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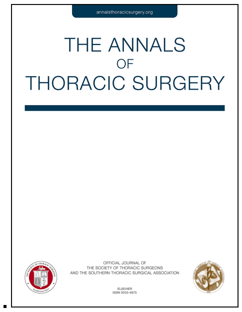

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Endovascular Versus Open Repair For Chronic Type B Dissection Treatment: A meta-analysis

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Abstract

Background: The respective place of endovascular versus open surgery in thoracic dissecting aneurysm treatment remains debatable. This comprehensive review seeks to analyse the outcomes of endovascular repair (ER) compared to open surgery (OS) in chronic type B aortic dissection treatment.

Methods: Embase and Medline searches (2000 – 2017)were performed following Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines. Outcomes data extracted comprised firstly early mortality and major complications: stroke, spinal cord ischemia (SCI), dialysis, respiratory complications; secondly, late survival and reinterventions. Reintervention causes were divided into proximal, adjacent, distal. Comparative studies provided comparative meta-analyses. Non-comparative studies were analysed in pooled proportion meta-analyses for each group.

Results: 39 studies were identified: 10 OS, 25 ER, 4 comparative. Comparative studies meta-analyses revealed lower early mortality for ER (OR: 4.13, 95% CI: 1.10 – 15.4), stroke (OR: 4.33, 95% CI: 1.02-18.35), SCI (OR: 3.3, 95% CI: 0.97 – 11.25) and respiratory complications (OR: 6.88, 95% CI:1.52- 31.02), but higher reintervention rate (OR: 0.34, 95% CI: 0.16 – 0.69). Mid-term survival was similar (OR: 1.19, 95% CI:0.42 – 3.32).

Non-comparative studies analyses showed distal causes as the principal reintervention indication in both groups: OS 73%; ER 59%. Reintervention procedures were mainly surgical for OS (85%), mainly endovascular for ER (75%). Rupture rates were: OS 1.2% , ER 3%.

Conclusions: This recent non -randomised data shows early ER benefit, unsustained at mid-term. Reintervention is higher after ER, necessitating improved technique. However, OS is exempt neither from reintervention nor rupture. Both techniques have their place, but patient selection is key.

The question regarding optimal treatment of thoracic or thoracoabdominal aneurysms, whether degenerative or dissecting, still divides the surgical community **(1)**. It has become more pertinent as the number of patients requiring repair during chronic phase of aortic dissection increases, due to improved imaging techniques, more sophisticated acute dissection management and better monitoring during follow-up.

Open surgery (OS) has long been considered as standard treatment for chronic dissection where medical management has failed to prevent disease progression. It nevertheless remains that the anatomical specificities of dissecting aneurysms render open repair challengingly complex. This is reflected in the high operative risks incurred, as demonstrated by early series reporting operative mortality as high as 27% with serious neurological complication rates of up to 28% **(2)**. These unfavourable outcomes, along with the emergence of endovascular treatment as a less invasive alternative for thoracic aneurysms, have prompted a gradual shift away from surgical repair.

Endovascular repair (ER) for aortic dissection was first applied in acute phase, and favorable results lead to recommendations in an Interdisciplinary Expert Consensus Document that it should be considered as first-line treatment **(3)**. Although the initial physiopathological mechanism is the same, chronic dissection is considered a different entity due to the fibrotic flap and multiple mature and stable communications between true and false lumen. These specific characteristics are responsible for a reputedly lower potential for remodelling, and consequently mid and long-term data have demonstrated higher reintervention rates **(4)**. This has restricted the widespread acceptance of thoracic endovascular aortic repair (TEVAR) for this indication and accounts for reluctance to consider ER as a durable alternative to OS.

This study aims to offer a comprehensive analysis of current literature to determine early outcomes, mid or long-term survival and reintervention rates after chronic dissection repair by either open or endovascular intervention.

Material and methods

Literature search

This review was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines **(5)**. To identify studies evaluating ER, OS, and those comparing the two techniques for chronic type B dissection treatment, an electronic search of Embase and Medline databases from 2000 to June 2017 was performed. The free-text search terms “aort*”, “dissection”, “type B”, “endovascular”, “repair”, “stent-graft”, “TEVAR”, “surgical treatment”, “open repair”, and the Medical Subheading term “dissection aneurysm” were used in combination with Boolean operators AND or OR. Additional hand-search was also undertaken in the Current Controlled Trials Register and Cochrane Database.

Search was limited to English language studies. Inclusion criteria comprised: (1) randomised controlled trials and retrospective or prospective observational studies, (2) dated after 2000, (3) reporting at least 15 patients treated for chronic dissection, (4) either by open or endovascular repair, (5) providing sufficient data of early, mid or long-term outcomes. Exclusion criteria comprised: (1) arch or hybrid repair series, (2) reports with less than one-year follow-up, (3) mixed acute and chronic dissection series or degenerative and dissecting aneurysm series, where data regarding chronic patients or dissection could not be separated from the rest of the cohort, (4) randomised trials comparing TEVAR to medical treatment.

Definitions and endpoints

- Chronic type B dissections were defined by a more than 2-week time frame following onset of symptoms and included any non-traumatic dissection. Data pooling from subacute and true chronic dissection was dictated by the limited number of publications adopting the categorization into acute, subacute and chronic.
- Early mortality corresponded to death occurring either within 30 days of procedure or in hospital prior to discharge.
- Endpoints were firstly, early mortality and major postoperative complications: stroke, spinal cord ischemia (SCI), de novo dialysis, respiratory complications; secondly, late survival and reinterventions.

Aortic related reintervention comprised all aortic procedures occurring during follow-up, > 30-days after index TEVAR, whether surgical or endovascular, and whether related to treated segment or at remote sites. Reinterventions unrelated to dissection were disregarded. Further details regarding indication type, treatment required and outcomes in terms of reintervention related mortality were also extracted. According to indication type, reintervention was divided into three subgroups: proximal, adjacent, distal to repair. For OS, proximal reintervention corresponded to proximal aneurysmal degeneration, type A dissection, proximal anastomotic pseudoaneurysm, whereas distal subgroup comprised distal aneurysmal degeneration. Graft infection, patch pseudoaneurysm, aortoesophageal fistula or visceral artery stenosis were categorized as adjacent subgroup. For ER, proximal subgroup encompassed retrograde dissection, type Ia endoleak and proximal extension. Distal reintervention was linked to distal aneurysmal degeneration. Type II or III endoleak, or other problems along the stented aorta, were considered as adjacent causes.

Data collection and analysis

Data extracted from each study were related to patients and pathology on the one hand, and on the other, to early, mid or long-term outcomes (26 variables, see **Appendix 1**). Two authors independently identified and analysed eligible articles. Any discordance was discussed with a third reviewer. The variable "pathology extent" differed from "extent of repair" and was categorized according to Debakey classification: residual type I, types IIIa or IIIb. When extension above or below coeliac axis was not specified, categorization was type III. Neither neurologic deficit < 72 hours nor temporary symptoms related to SCI, nor temporary dialysis were considered for calculation of major event rates. Respiratory complications encompassed various forms of pulmonary adverse events leading to prolonged ventilation. Survival data was obtained from at-risk scores tables or extracted from Kaplan Meier curves. Missing or lacking endpoint were not considered as nil.

The Scottish Intercollegiate Guidelines Network tool was used for quality assessment **(6)**.

Statistical analysis

Comparative meta-analyses (ER vs OR) were performed for outcomes: hospital mortality, stroke, SCI, dialysis, respiratory complications, reintervention and mid-term survival. Survival rates were calculated at two time points (1 and 3 years). Pooled odds ratio (OR) with 95% confidence intervals (CIs) were calculated. Fixed or random effect was used according to heterogeneity degree which was examined by Cochrane's Q statistic and I^2 test. I^2 value >50% indicated high heterogeneity and thus implies that the random effects model was used.

Non-comparative studies referring to single treatment modality were not used for comparative meta-analysis but analysed separately in pooled proportion meta-analyses for each group. The latter data were presented as weighted frequencies or means with 95% CIs. For primary analysis, aggregated data from descending thoracic aorta (DTA), thoracoabdominal aorta (TAA) repair and mixed DTA and TAA studies were presented. Sub-analysis within series targeting TAA repair was then performed. Exclusively DTA repair data were limited, precluding reliable statistical analysis.

Funnel plot was used to evaluate publication bias. A two-sided p value < 0.05 was considered statistically significant. Statistical analysis was performed using Comprehensive Meta-Analysis Software version 2 (Biostat, New Jersey).

Results

Of the 1238 abstracts initially identified as potentially eligible, 39 studies met the inclusion and exclusion criteria and were selected to serve as the basis for the current review **(Fig 1)(7- 45)**. Only 4 articles compared the two techniques. Most studies were retrospective and based on single-centre experiences. There were 4 multi-centre studies, all of which reported on patients treated with TEVAR.

Data from non-comparative studies

Pre- and intra-operative details

10 studies reported 1079 patients treated with OS, mean age 58.1± 0.9 years. Overall, aortic dissection was mainly classified as Debakey IIIb (81.5%) and preoperative maximum aortic diameter was 63.5 ± 2.6 mm. The procedure was performed urgently or emergently in 14.4% of cases, most of which (89%) were due to rupture or impending rupture. Aorta replacement was extended to TAA in 63.2% of cases and limited to DTA in only 36.8 % **(Appendix 2)**.

TEVAR data stemmed from 25 studies totalling 1271 patients, mean age 59± 0.9 years. Dissection extent was Debakey IIIb in 79.6 % of patients and preoperative maximum aortic diameter ranged from 52 to 76.8 mm, mean= 61± 1.8 mm. Urgent or emergent repair was required in 4.7% of cases, of which 52% were related to rupture or impending rupture **(Appendix 2)**. Treatment consisted of standard TEVAR for all studies but two, which reported their experience with fenestrated or branched TEVAR.

Early outcomes

Cumulative all-cause early mortality was 9.3% (95% CI: 0.07 – 0.12) in OS group **(table 1)** and 2% (95% CI: 0 – 0.03) in ER group **(table 2)**.

Cumulative stroke and SCI rates were respectively 4.5% (95% CI: 0.03 - 0.06) and 5% (95% CI: 0.03 – 0.08) after OS, whereas in ER group stroke and SCI rates were 2.7% (95% CI: 0.017 - 0.041) and 2.2% (95% CI: 0.014- 0.034). The overall need for dialysis was 5.2% (95% CI: 0.02 – 0.11) after OS and 0% (95%: 0 – 0.01) after TEVAR.

OS was associated with respiratory complications in 24.9% of cases (95% CI: 0.14- 0.39) compared to 4% (95% CI: 0.02 – 0.06) following TEVAR.

Late survival

In OS cohort, survival rates at 1 and 3 years were respectively 84% (95% CI: 0.78 - 0.88) and 79.9% (95% CI: 0.71-0.86) **(table 1)**. Only one study reported on aortic related mortality, which was 2.1% **(table 3)**.

In ER cohort, 1 and 3-year survival rates were similar: 91% (95% CI: 0.88- 0.95)**(table 2)**. Aortic related death was mentioned in most studies, with a 3.2%(95% CI: 0.02 - 0.04) cumulative rate **(table 3)**, while all-cause late mortality was 9%.

Reintervention, rupture and aortic remodelling

For OS group, during an overall 65.5 months' mean follow-up, reintervention was required in 11.8 % of cases (95% CI: 0.08- 0.16), and rupture reported in only 3 studies, representing a 1.2% (95% CI: 0.005 - 0.032) cumulative rate **(table 3)**.

For ER group, mean follow-up time was 30.4± 2.8 months. Reintervention rate was 20.2% (95% CI: 0.15 – 0.26%), time to reintervention 15.4 months (range: 8.5- 23) and rupture rate 3% (95% CI: 0.02 – 0.04) **(table 3)**.

Indications for reintervention and its treatments for both groups are listed in **table 3**.

After OS, causes for reintervention were considerably more frequent distal to the treated segment (73%) than adjacent (16.7%) or proximal (10.5%). Similarly for ER the main causes leading to reintervention were distal (59%), followed by proximal (32%) and adjacent to stent-graft (9%). For OS, reintervention procedures were mainly surgical (85%), while for ER they were endovascular (75%). Outcomes data after secondary intervention were described only in TEVAR studies, with reintervention related mortality rate of 1.4% (95% CI: 0.008 – 0.026).

After ER, aortic remodelling was assessed at various anatomic levels and according to different morphological parameters **(Appendix 2)**. Cumulative complete thoracic aorta thrombosis was 71.7% (95% CI: 0.57- 0.82). Association between survival and remodelling was analysed by 2 studies: contrary to Scali et al **(35)**, Mani et al **(33)** observed positive effect on mid-term-survival,

Data from comparative studies

<u>Pre- and intra-operative details</u>

Four studies involving 195 patients treated with OS and 139 with ER contributed to meta-analysis. Comparison of demographic characteristics showed that patients receiving ER were older than those receiving OS (64.3 ± 2 years vs 58± 2 years, p= 0.01) with more frequent coronary artery disease, chronic obstructive pulmonary disease and renal failure, yet the differences were not statistically significant (18.2% vs 16.2%, p=0.742; 25.4% vs 14.7%, p=0.284; 19.3% vs 13.3%, p=0.575). Dissection was more likely to be associated with connective tissue disorder in OS: 17.6% vs 2% (p= 0.002). The proportion of procedures performed in urgent or emergent setting was similar between the 2 groups (19.2% for OS vs 27.9% for ER, p= 0.55). Mean time from dissection to index intervention was higher for OS (30.9± 10.4 vs 22.1± 10.4 months, p=0.55). Anatomic characteristics comparison revealed that dissection was more commonly extensive in OS (Debakey IIIb 80.2% in OS versus 60.7% in ER, p=0.30) with larger maximum aortic diameter (63 ± 4 mm vs 55.8 ± 3 mm, p= 0.15). Repair extent was limited to DTA in 97.7 % of cases in ER and, on the contrary, extended to TAA in 72.4% of cases in OS (p=0.001).

Early outcomes

Cumulative all-cause early mortality was significantly lower in ER versus OS (OR: 4.13, 95% CI: 1.10 – 15.4, p=0.035) **(Fig 2A)**. Adverse neurologic events were significantly higher after OS for overall risk of stroke and SCI, respectively (OR: 4.33, 95% CI: 1.02-18.35, p=0.04) and (OR: 3.3, 95% CI: 0.97 – 11.25, p=0.05) **(Fig 2B, 2C)**. Following OS, patients were more likely to develop severe respiratory complications (OR: 6.88, 95% CI:1.52- 31.02 , p=0.01)**(Fig 2D).** Surprisingly the need for permanent dialysis in postoperative course did not significantly differ between ER and OS (OR: 2.99, 95% CI: 0.56 - 15.97, p=0.20) **(Fig 3A)**.

Late survival

Survival analysis at 1 and 3 years showed no benefit of one technique over the other: (OR: 0.73, 95% CI: 0.34 – 1.55, p=0.41) and (OR: 1.19, 95% CI: 0.42 – 3.32, p= 0.73) **(Fig 3B,3C)**. Funnel plots did not indicate a significant risk of bias for mortality outcome.

Reintervention and rupture

Compared to OS, endovascular repair significantly increased reintervention risk (OR: 0.34, 95% CI: 0.16 – 0.69, p=0.003) **(Fig 3D)**. There was no difference between OS and ER in terms of indication type, whether proximal (p=0.81), adjacent (p=0.06) or distal (p=0.27) to the treated segment. However reintervention was more often managed using endovascular techniques in ER group (OR: 0.24, 95% CI: 0.08 – 0.69, p=0.008). Reintervention related mortality was noted in only 2 studies and did not significantly differ between OS and ER (OR: 0.49, 95% CI: 0.10 – 2.46, p=0.39).

Since details about rupture were not provided in the OS group, comparative meta-analysis was impossible for this outcome.

Thoracoabdominal aneurysmal dissection repair

Five studies reported data on TAA repair: OS cohort =160 patients; ER cohort = 63 patients.

Early outcomes

Cumulative all-cause early mortality was 7.5% (95% CI: 0.04 – 0.13) in OS group and 8.9 % (95% CI: 0.02 – 0.26) in ER.

Cumulative stroke and SCI rates were respectively 3.9% (95% CI: 0.02 – 0.08) and 9.2% (95% CI:0.05 – 0.15) after OS, whereas for ER cumulative SCI rate was 0%. Stroke rate was provided by only one study: 0% **(Appendix 3)**.

Late survival

One- year survival was 86.6% (95% CI: 0.80 – 0.91) and 87.5% (95% CI: 0.71- 0.95) respectively for OS and ER cohorts. Three-year survival was provided by only one study: 75% for OS and 85% for ER.

Reintervention

Reintervention rates were 14.7% (95% CI:0.03 – 0.44) for OS and 34 % (95% CI:0.09 – 0.72) for ER.

Comment

Given the advances in imaging, surgical techniques, critical care and knowledge of aortic dissection in the last decades, and to avoid bias related to the use of historical series, this comprehensive review search was limited to concurrent series. In contemporary literature surgical series are considerably less plentiful than endovascular. This may be partly explained by the fact that such complex aortic surgery is limited to high- volume centers, whereas TEVAR can be performed in less restrictive environments. The higher median of patients in surgical (n=79) compared to endovascular series (n=40) supports this observation. It must nevertheless be noted that, beyond simple stent-graft deployment in diseased aorta, appropriate TEVAR for aortic dissection is challenging. Technical success requires preliminary fine-tune imaging analysis with exact anatomical characterization, notably intimo-medial tear location; high endovascular skill level to overcome procedural pitfalls; accumulated experience permitting adapted algorithmic approach.

One concern raised by some authors is that comparison between open and endovascular repair is difficult because of differing patient populations **(9, 42)**, and this was indeed the case in our comparative studies cohort. Similar maximum aortic diameter noted in both groups, indirectly indicates that the reputedly less invasive nature of endovascular approach has not led to a size threshold lowering.

Despite the fact that pathology extended to TAA in most cases in both groups, repair extent differed, with more need to involve TAA in OS group. This can be explained by the two different treatment principles. OS is based on replacement of aneurysmal aortic segment, but, to successfully perform distal anastomosis, this segment must be relatively healthy, yet is not always readily available within thoracic aorta. On the other hand, TEVAR aims to seal the entry tear and achieve false lumen thrombus with less concern about distal landing zone. This difference could be a potential confounding factor to be considered when interpreting results, and could explain the higher mortality and morbidity rates noted in OS cohort.

This review provides evidence of the early mortality and morbidity benefit of TEVAR: lower all-cause hospital mortality, lower stroke and SCI rates. In comparison to what has been reported in OS literature in the last 20 years, the rate of major complications is undoubtedly lower in the present review, yet remains higher compared to ER.

The higher rate of permanent neurological events after OS generates functionality and autonomy loss, thus reducing life quality. No comparative study objectively documented this. Despite wide use of protective techniques, such as spinal fluid drainage in both types of intervention, SCI still remains more of an issue for surgical repair.

Endovascular sceptics often cite the more frequent need for reintervention associated with ER in mid or long term. Even if effectively more frequent after ER, this review showed that OS was not exempt from reintervention risk. Indeed, in open group, the rate was as high as 12% with over half to treat distal expansion of dissected aorta, even though distal anastomosis is usually performed in apparently healthy aorta. Pujara et al **(10)** found maximum aortic diameter, as well as diameter at diaphragm or renal artery levels, as predictive of poor late outcomes in terms of death and reintervention after OS.

Similarly, after TEVAR, causes distal to stent-graft accounted for about 60% of reinterventions, in line with recent systematic review report **(46)**. The latter identified aneurysmal dilatation of distal aorta secondary to retrograde false lumen perfusion as the most common reason for reintervention. This probably implies that some kind of reintervention is unavoidable because inherent to the pathology itself, and not to the technique, whether surgical or endovascular. While reintervention is certainly frequent after TEVAR, it can mostly be treated by endovascular means, and related mortality was similar in both repair groups.

Secondary rupture rates were very low for both techniques. Proponents of OS advocate that once dissected segment is eliminated, risk of secondary rupture is nil **(16)**. This review reveals that even if rupture rate is lower after OS, it still occurs. Additionally, this cumulative rupture rate may be underestimated since numerous surgical studies failed to expressly mention this complication.

This study indicates that mid-term survival after ER is no better than after OS, a result which should be interpreted cautiously, since, of the 25 studies reviewed, only 15 reported on 3-year survival. The decline of initial ER survival benefit could be attributed to higher aortic related death secondary to reintervention and/or to increased cardiopulmonary death unrelated to dissection. The fact that ER patients were more frail with more advanced atherosclerosis, a tendency reflected in preoperative demographic characteristics, argues in favour of the second hypothesis, as does the absence of difference in reintervention related mortality found in the comparative studies. Goodney et al **(47)** reached a similar conclusion to explain unsustained ER mid or long-term survival benefit after degenerative aneurysm repair. Moreover, the fact that chronic phase is less likely to promote aortic remodelling may account for this finding. Indeed authors postulate that FL patency is indicative of poorer survival **(32, 33)**. However, data in this meta-analysis was not conclusive since only 2 studies analysed association between remodelling and survival, and reported contradictory results

Endovascular device progress, in particular fenestrated and branched stent-graft availability, now enables more extensive dissecting aneurysm treatment. Surprisingly, this review showed similar hospital mortality and 1-year survival rates in both groups. Greenberg et al's comparative study mixing degenerative and dissecting aneurysm reported analogous results. However, a 2-year survival benefit was noted for ER**(48)**.

Limitations

A significant limitation stems from existing data, which, in most OS studies, combined DTA and TAA repair, whereas, with the exception of two series, ER studies reported only on DTA repair, which may have biased outcomes in favor of ER. This difference is however inevitable and inherent to the principles of each technique, and cannot therefore be considered as heterogeneity of available data. For this reason a subanalysis focussed on TAA repair was provided in this review. These TAA cohort results should however be interpreted with caution, given the limited existing reports. Other differences in patient populations between ER and OS were detected and may have been a source of bias.

Another limitation in the comparative meta-analyses is inherent to the small populations treated and to bias related to ER or OS patient-selection based on anatomy and clinical status. However, if ever such bias occurred, it would have favored TEVAR for anatomical suitability and OS for clinical status, since better outcomes are expected in younger and fitter patients.

Furthermore, major event rates are probably underestimated for both techniques, since neither temporary dialysis nor temporary neurological complications were considered.

Finally, neither OS nor ER was compared to hybrid repair, which remains an accepted treatment modality. These hybrid series were excluded given the mixed population treated.

Conclusion

Available surgical and endovascular chronic dissection treatment guidelines are based on retrospective studies, and well-conducted prospective trials comparing the two techniques are lacking. Optimal management of complicated chronic dissection still needs to be precisely defined and no firm recommendation favoring either technique can be advanced.

Nevertheless, compared with OS, this study shows that ER had better early outcomes, although this benefit was not sustained for mid-term survival. Assumption that reintervention is a major problem after ER may be unfounded, as survival seemed unaffected and secondary rupture rare. Conversely, during OS, diseased aorta resection does not completely eliminate either reintervention risk or rupture, especially regarding dilatation of distal untreated segment. Both techniques undoubtedly have their place, but patient selection is key.

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Author/study and year	All-cause early mortality n(%)	Stroke n (%)	SCI n (%)	Definitive dialysis n (%)	Respiratory complications n (%)	Survival (%)		Quality assessment
						1-year	3-year	
Miyamoto 2008	0	2 (5)	0	-	5 (12.5)	96	94	++
Mutsuga 2010	0	2 (6.1)	3 (9.1)	-	8 (24.3)	-	-	+
Zoli 2010	10 (9.6)	6 (5.8)	5 (4.8)	1 (0.9)	16 (15.4)	78	75	+++
Conrad 2011	8 (11)	2 (3)	12 (16.4)	-	36 (49)	72	64	++
Pujara 2012	16 (9.4)	8 (4.7)	4 (2.4)	10 (5.9)	22 (13)	-	-	+++
Bashir 2014	14 (22.6)	7 (11.3)	2 (3.2)	16 (15.8)	-	76	73	++
Conway 2014	5 (5.8)	2 (2.3)	3 (3.4)	2 (2.3)	53 (62)	97	88.4	++
Estera 2015	18 (8.6)	5 (2.4)	5 (2.4)	11 (5.2)	-	83	-	+++
Fujikawa 2015	20 (8.5)	7 (3)	14 (5.9)	9 (3.8)	78 (33.3)	87.6	86.5	++
Kouchoukos 2015	4 (5.8)	2 (3)	4 (6.1)	3 (4.5)	7 (10.6)	86.6	75	++
Cumulative data(weighted average)	**95/1079 9.3%**	**43/1079 4.5%**	**52/1079 5%**	**52/929 5.2%**	**225/808 24.9%**	**84%**	**79.9%**	

Table 1: Early outcomes and late survival after open surgery

Data are n (%) or %

SCI = spinal cord ischemia

- = not reported

Author/study and year	All-cause early mortality n (%)	Stroke n (%)	SCI n (%)	Definitive dialysis n (%)	Respiratory complications n (%)	Survival %		Quality assessment
						1-year	3-year	
Kusagawa 2005	0	-	-	-	-	100	100	+
Eggebrecht 2005	0	0	0	-	-	86.4	78.8	+
Bockler 2006	0	0	0	0	-	100	-	+
Song 2006	2 (11.8)	1 (5.9)	0	-	-	-	-	+
Jing 2008	0	0	0	-	-	-	-	+
Sayer 2008	3 (7.5)	0	0	-	-	80	66.5	++
Alves 2009	2 (3.3)	-	-	-	-	-	-	++
Guangqi 2009	4 (8.2)	1 (2)	0	0	4 (8)	82.9	64.7	++
Kim 2009	0	0	0	0	-	-	-	++
Xu 2010	1 (1.2)	0	0	-	-	93	90	++
Parsa 2011	0	0	0	1 (2)	-	86.7	77.7	++
Kang 2011	4 (5)	1 (1.3)	0	0	7 (9.2)	86	80	++
Oberhuber 2011	0	0	1 (5.2)	0	-	-	-	+
Andachech 2012	10 (14)	1 (1.3)	1 (1.3)	0	-	81	-	++
Yang 2012	2 (7.1)	1 (3.6)	0	1 (3.6)	3 (10.7)	89	89	++
Qing 2012	0	0	1 (3)	-	-	-	-	+
Mani 2012	3 (5.1)	0	0	-	2 (3.4)	89	64	++

Jia 2013	0	0	2 (0.9)	-	-	95	82.7	+++
Scali 2013	2 (2.5)	6 (7.5)	5 (6.2)	-	3 (4)	89	80	++
Lee 2013	1 (1.4)	0	0	-	-	97.1	88.9	++
Kitagawa 2013	0	0	0	0	0	85	85	+
Song 2014	0	0	0	0	0	-	-	+
Virtue registry 2014	0	0	1 (2)	-	-	-	86	++
Kitamura 2014	0	2 (3.8)	0	1 (1.8)	1 (1.2)	100	90	+++
Oikonomou 2014	2 (11.8)	-	0	1 (5.9)	-	88.2	-	+
Cumulative data(weighted average)	**36/1271** **2%**	**13/1176** **2.7%**	**11/1193** **2.2%**	**4/490** **0%**	**20/379** **4%**	**91%**	**91%**	

Table 2: Early outcomes and late survival after endovascular repair

Data are n (%) or %

SCI = spinal cord ischemia

- = not reported

Author/study	Follow-up (months)	Reintervention delay (months)	Reintervention n (%)	Indication of reintervention			Reintervention type			Rupture n (%)	Aorta related late mortality n(%)	Reintervention related mortality n(%)
				proximal	adjacent	distal	Endovascular	surgical	hybrid			
Open repair												
Miyamoto	117±56.4	128 ±103	3(7.5%)	0	0	3(100)	0	3(100)	0	-	-	-
Mutsuga	-	-	-	-	-	-	-	-	-	-	-	-
Zoli	68.4 ±54	68.4±34.8	9 (8.6)	0	0	9(100)	0	9(100)	0	-	-	-
Conrad	53± 61.8	-	-	-	-	-	-	-	-	-	-	-
Pujara	23±15.6	-	23 (14)	14*(35)	12*(30)	14*(35)	22(55)	18 (45)	0	1 (0.6)	-	-
Bashir	43.2±44.6	-	-	-	-	-	-	-	-	-	-	-
Conway	55.2±13.9	Median 51.6	5 (5.8)	0	1(20)	4(80)	0	5(100)	0	-	-	-
Estera	102±44.6	41.6±39	19 (9)	-	-	-	0	19(100)	0	-	-	-
Fujikawa	-	-	31 (13.2)	5(16.2)	7(22.5)	19(61.3)	10(32.3)	21(67.7)	0	1 (0.4)	5(2.1)	-
Kouchoukos	64.8±66	-	18 (26)	6*(30)	10*(50)	4*(20)	-	-	-	2 (2.9)	-	-

Cumulative data(weighted average)	**65.5±11**	**65±9**	**108/911** **11.8%**	**25/108** **10.5%**	**30/108** **16.7%**	**53/108** **73%**	**32/107** **15 %**	**75/107** **85%**	**0%**	**4/472** **1.2%**	**-**	**-**
Endovascular repair												
Kusagawa	43.2±18	-	0	0	0	0	0	0	0	0	0	0
Eggebrecht	18(1-55)	-	-	-	-	-	-	-	-	3(9)	-	-
Bockler	24	-	4(23.5)	1(25)	0	3(75)	-	-	-	1(5.8)	2(11.7)	0
Song	11	-	2(12)	0	0	2(100)	2(100)	-	-	0	0	0
Jing	17±14	-	-	-	-	-	-	-	-	0	-	-
Sayer	-	-	14(35)	3(21.4)	1(0.7)	10(71.4)	-	-	-	0	-	-
Alves	36±28.5	-	13(22)	-	-	-	-	-	-	-	-	-
Guangqi	22.1±20.8	-	-	-	-	-	-	-	-	0	0	-
Kim	64.4 ±38.8	-	9(12.5)	1(11.1)	0	8(88.9)	7(77.8)	2(22.2)	0	1(1.4)	1(1.4)	0
Xu	33.2±19.2	-	5(6)	4(80)	0	1(20)	4(80)	1(20)	0	4(4.7)	4(4.7)	0
Parsa	27±16.5	-	11(21.5)	4(36.4)	3(27.2)	4(36.4)	9(81.8)	2(18.2)	0	-	1(1.9)	1(1.9)

Kang	33.5 ± 29.4	15±16.7	17(22)	5*(29.4)	1*(5.9)	12*(70.6)	9*(50)	9*(50)	0	1(1.3)	1(1.3)	0
Oberhuber	13(1-124)	23(6-59)	9(47.3)	-	-	-	7(77.8)	2(22.2)	0	-	0	0
Andachech	Mean 18	-	11(15)	7(63.6)	0	4(36.4)	9(81.8)	0	2(18.2)	0	0	0
Yang	26.1±17.8	-	4(10.7)	1(25)	0	3(75)	3(75)	1(25)	0	0	1(3.6)	1(3.6)
Qing	31.7±17	34	2(6.2)	1(50)	0	1(50)	1(50)	1(50)	0	0	0	0
Mani	38±28	15±18	12(25.5)	3*(17.6)	3*(17.6)	11*(64.7)	5*(29.4)	12*(70.6)	0	1(1.7)	2(3.4)	1(1.7)
Jia	28.5±16.3	-	9(4)	3(33.3)	0	6(66.7)	6(66.7)	3(33.3)	0	6(2.9)	6(2.9)	1(0.4)
Scali	24±21.4	17(4-33)	23(29)	-	-	-	16*(55.2)	13*(44.8)	0	0	-	0
Lee	-	-	25(35.2)	13*(46.4)	2*(7.1)	13*(46.4)	12*(42.8)	15*(53.6)	1*(3.6)	2(3)	2(3)	0
Kitagawa	20.4±18	-	8(53.3)	-	-	-	8(100)	0	0	-	1(6.7)	-
Song	10.3± 5	8.5±4.9	2(10)	0	0	2(100)	2(100)	0	0	0	0	0
Virtue registry	-	-	14(28)	4(28.6)	2(14.3)	8(57.1)	12(85.7)	1(7.1)	1(7.1)	1(2)	2(4)	-

Kitamura	90±46	-	21(40)	-	-	-	-	-	-	2(3.7)	-	-
Oikonomou	12(4-28)	-	3(17.6)	0	2(66.7)	1(33.3)	-	-	-	-	0	0
Cumulative data(weighted average)	**30.4±2.8**	**15.4 ±2.3**	**218/1159 20.2%**	**50/153 32%**	**14/153 9%**	**89/153 59%**	**110/176 75%**	**62/176 16%**	**4/176 9%**	**22/1108 3%**	**29/974 3.2%**	**4/940 1.4%**

Table 3: Late outcomes data after open surgery and endovascular repair

Data are n (%)

- = not reported

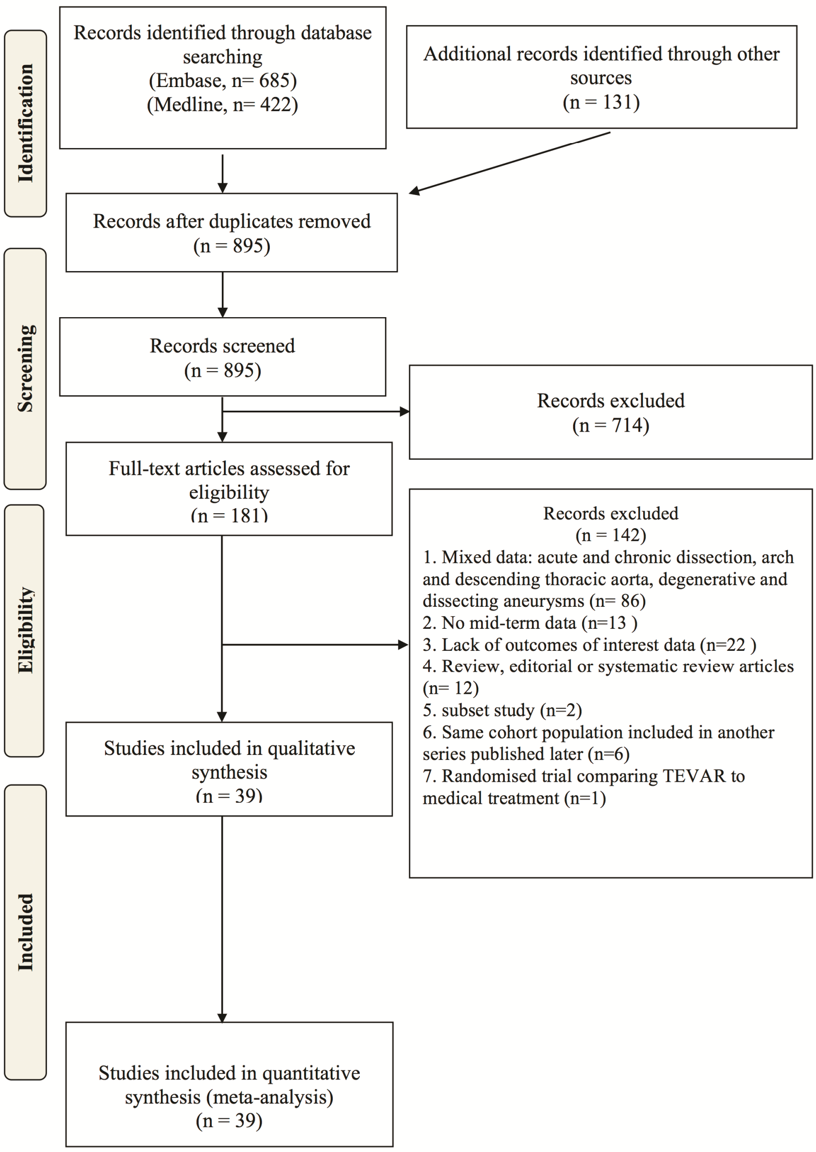
* number of procedures

Figure Legends

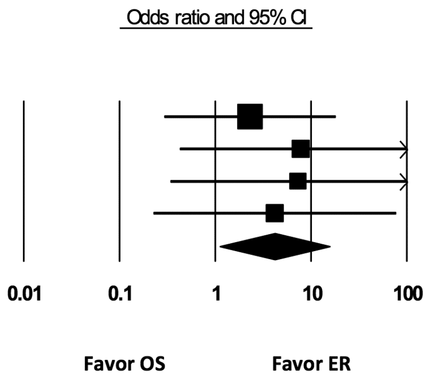
Fig 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart

Fig 2: (A) Random-effect meta-analysis plot for all cause early mortality comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval (B) Random-effect meta-analysis plot for stroke comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval (C) Random-effect meta-analysis plot for spinal cord ischemia comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval (D) Random-effect meta-analysis plot for respiratory complications comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval

Fig 3: (A) Random-effect meta-analysis plot for dialysis comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval (B) Random-effect meta-analysis plot for 1-year survival comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval (C) Random-effect meta-analysis plot for 3-years survival comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval (D) Random-effect meta-analysis plot for reintervention comparing endovascular repair (ER) and open surgery (OS); CI= confidence interval


Identification
Screening
Eligibility
Included
Records identified through database searching (Embase, n= 685) (Medline, n= 422)
Additional records identified through other sources (n = 131)
Records after duplicates removed (n = 895)
Records screened (n = 895)
Records excluded (n = 714)
Full-text articles assessed for eligibility (n = 181)
Records excluded (n = 142)
1. Mixed data: acute and chronic dissection, arch and descending thoracic aorta, degenerative and dissecting aneurysms (n= 86)
2. No mid-term data (n=13)
3. Lack of outcomes of interest data (n=22)
4. Review, editorial or systematic review articles (n= 12)
5. subset study (n=2)
6. Same cohort population included in another series published later (n=6)
7. Randomised trial comparing TEVAR to medical treatment (n=1)
Studies included in qualitative synthesis (n = 39)
Studies included in quantitative synthesis (meta-analysis) (n = 39)

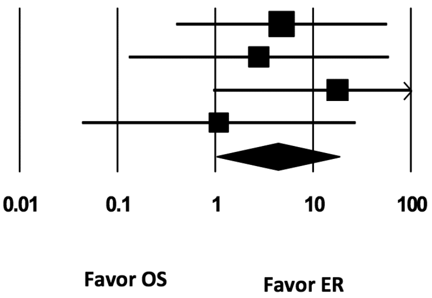
Study name	Statistics for each study				Relative weight
	Odds ratio	Lower limit	Upper limit	p-Value	
Nordrzykowski 2013	2.308	0.293	18.200	0.427	40.73
Leshnower 2013	7.800	0.425	143.206	0.167	20.51
Andersen 2014	7.295	0.338	157.326	0.205	18.42
Van Bogerijen 2015	4.181	0.225	77.767	0.337	20.33
	4.133	1.106	15.441	0.035	



Study name	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight
Nordrzykowski 2013	4.769	0.397	57.310	0.218	33.68
Leshnower 2013	2.788	0.130	59.899	0.512	22.13
Andersen 2014	17.800	0.947	334.632	0.054	24.19
Van Bogerijen 2015	1.089	0.043	27.421	0.959	20.01
	4.334	1.024	18.345	0.046	

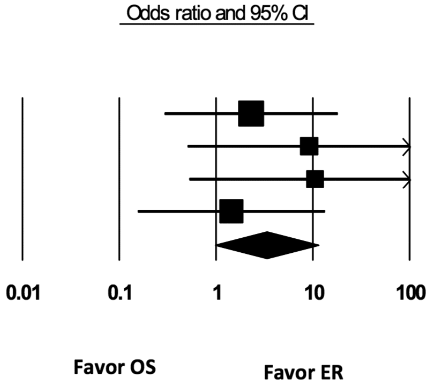
Statistics for each study

Odds ratio and 95% CI



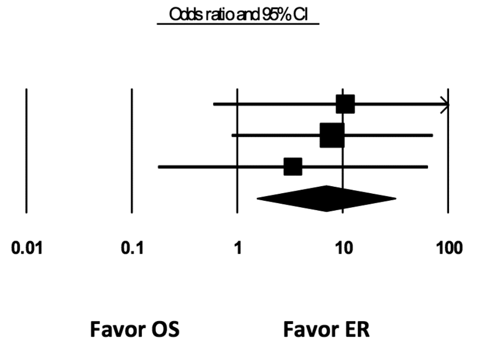
Study name	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight
Nordrzykowski 2013	2.308	0.293	18.200	0.427	35.21
Leshnower 2013	9.175	0.506	166.217	0.134	17.89
Andersen 2014	10.559	0.526	211.984	0.124	16.69
Van Bogerijen 2015	1.442	0.155	13.402	0.748	30.21
	3.303	0.970	11.250	0.056	

Statistics for each study



Model	Study name	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight
	Leshnower 2013	10.604	0.591	190.166	0.109	27.18
	Andersen 2014	7.963	0.882	71.888	0.065	46.78
	Van Bogerijen 2015	3.382	0.177	64.571	0.418	26.04
		6.887	1.529	31.020	0.012	

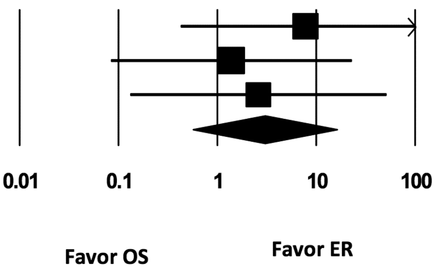
Statistics for each study



Study name	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight
Leshnower 2013	7.800	0.425	143.206	0.167	33.12
Andersen 2014	1.387	0.084	23.040	0.819	35.52
Van Bogerijen 2015	2.600	0.131	51.724	0.531	31.36
	2.993	0.561	15.973	0.200	

Statistics for each study

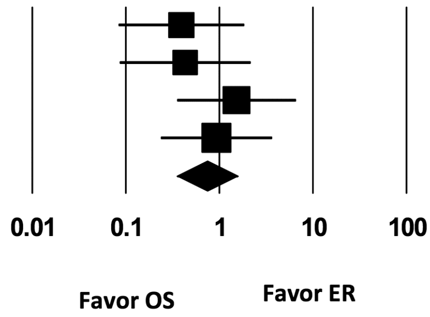
Odds ratio and 95% CI



Study name	Odds ratio	Lower limit	Upper limit	p-Value
Nordrzykowski 2013	0.393	0.083	1.854	0.238
Leshnower 2013	0.431	0.086	2.169	0.307
Andersen 2014	1.526	0.352	6.623	0.572
Van Bogerijen 2015	0.931	0.236	3.678	0.919
	0.735	0.348	1.551	0.419

Statistics for each study

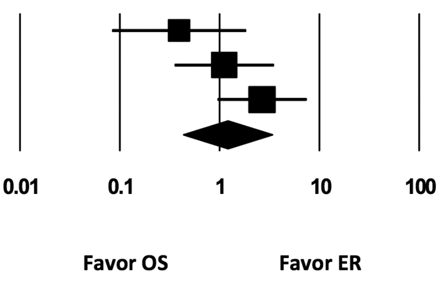
Odds ratio and 95% CI



Study name	Odds ratio	Lower limit	Upper limit	p-Value	Relative weight
Nordrzykowski 2013	0.393	0.083	1.854	0.238	25.93
Andersen 2014	1.114	0.353	3.522	0.854	35.39
Van Bogerijen 2015	2.667	0.947	7.511	0.063	38.68
	1.192	0.428	3.321	0.737	

Statistics for each study

Odds ratio and 95% CI



Study name	Statistics for each study				Odds ratio and 95% CI	
	Odds ratio	Lower limit	Upper limit	p-Value		Relative weight
Nordrzykowski 2013	0.080	0.004	1.472	0.089		5.80
Leshnower 2013	0.309	0.080	1.192	0.088		27.02
Andersen 2014	0.306	0.090	1.042	0.058		32.88
Van Bogerijen 2015	0.527	0.159	1.747	0.295		34.30
	0.342	0.169	0.690	0.003