Statistical analysis: MA
Obtained funding: MM
Overall responsibility: MM

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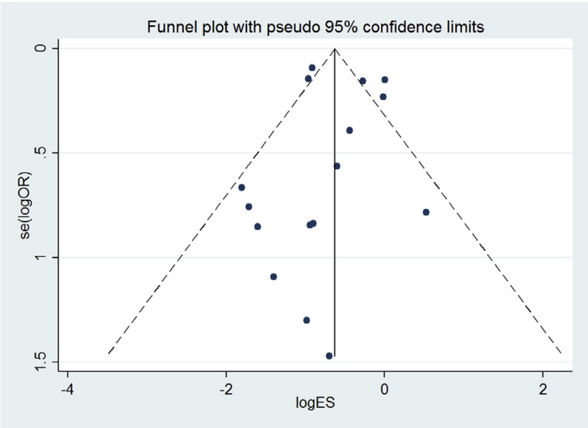
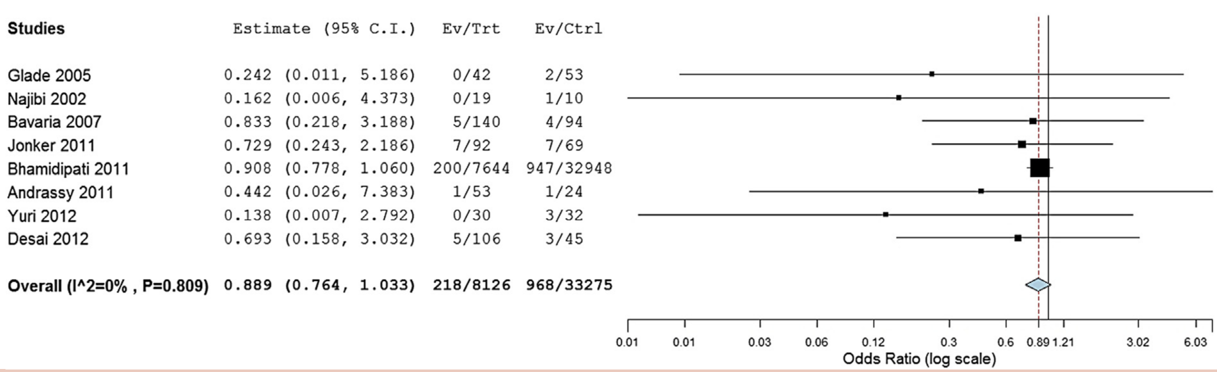
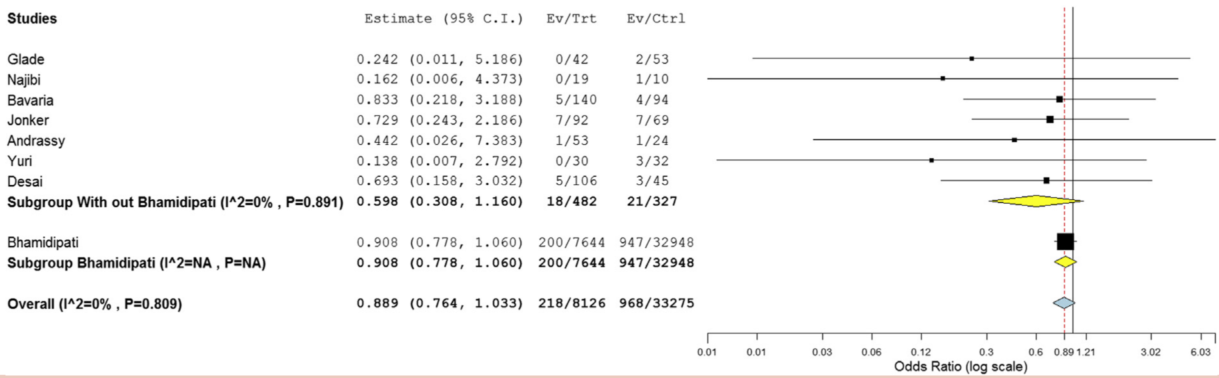
APPENDIX (online only).



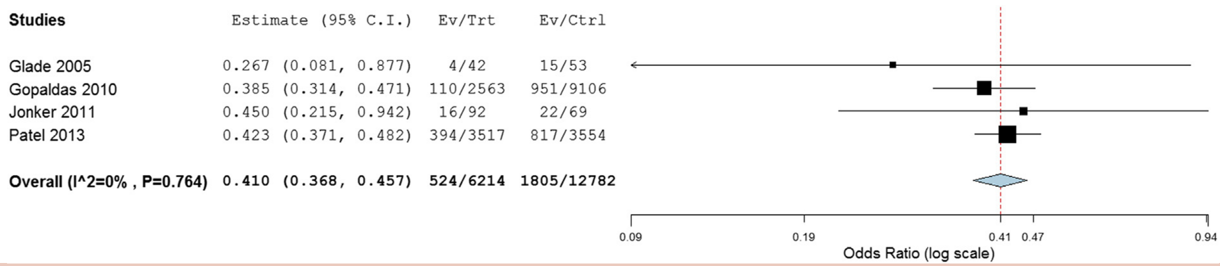
Supplementary Fig 1 (online only). Funnel plot for 30-day mortality in thoracic endovascular aortic repair (TEVAR) vs open repair showing an empty space in the right base of the triangle, suggesting the presence of small unpublished studies that can be caused by publication bias. *ES,* Effect size; *OR,* odds ratio; *se,* standard error.



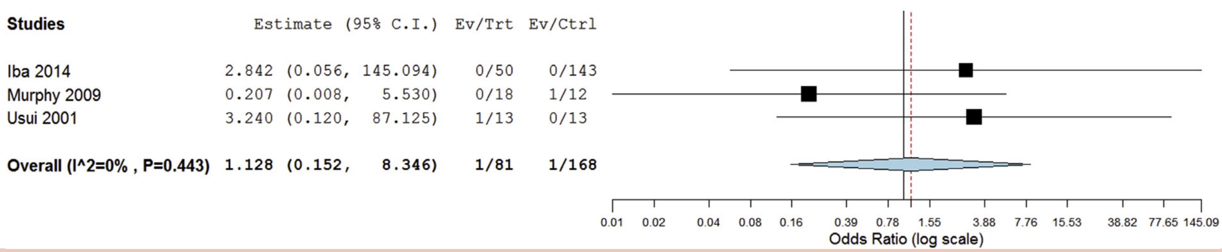
Supplementary Fig 2 (online only). The 30-day stroke rate for thoracic endovascular aortic repair (TEVAR) vs open repair. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.



Supplementary Fig 3 (online only). Sensitivity analysis for 30-day stroke, thoracic endovascular aortic repair (TEVAR) vs open repair, with and without Bhamidipati study. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.



Supplementary Fig 4 (online only). The 30-day pulmonary complications of thoracic endovascular aortic repair (TEVAR) vs open repair. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.



Supplementary Fig 5 (online only). The 30-day paraplegia or ischemic spinal cord odds ratio (OR) for hybrid vs open repair. *CI,* Confidence interval; *Ev/Trt,* observed number of events in the treatment group; *Ev/Ctrl,* observed number of events in the control group.

Supplementary Table I (online only). Characteristics of studies, open vs hybrid approach

				Aneurysm location					
First author, year	Data source	Study period	Country	Asc	Arch	Des	TA	Open, No.	Hybrid, No.
Iba,[45] 2014	Single center	2008-2013	Japan		X			143	50
Usui,[46] 2001	Single center	1997-2000	Japan		X			13	13
Murphy,[47] 2009	Single center	2005-2006	United States		X			12	18

Asc, Ascending; *Des,* descending; *TA,* thoracoabdominal.

Supplementary Table II (online only). Characteristics of studies, open surgery vs medical treatment

				Aneurysm location					
First author, year	Data source	Study period	Country	Asc	Arch	Des	TA	Open, No.	Medical, No.
Kurazumi,[44] 2014	Single center	2003-2012	Japan		X			20	27

Asc, Ascending; *Des,* descending; *TA,* thoracoabdominal.

Supplementary Table III (online only). Grading the quality of evidence, thoracic endovascular aortic repair (*TEVAR*) vs open repair

Quality assessment							No. of patients (%)		Effect		
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TEVAR	Open repair	Relative (95% CI)	Absolute (95% CI)	Quality
30-day mortality											
18	Observational studies	Serious	Serious	Not serious	Not serious	Publication bias strongly suspected	507/7927 (6.4)	1217/14,775 (8.2)	**OR, 0.546** (0.402-0.743)	**36 fewer per 1000** (from 20 fewer to 48 fewer)	⊕◯◯◯ Very low
30-day paraplegia											
6	Observational studies	Serious	Not serious	Not serious	Not serious	None	22/420 (5.2)	47/351 (13.4)	**OR, 0.348** (0.200-0.608)	**83 fewer per 1000** (from 48 fewer to 104 fewer)	⊕◯◯◯ Very low
30-day stroke											
8	Observational studies	Serious	Not serious	Not serious	Not serious	None	218/8126 (2.7)	968/33,275 (2.9)	**OR, 0.889** (0.764-1.033)	**3 fewer per 1000** (from 1 more to 7 fewer)	⊕◯◯◯ Very low
30-day pulmonary complications											
4	Observational studies	Serious	Not serious	Not serious	Not serious	None	524/6214 (8.4)	1805/12,782 (14.1)	**OR, 0.410** (0.368-0.457)	**78 fewer per 1000** (from 71 fewer to 84 fewer)	⊕◯◯◯ Very low
Length of hospital stay											
6	Observational studies	Serious	Very serious	Not serious	Serious	None	2815	9324	—	MD, **5.173 days lower** (2.573 lower to 7.774 lower)	⊕◯◯◯ Very low
Length of ICU stay											
4	Observational studies	Serious	Serious	Not serious	Not serious	None	222	186	—	MD, **5.885 days lower** (2.121 lower to 9.649 lower)	⊕◯◯◯ Very low

CI, Confidence interval; *ICU,* intensive care unit; *MD,* mean difference; *OR,* odds ratio.

Supplementary Table IV (online only). Grading the quality of evidence, hybrid vs open repair

Quality assessment							No. of patients (%)		Effect		
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Hybrid**	**Open**	**Relative (95% CI)**	**Absolute (95% CI)**	**Quality**
30-day mortality											
3	Observational studies	Serious	Not serious	Not serious	Serious	None	2/81 (2.5)	7/168 (4.2)	**OR, 0.441** (0.100-1.950)	**23 fewer per 1000** (from 36 more to 37 fewer)	⊕◯◯◯ Very low
30-day paraplegia or ischemic spinal cord odds											
3	Observational studies	Serious	Not serious	Not serious	Very serious	None	1/81 (1.2)	1/168 (0.6)	**OR, 1.128** (0.152-8.346)	**1 more per 1000** (from 5 fewer to 42 more)	⊕◯◯◯ Very low
Length of hospital stay											
3	Observational studies	Serious	Not serious	Not serious	Not serious	None	81	168	—	MD, **8.827 days lower** (3.288 lower to 14.365 lower)	⊕◯◯◯ Very low
Length of ICU stay											
3	Observational studies	Serious	Not serious	Not serious	Serious	None	81	168	—	MD, **3.168 days lower** (0.794 lower to 5.542 lower)	⊕◯◯◯ Very low

CI, Confidence interval; *ICU,* intensive care unit; *MD,* mean difference; *OR,* odds ratio.

SEARCH STRATEGY

Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1946 to Present			
#	Searches	Results	Search type
1	aortic aneurysm, thoracic/dt, th, su	7109	Advanced
2	"thorac* aortic aneurysm*".mp.	3415	Advanced
3	aortic aneurysm, thoracic/ or 2	10,357	Advanced
4	aneurysm, rupture/dt, th, su or aortic rupture/dt, th, su or aneurysm, dissecting/dt, th, su	11,832	Advanced
5	3 and 4	3374	Advanced
6	((medical or clinical) adj2 manage*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	56,101	Advanced
7	exp antihypertensive agents/ad, tu or exp hypertension/dt, pc or exp adrenergic beta antagonists/	174,649	Advanced
8	(beta adj2 block*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	42,636	Advanced
9	(monitor* or surveillance or progress* or risk*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	3,230,692	Advanced
10	or/6-9	3,415,753	Advanced
11	3 and 10	3466	Advanced
12	aortic aneurysm, thoracic/su or (3 and (open or thoractom* or sternotom* or anastomosis or repair or "cross clamp").mp.) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	7407	Advanced
13	3 and (blood vessel prosthesis/ or blood vessel prosthesis implantation/ or vascular surgical procedures/ or elective surgical procedures/)	4879	Advanced
14	3 and (angioplast* or endovascul* or stent* or tevar or endograft*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	3483	Advanced
15	11 and (12 or 13 or 14)	2857	Advanced
16	12 and (13 or 14)	5339	Advanced
17	13 and 14	2598	Advanced
18	1 or 5 or 15 or 16 or 17	7732	Advanced
19	(mortality or death* or surviv* or complicat*).mp. or co.fs. or ae.fs. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	5,050,895	Advanced
20	(postoperative* or intraoperative*).mp. or exp cerebrovascular disorders/ or stroke*1.mp. or los.mp. or "length of stay".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	1,213,845	Advanced
21	(outcome* or tracheostom* or ventilat* or work* or employ* or cost* or economic*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	3,581,114	Advanced

(Continued on next page)

Continued.

Ovid MEDLINE In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1946 to Present			
#	**Searches**	**Results**	**Search type**
22	(paralysis or transfus* or hemorrhag* or bleed* or haemorrhag*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	563,763	Advanced
23	or/19-22	7,981,950	Advanced
24	18 and 23	6567	Advanced
25	limit 24 to comparative study	599	Advanced
26	24 and (compar* or versus or vs).tw.	1154	Advanced
27	25 or 26	1386	Advanced
28	27 and (series or "case control*" or cohort* or prospective* or retrospective* or "cross section*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	837	Advanced
29	25 or 28	1031	Advanced
30	27 and observation*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	39	Advanced
31	limit 29 to yr="1995 - 2016"	998	Advanced
32	limit 30 to yr="1995 - 2016"	37	Advanced
33	31 or 32	1005	Advanced
34	33 not (letter or note or comment or editorial).pt.	992	Advanced
35	remove duplicates from 34	988	

CENTRAL – SAME STRATEGY = 29

Embase 1988 to 2016 Week 04			
#	Searches	Results	Search Type
1	thoracic aorta aneurysm/	5995	Advanced
2	*thoracic aorta aneurysm/su, dt, th	3316	Advanced
3	aneurysm surgery/	10,217	Advanced
4	endovascular surgery/ or endovascular aneurysm repair/	23,238	Advanced
5	vascular surgery/ or exp blood vessel transplantation/	102,275	Advanced
6	angioplasty/ or percutaneous transluminal angioplasty/	40,623	Advanced
7	exp conservative treatment/	402,571	Advanced
8	vascular implant/ or exp vascular stent/	25,992	Advanced
9	4 or 6 or 8	82,047	Advanced
10	3 or 5	110,561	Advanced
11	thoracic aorta aneurysm/dt, th, co, su	4404	Advanced
12	11 and (9 or 10 or 7)	2676	Advanced
13	12 and (comparative study/ or intermethod comparison/)	164	Advanced
14	11 and (7 or 9 or 10)	2676	Advanced
15	14 and (comparative study/ or intermethod comparison/ or compar*.mp.) [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	443	Advanced
16	13 or 15	443	Advanced
17	..l/ 16 hu=y and yr=1995-2016	428	Advanced
18	11 and 7	67	Advanced
19	11 and 9	1298	Advanced
20	11 and 10	1946	Advanced
21	18 and 19	29	Advanced
22	18 and 20	28	Advanced
23	19 and 20	589	Advanced
24	or/21-23	624	Advanced
25	exp case control study/ or exp case study/ or exp intervention study/ or exp major clinical study/ or exp prospective study/ or exp retrospective study/	2,430,371	Advanced
26	24 and 25	115	Advanced
27	24 and (cohort* or series or "cross-section*").mp.	60	Advanced
28	17 or 26 or 27	528	Advanced
29	28 not case report/	490	Advanced
30	29 not (letter or editorial or note or comment).pt.	470	

Scopus. (TITLE-ABS-KEY ((thoracic OR thoracoabdominal) W/4 (dissect* OR rupture* OR aneurysm*)) AND TITLE-ABS-KEY (open OR surgical OR surgery OR operation* OR prosthesis* OR conventional* OR prosthesis OR anastomo*) AND TITLE-ABS-KEY ((medical OR clinical OR conservative) W/3 (manage* OR care OR therapy))) 594

((TITLE-ABS-KEY ((thoracic OR thoracoabdominal) W/4 (dissect* OR rupture* OR aneurysm*)) AND TITLE-ABS-KEY (repair* open OR surgical OR surgery OR operation* OR prosthesis* OR conventional* OR prosthesis OR anastomo*) AND TITLE-ABS-KEY (stent* OR endograft* OR endovascular* OR tevar))) AND ((outcome* OR complicat* OR compar* OR death* OR mortality OR pulmonary OR cardiopulmonary OR stroke* OR paralysis OR paraplegi* OR surviv* OR morbid* OR reintervention* OR reoperat* OR transfusion*r)) AND (compar*) 1902

1 AND 2 = 154

Publication Types

- Comparative study
- Meta-analysis
- Review

MeSH Terms

- Aneurysm, dissecting/surgery

- Aorta, thoracic/injuries
- Aorta, thoracic/surgery*
- Aortic aneurysm, thoracic/surgery
- Aortic diseases/mortality
- Aortic diseases/surgery*
- Aortic rupture/surgery
- Blood vessel prosthesis implantation/adverse effects
- Blood vessel prosthesis implantation/instrumentation*
- Elective surgical procedures
- Emergency treatment
- Humans
- Intensive care units
- Length of stay
- Odds ratio
- Reoperation
- Risk assessment
- Stents*
- Trauma, nervous system/etiology
- Treatment outcome
- Vascular surgical procedures/adverse effects
- Vascular surgical procedures/methods*

Medical management—aggressive blood pressure control, beta blockers

Surveillance, patient education, elective surgical repair

Serial imaging—CT, MR angiography

Preoperative evaluation

Risk assessment

Pulmonary function tests

Thoracotomy

Perioperative monitoring

Open repair = median sternotomy

Revascularization distal anastomosis, arterial reimplantation, endarterectomy, bypass graft

Cardiopulmonary bypass/cross-clamp aorta

Tevar

Endovascular aortic repair

Stent—graft/endograft

Publication Types
- Clinical trial, phase II
- Comparative study
- Multicenter study
- Research support, non-U.S. government

MeSH Terms
- Aged
- Aged, 80 and over
- Angiography
- Angioplasty/adverse effects
- Angioplasty/methods*
- Aortic aneurysm, thoracic/mortality
- Aortic aneurysm, thoracic/radiography
- Aortic aneurysm, thoracic/surgery*
- Aortic aneurysm, thoracic/therapy
- Blood vessel prosthesis implantation/adverse effects
- Blood vessel prosthesis implantation/methods*
- Equipment safety
- Female
- Follow-up studies
- Humans
- Male
- Middle aged
- Postoperative complications/diagnosis
- Postoperative complications/mortality*
- Probability
- Risk assessment
- Severity of illness index
- Statistics, nonparametric
- Stents*
- Survival rate
- Tomography, X-ray computed
- Treatment outcome
- Vascular surgical procedures/adverse effects
- Vascular surgical procedures/methods