Systematic Review

Open, closed or a bit of both: a systematic review and meta-analysis of staged thoraco-abdominal aortic aneurysm repair

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Background: Staged procedures are one strategy found to be beneficial for medium- to high-risk Crawford extent I–III thoraco-abdominal aortic aneurysm (TAAA) repair patients and may be performed through a variety of techniques. This review sought to compare the primary outcomes of spinal cord ischemia (SCI) and long-term mortality between three cohorts grouped by approach: open, endovascular, and hybrid.

Methods: In accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a total of 919 references were extracted from a search of three online databases (Embase, PubMed, Scopus). Following application of inclusion/exclusion criteria and data extraction, quantitative meta-analysis was undertaken utilizing a random effects model. Kaplan-Meier (KM) curves were digitized and aggregated to graph estimated survival.

Results: A total of 20 studies representing 924 patients were included. SCI was highest in the endovascular group, at 9.8% of weighted means, followed by hybrid, and open groups at 3.2% and 1.4%, respectively. However, 30-day mortality was highest in the open group at 6.0%, followed by the hybrid group at 3.8%, and endovascular at 3.6%. Aggregated long-term survival estimations are shown graphically, extending to 5 years for open and endovascular cohorts, and 3 years for the smaller hybrid cohort.

Conclusions: While all cases incorporated spinal drainage, monitoring and staging for spinal protection, there is innate difference in approach when examining for cord ischemia. This systematic review and meta-analysis of staged TAAA repair describes the first comparison between cohorts of open and endovascular approach, revealing the increased risk of SCI and long-term mortality in endovascular repair.

Keywords: Thoraco-abdominal aortic aneurysm repair (TAAA repair); staged; spinal cord ischemia (SCI)

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Introduction

Whether an emergent or planned operation, extensive thoraco-abdominal aortic aneurysm (TAAA) repair remains a highly complex procedure, with known risk to patient life as well as spinal cord function (1). With post-operative permanent paraplegia of up to 20%, neuroprotection strategies have been placed at the forefront of operative management in recent decades (2). Staging of operations into two or more individual procedures, usually separated by a timeframe of 1 week up to several months, is one technique which is now commonplace in expert aortic centers to reduce the significant rate of spinal cord ischemia (SCI). The aim of this concept is to provide sufficient time for the partially impaired spinal vasculature to repair itself and develop collateral networks (3). The effective preconditioning of the spinal arteries reduces the overall insult to the spinal cord, lowering the rate of major adverse outcomes compared to single-stage procedures (4). Other

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techniques have also been described to contribute to spinal protection, notably, cerebrospinal fluid drainage (CSFD), intraoperative monitoring, temporary aneurysm sac perfusion (TASP), and segmental artery embolization. A novel form of spinal protection, called minimally invasive segmental spinal artery coil embolization (MISSACE), first reported by Etz *et al.* in 2015, and currently undergoing multi-center trials in European centers, is a promising technique for future reduction of SCI in TAAA surgery (5).

Any TAAA characterized as an extent I, II, or III aneurysm, according to the Crawford classification (6), is commonly perceived as 'extensive', due to the propensity for these to cross the diaphragm and increase the technical complexity of the subsequent repair. While the extent V aneurysm, added by Safi *et al.* in 1999, has anatomical dilatation on both supra- and infra-diaphragmatic aortic segments, it does not span far enough to commonly be considered 'extensive' (7). It follows that the larger the extent of the aortic injury and subsequent dilatation, the larger the required repair or replacement of the native aorta. This is therefore more likely to inhibit the spinal collateral network and lead to SCI, including permanent paraplegia. This report aims to compare the spinal cord and mortality outcomes following the second stage intervention between three grouped combinations of surgical approaches. These are defined as: (I) the "open" group, consisting of two consecutive open surgical procedures, such as supra-diaphragmatic repair followed by infra-diaphragmatic repair, or vice versa; (II) the "endovascular" or "endo" group, consisting of consecutive endovascular procedures such as thoracic endovascular aortic repair (TEVAR) or fenestrated/branched endovascular aortic repair (f/bEVAR); and (III) the "hybrid" group, which for simplicity amalgamates patients who have received one open and one endovascular procedure in either order, i.e., open/endo or endo/open. Time between procedures was not controlled but rather accounted for and presented through demographic data in *Table 1*.

Methods

Literature search

Three electronic databases were selected to complete the initial literature search, specifically PubMed, Embase, and Scopus, from inception of records until 3rd January 2023. The search strategy employed Medical Subject Headings (MeSH) and focused keywords including: ("TAAA" OR "Thoracoabdominal aortic aneurysm" OR "Thoraco-abdominal aortic aneurysm" OR "Thoracic endovascular aortic repair" OR "TEVAR") AND ("staged" OR "hybrid").

After removal of duplicate records and those published before the year 2000, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in accordance with pre-written inclusion and exclusion criteria to screen the remaining records (8). Papers selected for full-text review were then exposed to stricter inclusion criteria which aimed for more homogeneity between the cohorts of included papers. Screening was conducted by two authors independently (Bilbrough J and Bushati Y) with any discrepancies being finalized through team discussion, with ultimate ruling by the leading author (Muston BT). A PRISMA diagram of the search strategy and list of records at each stage is depicted in *Figure 1*. Once full-text review was completed, the reference lists of all included papers were searched to assess for previously missed publications fitting the inclusion criteria.

Inclusion and exclusion criteria

Eligibility criteria was established prior to initial screening for this meta-analysis, focusing on maintaining a cohort of patients who had extensive repair of the aorta, spanning both thoracic and abdominal segments. For this reason, Crawford IV repairs were excluded so as to not artificially alter presented data, due to a recorded reduction of SCI in this patient group (9). In order to directly test the differences in SCI and mortality rates between the surgical interventions, similar extent of aortic repair, intervention type, and demographic data were controlled. Strict reporting of baseline patient data and procedural technique was sought to reduce confounding factors when measuring outcomes between studies. Only English language studies were included.

Studies were included if they met the following criteria: (I) the entire cohort consisted of TAAA repair patients with isolated outcome data; (II) the cohort specified Crawford types or extent of aneurysm repair; (III) data was presented following the second stage procedure; (IV) the type of repair was described (i.e., open/open, endo/endo, or a combination of both); (V) SCI was a recorded outcome. Studies were excluded if they: (I) included a pediatric population; (II) had a sample size smaller than ten patients; (III) had overlapping cohorts with larger included studies. All conference abstracts, reviews, editorials, and animal studies were also excluded.

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Table 1 Baseline cohort characteristics

Variables	Overall	Open	Endovascular	Hybrid	P value†
Studies	20	6	7	7	N/A
Patients	924 (100.0)	323 (35.0)	402 (43.5)	199 (21.5)	N/A
Males	581 (62.9)	173 (53.6)	277 (68.9)	131 (65.8)	0.67
Age (years)	64.6±12.1	59.5±13.8	70.8±10.8	61.9±10.7	0.014
Crawford type					N/A
Extent I	151	112	25	14	
Extent II	326	89	87	150	
Extent III	83	5	66	12	
Other‡	87	55	29	3	
Reporting frequency (%)	68.2	80.8	51.5	89.9	
Time between stages (months)	16.2±16.8	25.0±23.0	16.1±18.0	5.2±4.1	0.62
Urgent cases	83 (9.0)	57 (17.6)	16 (4.0)	10 (5.0)	0.27
Aneurysm diameter (cm)	6.6±1.1	6.4±0.87	6.7±1.1	6.6±1.4	0.44
Comorbidities§					N/A
Cardiac disease	130 (58.7)	58 (79.9)	37 (24.9)	35 (92.5)	
DM	97 (72.1)	21 (56.0)	55 (71.1)	21 (100.0)	
PVD	109 (34.4)	12 (20.1)	14 (23.4)	83 (79.9)	
Hypertension	729 (87.6)	176 (64.4)	373 (100.0)	180 (100.0)	
Smoking history	375 (65.8)	103 (56.0)	168 (68.4)	104 (76.4)	
CVA	56 (39.0)	24 (56.0)	3 (7.5)	29 (74.9)	
Previous aortic surgery	267 (28.9)	18 (5.6)	109 (27.1)	140 (70.4)	0.39
Connective tissue disorder	74 (8.0)	38 (11.8)	7 (1.7)	29 (14.6)	0.10

Values are n (%) or mean ± SD (weighted average) unless otherwise specified. †, P values are determined by comparison between open and endovascular groups (not given for variables with low reporting frequency); ‡, other aneurysm types making up a minority of the cohort, including: extent IV, extent V and descending thoracic aortic aneurysm; §, n = reporting frequency. N/A, not applicable; DM, diabetes mellitus (any type); PVD, peripheral vascular disease; CVA, cerebrovascular accident; SD, standard deviation.

Outcome measures

The primary outcome for this study was a pooled analysis of in-hospital SCI, reported as both a ratio with permanent paraplegia and overall temporary or permanent ischemia. SCI was defined as temporary or permanent motor or sensory dysfunction following surgery and was extracted either from direct SCI statistics or through provided modified Tarlov scale scores. Due to differences in use of modified Tarlov scales, SCI was defined as any score less than the highest available, or 'normal' ambulation. Paraplegia was defined as permanent motor SCI that did not resolve in the assessed post-operative period.

The secondary outcome was long-term mortality, assessed in two separate methods. The first involved all cohorts reporting mortality, which received weighted mortality analysis to be described quantitatively. The second method incorporated all manuscripts which included Kaplan-Meier (KM) curves, using a graphical approach to portray the data. Mortality was separated and compared by operative technique.

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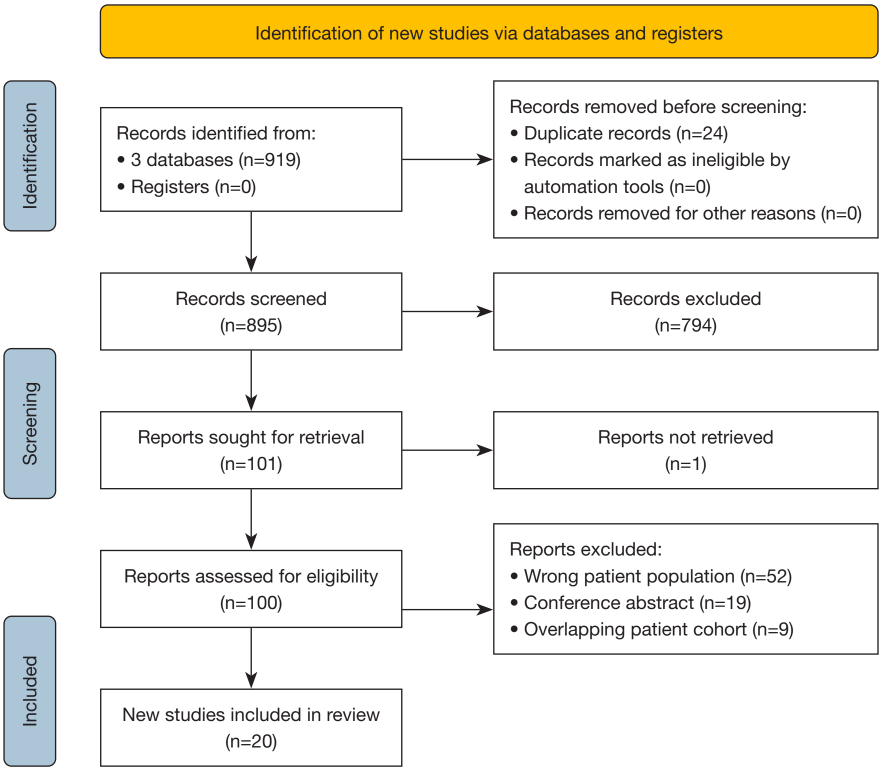

Figure 1 PRISMA flowchart of included studies. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Quality assessment

The quality of each study was assessed using the modified Canadian National Institute of Health Economics (CNIHE) assessment tool for case series (10). Of a possible total of 20 criteria to be met from the CNIHE tool, a study was considered high quality if it scored 17 or higher, moderate quality if it scored between 13 and 16, and low quality if it scored 12 or below. Study quality was independently assessed by two investigators (Muston BT and Bilbrough J) with review and consensus completed by the senior author (Muston BT).

Publication bias

The evaluation of inter-study bias was performed using Stata (version 17.0, StatCorp, College Station, TX, USA) in the form of a funnel plot. The data used to conduct this graphical analysis was extracted from the reporting of the primary outcome of SCI following any of the three intervention types, as this was reported by all studies. As opposed to an odds ratio commonly used when comparing randomized controlled trials, effect sizes should be used on a funnel plot comparing single-arm studies.

Statistical analysis

Baseline characteristics and operative details were extracted from the text, tables, and figures of included papers by three independent authors (Muston BT, Bilbrough J, and Bushati Y). Discrepancies were discussed then finally reviewed by the senior author (Muston BT). Statistical analysis was carried out using Stata (version 17.0, StataCorp) and R (version 4.1.1. R Core Team, Vienna, Austria) utilizing meta-analysis of proportions and means with a random effects model where necessary. Values were considered statistically significant if the reported P value was <0.05. For continuous data with central tendency described using median values and interquartile range, the mean and standard deviation were estimated using calculations described by Wan and colleagues (11). Survival data was calculated using aggregated KM curves collected from included studies, where reported, using

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the methods described by Guyot and colleagues (12). Digitization of source KM curves was performed using DigitizeIt (version 2.5.9, Braunschweig, Germany) and in the case where multiple cohorts were represented on the same curve, individual KM curves were first generated then subsequently merged with the rest of the data, to be analyzed together.

Results

After independent screening by three authors, 20 studies were included for analysis. Notably, a study by Safi *et al.*, published as an update of a previously written report, was included, but extraction of demographic data from the original paper was required to supplement the outcome data in the latter study (13,14). Furthermore, the study by Tsilimparis *et al.* was represented twice, with two eligible cohorts (15). These caveats are responsible for the final inclusion of 21 cohorts from 20 papers (14-33). Nine studies were excluded for patient overlap with other included studies after previously adhering to all inclusion criteria.

Quality analysis using the CNIHE tool resulted in nine studies being classed as of a high standard of quality, 11 studies being of medium quality and zero studies being of low quality (Table S1). Therefore, no further sub-group analysis for outcome data or heterogeneity was required as low-quality evidence was not a confounding factor in this meta-analysis.

Baseline study characteristics

Baseline cohort characteristics are reported in *Table 1*, along with reporting frequencies for each of the three operative methods. A total of 924 patients were followed in this systematic review, of whom 581 (62.9%) were male. The studies ranged in cohort size from ten to 122. The mean age of the overall cohort was 64.6±12.1 years with 83 (9.0%) being urgent or emergency cases. Patient comorbidities were infrequently reported. The mean aneurysm size before second-stage intervention was 6.6±1.1 cm overall, with no significant difference between the operative approaches. Study details are shown in Table S1, with most originating from centers in the USA (n=11), followed by Italian (n=5) and other European centers (n=4). Notably, the time between first and second stages of TAAA repair was significantly different between the comparator groups, attributed to the fact that planned staging reduced time between stages when compared to unintentional staging groups. This is clearly seen amid the open and hybrid cohorts, which spent 25.0±23.0 and 5.2±4.1 months between operations, respectively. The endovascular sub-group was the largest, including 402 patients, followed by the open and hybrid sub-groups at 323 and 199, respectively. Crawford extent II aneurysms were the commonest overall, involving the longest extent of repaired aorta and hence increased risk of SCI. The hybrid cohort had the highest proportion of data points involving this TAAA type, at 83.8% of reported cases, while the open cohort had the lowest ratio, at just 34.1%. Furthermore, 267 of 924 patients had received previous aortic surgery (prior to staged intervention) and 74 cases were reported with an associated connective tissue disorder.

Primary outcome evaluation: long-term SCI and paraplegia

All studies included data on overall SCI rates as well as permanent paraplegia, as per previously outlined inclusion criteria. Reported long-term follow-up for the primary outcome exceeded 2 years, with a mean of 27 months between studies. Pooled rate of SCI (temporary or permanent) was 5.4% [95% confidence interval (CI), 5.1–5.8%; I^2=31.7%; *Table 2*]. When subgroups were compared, the open approach resulted in the lowest proportion of SCI, at 1.4% (95% CI, 1.3–1.5%; I^2=0.0%), followed by the hybrid cohort with 3.2% (95% CI, 2.8–3.6%; I^2=0.0%) and the endovascular approach, which showed the highest presence of SCI postoperatively, at 9.8% (95% CI, 9.2–10.4%; P<0.01; I^2=23.8%) of cases.

Following sensitivity analysis, these results remained robust, with minimal deviation from the pooled effect size. Permanent paraplegia was also quantified using weighted means, showing the open approach subgroup to have the lowest rate at 0.7% (95% CI, 0.6–0.8%). When this metric is divided by the weighted means for SCI, the propensity for SCI to become permanent paralysis/paraplegia was highest in the hybrid subgroup, at 90.5%. The endovascular approach proved to be more favorable in this analysis than the open approach, with paraplegia occurring from associated SCI 26.2% *vs.* 49.9% of the time, respectively.

Secondary outcome evaluation: 30-day mortality following second-stage intervention

Data for the analysis of 30-day mortality were present in 19 studies, totaling 808 of 924 patients. The overall pooled 30-day mortality rate was 4.6% (95% CI, 4.3–4.8%;

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Table 2 Operative outcomes and early morbidity

Operative outcomes	Overall	Open	Endovascular	Hybrid	P value[†]	I^2 (%)
Patients	924 (100.0)	323 (35.0)	402 (43.5)	199 (21.5)	N/A	–
SCI (%)	5.4	1.4	9.8	3.2	<0.01	31.7
Paraplegia (%)	2.0	0.69	2.6	2.9	0.17	–
30-day mortality (%)	4.6	6.0	3.6	3.8	0.069	55.4
Hospital LOS (days)	19.5±9.0	26.6±7.4	15.2±7.6	14.8±5.9	0.34	–
ICU LOS (days)	11.2±7.4	16.1±7.7	5.3±1.7	7.4±2.0	0.42	–
Adverse events[‡]					N/A	–
MI	6 (24.2)	1 (22.6)	3 (22.1)	2 (31.2)		
Stroke/CVA	15 (41.3)	8 (64.4)	1 (15.4)	6 (56.3)		
AKI	83 (57.9)	25 (64.4)	8 (38.1)	50 (87.4)		
Respiratory failure	16 (15.6)	7 (10.8)	5 (15.4)	4 (23.6)		
Endoleak[‡]	–	–	2 (8.0)	11 (36.2)	0.29[§]	–

Values are n (%) or mean ± SD (weighted average) unless otherwise specified. [†], P values are determined by comparison between open and endovascular groups; [‡], n = reporting frequency; [§], endoleak assessed for endovascular and hybrid groups. N/A, not applicable; SCI, spinal cord ischemia; LOS, length of stay; ICU, intensive care unit; MI, myocardial infarction; CVA, cerebrovascular accident; AKI, acute kidney injury; SD, standard deviation.

I^2=55.4%; *Table 2*). Pooled mortality was greater in the open cohort than the endovascular cohort, at 6.0% (95% CI, 5.5–6.4%) *vs.* 3.6% (95% CI, 3.2–3.9%), however, this was not statistically significant (P=0.069). Hybrid operations achieved a similar 30-day mortality rate to the endovascular approach (3.8%; 95% CI, 3.3–4.2%).

KM curves were used to assess the less frequently reported long-term mortality rate and were aggregated and digitized to present this extended mortality rate (*Figures 2,3*). Actuarial survival at 1, 3, and 5 years for the open cohort was 76.5%, 61.7%, and 55.0%, respectively. This compared to the 1- and 3-year survival of the endovascular cohort (76.1% and 45.8%, respectively) shows a similar initial level of mortality but superior lasting survival for the open cohort. Five-year data was not presented for the endovascular cohort. Interestingly, the hybrid cohort showed the most impressive actuarial survival data, with 92.7%, 88.8%, and 85.8% at 1, 3, and 5 years, respectively. However, this was the least frequently reported and is likely impacted by bias and confounders.

Spinal cord protection techniques and comorbidities

All but two studies reported using some form of spinal cord protection outside of standard practice of induced hypothermia and rewarming. In total, 597 patients from a possible 805 patients received CSFD, whether prophylactic or interventional, following surgery. An additional 46 patients from the endovascular cohort were reported to have received TASP as an alternative SCI prevention modality. Limited data were presented on use of motor evoked potential (MEP) and somatosensory evoked potential (SSEP) monitoring from collected studies. Major adverse events following second-stage procedures are listed in *Table 2*. As expected, hospital and intensive care unit (ICU) length of stay (LOS) were longest in the open group, at 26.6±19.1 and 16.1±12.6 days, respectively. Notably, acute kidney injury (AKI) was more common in the open subgroup than those undergoing endovascular intervention, at 4.5% (95% CI, 4.0–5.0%) *vs.* 1.6% (95% CI, 1.5–1.7%), respectively.

Study bias evaluation

Publication bias was assessed using a funnel plot, with data provided from the pooled primary outcome of all included studies, in this case being SCI after intervention. The resulting funnel plot (*Figure 4*) shows some skew,

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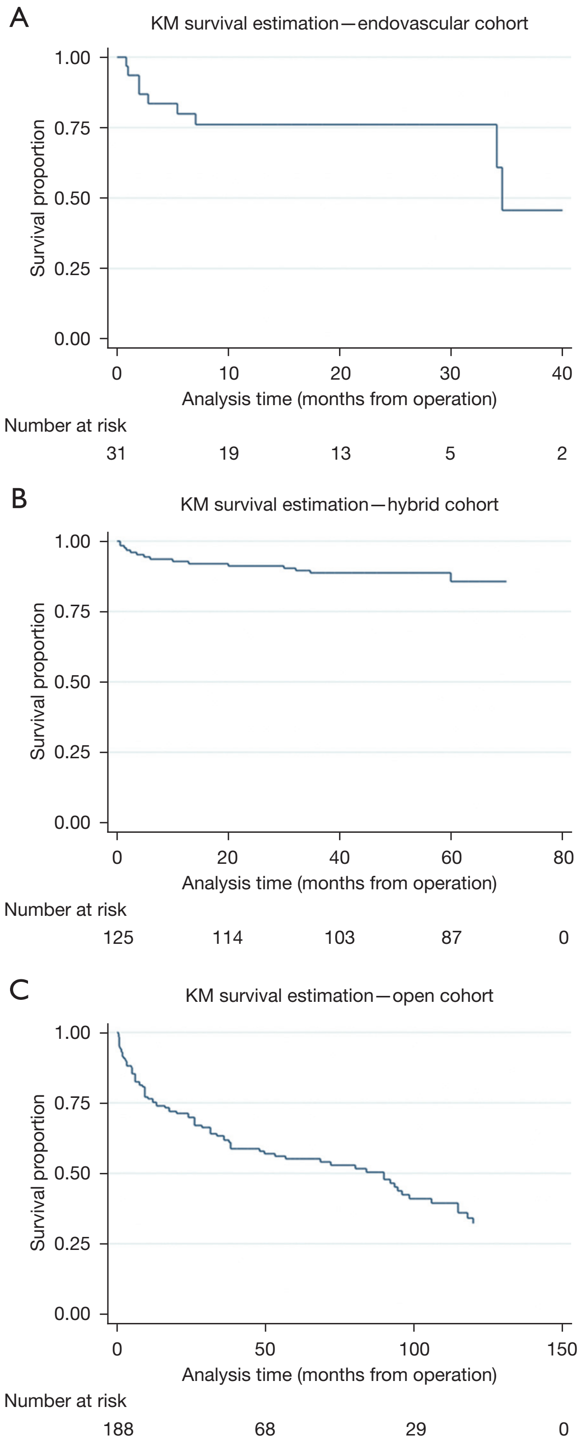

Figure 2 KM curve showing non-parametric survival analysis of: (A) endovascular cohort; (B) hybrid cohort; (C) open cohort. KM, Kaplan-Meier.

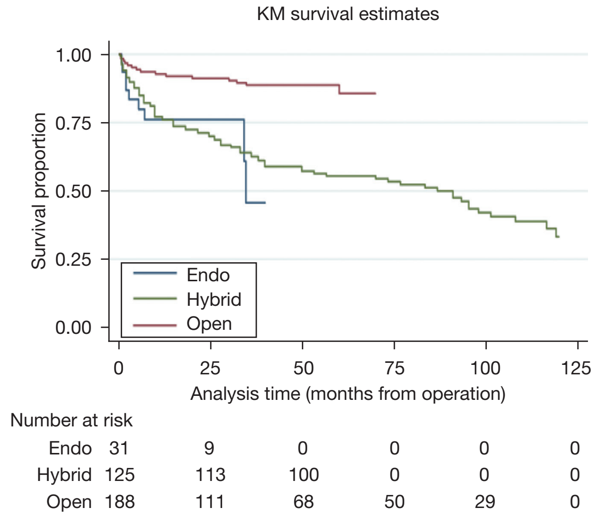

Figure 3 KM curve overlay for all included cohorts. KM, Kaplan-Meier; endo, endovascular.

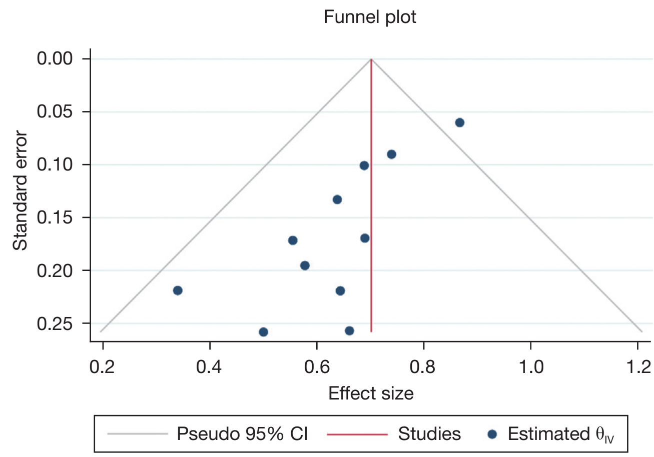

Figure 4 Funnel plot for SCI overall. CI, confidence interval; SCI, spinal cord ischemia.

suggesting the possibility of some bias in the publication of results between studies. The reasons for this skew are likely due to publication bias, heterogeneity between studies, differing methodology or random chance. Notably, this meta-analysis showed some moderate heterogeneity, requiring the use of a random-effects model, as despite I^2<50%, the Q test was not statistically significant (P=0.2).

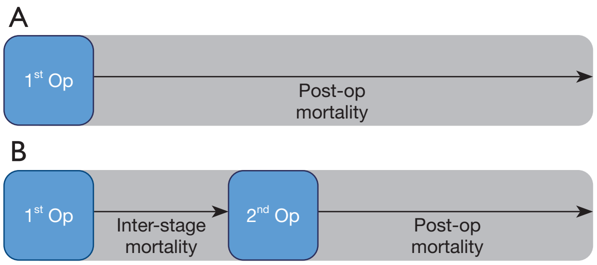

Figure 5 Timeline of possible mortality. (A) Single stage TAAA repair; (B) two-stage TAAA repair. Most reported risks are during each operation (blue boxes), or solely in the postoperative period, however total risk should be marked by mortality in its entirety. Op, operation; TAAA, thoraco-abdominal aortic aneurysm.

Discussion

While the benefit of staging as a method of spinal cord protection for extensive TAAA repair has long been recognized, with recent meta-analyses being performed for both open and endovascular cohorts (34,35), comparisons between staged cohorts have been lacking. Moreover, the current literature has a paucity of well-defined staged repair cohorts, whereby the morbidity and mortality data are published for a homogeneous patient group which can then be compared between centers. Nevertheless, this systematic review reported a pooled SCI rate of 5.4% and a pooled paraplegia rate of 2.0% from 924 patients distributed between 21 studies. The discrepancy between surgical approaches was noteworthy, showing open repair to be most favorable when solely analyzing this metric at 1.4%, and endovascular repair to be least favorable, at 9.8% of patients suffering SCI. These figures are verified in the literature yet have not previously been directly compared. Pini *et al.*, during a very comprehensive meta-analysis of 18 studies reporting endovascular TAAA repair for Crawford extents I, II, III, and V, found a similar rate of 9% when reporting overall SCI percentage (34). The rate of permanent paraplegia in their review were found to be slightly higher, at 6%, where this present review reports a rate of 2.6%. However, this may be due to variable reporting of permanent paraplegia between studies. This study was also valuable in portraying the importance of excluding the Crawford IV cohort when completing SCI analysis. A significantly lower percentage of patients suffered SCI in their Crawford IV cohort when compared to all other Crawford extents, at 6% *vs.* 13%, respectively. This is evidence for separation of these patients in future analyses in order to preserve homogeneity when comparing staging approaches. The reduced aortic coverage during repair of the extent IV aneurysm cohort can artificially reduce the risk of SCI when grouped into an overall TAAA repair population, which is why Crawford IV patients were excluded in this analysis.

Mortality differences also appeared between approaches for staged TAAA, however, this was most elucidated in the short-term. We found pooled 30-day mortality to be highest in the open cohort and lowest in the endovascular cohort, at 4.6% and 3.6%, respectively. Interestingly, this is a reversal of the order found in SCI outcomes. Differences in complexity between cases may be a reason for this discrepancy, as it is well established that surgical approach will be dictated based on the morphology of the aneurysm and complexity of the case. Usually, increased complexity leads to an open approach, which may be a confounding factor affecting the rate of mortality. An analysis of long-term mortality was also conducted, using digitized and aggregated KM curves for each surgical approach (*Figure 2*). While this is a useful visual representation of the survival data over 3 or more years, a relatively low sample size limits the comparability of the data. Four of the six open repair cohorts supplied a KM curve for aggregation, while 3/7 hybrid and only 2/8 endovascular cohorts had a KM curve able to be included in the final digitized graph. Regardless, at the 36-month interval, the hybrid group had the highest survival, at 88.7%, followed by the open group at 61.7%. The endovascular cohort had too few numbers-at-risk to make a meaningful interpretation of the aggregated survival estimate (*Figure 3*). It should also be noted that mortality was only assessed for the period during and following second stage intervention in this review, and that this only represents one of the four periods where the patient is at risk of death (*Figure 5*). Post-operative mortality was used in this review due to reporting frequency in included studies, however this is not to shroud or minimize the apparent risk of death for staged procedures. When using this review to report mortality in comparison to any non-staged procedures, a point of clarification must be made to also involve inter-operative mortality to fully express the incidence of death.

The nature of endovascular aortic repair using long landing zones, compared to the precise sutured attachment of open grafting, increases the extent of aortic coverage, making this approach more liable to SCI. Tenorio *et al.* suggest that this is a potential shortcoming of the endovascular repair in their review of the literature (36),

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which may be reflected in the present study's results as both endo and hybrid groups were inferior to the open group. Previous literature has established the importance that aortic coverage holds when analyzing rates of SCI (37,38), whether by multiple stent grafts or through extensive involvement by open repair, first denoted by Greenberg and colleagues (39). Multivariate analysis in a study assessing neurological complications associated with endovascular repair of the aorta by Buth *et al.* found statistically significant correlation between aortic length coverage and rates of SCI, an issue less prevalent in open repair (40).

The hybrid group described in this review included a mixed population undergoing TEVAR, f/bEVAR, frozen elephant trunk and open procedures as their first or second stage. However, this sub-group did have a high proportion of Crawford extent II patients (83.8%) and intentionally staged procedures, leading to a short, pooled interval between operations of 5.2 months. Good long-term survival was also shown through the composite KM curve (*Figure 2*) with 3-year survival of 86%. Our staged hybrid cohort proved to have substantially more promising results than a previous meta-analysis conducted by Moulakakis *et al.*, who found 14 single-stage hybrid cohorts comprising of 528 patients (41). This study established an operative mortality of 14.3% and a risk of SCI at 7.0%, both of which were higher than our results, which should be attributed to the lack of staging.

Further research should be conducted not only on prospective patient-matched randomized controlled trials, in order to make comparisons more directly between the surgical cohorts, but also longitudinal studies taking into account mortality rates between and after staged procedures, whether they are done with an open, endovascular or hybrid approach. This would allow incidence statistics to be unveiled regarding the risks of delaying complete aneurysmal repair during the staging process.

Limitations

Heterogeneity between and within sub-groups formed the predominant basis for impaired validity in this study. Firstly, between groups, inconsistent reporting of aortic coverage and co-morbidities as well as varying prevalence of Crawford extent II reduces the ability for the cohorts to be fairly compared to each other. While a great degree of caution was undertaken during selection of inclusion criteria, population differences still exist between intervention groups. Secondly, within groups, there was a notable difference in the time interval between staged procedures, which can be attributed to the number of intentionally *vs.* unintentionally staged patients. This could possibly skew survival data in the favor of those with longer intervals as these patients have survived longer after the first procedure and are therefore more likely to be stable and less complicated (13). Some cohorts within each sub-group also received different procedures despite being merged under the same heading. For example, the endovascular cohort had patients undergoing f/bEVAR initially before then receiving TEVAR, while other patients had both operations in the reverse order.

Furthermore, a preponderance for retrospective observational studies with most (15/21) analyzing cohorts of fewer than 40 patients can limit the generalizability of these data. Many of these reports (17/21) pulled data from only one institution, which heightens the impact of surgeon skill and the protocols of the single center on the survival outcomes.

Conclusions

This systematic review and meta-analysis describes the post-operative rates of SCI, permanent paraplegia and mortality following staged repair of TAAAs. We compared the outcomes between cohorts receiving total open, total endovascular and hybrid repair of the aorta and found that the open cohort had the lowest rate of SCI and permanent paraplegia, at just 1.4% and 0.7%, respectively. Hybrid repair showed promising long-term survival at 5-year with preliminary data. Overall, this study describes the first comparison between cohorts of open and endovascular approach, revealing the increased risk of SCI and long-term mortality in endovascular repair.

Acknowledgments

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Supplementary

Table S1 Study details and quality findings

Author, year	Cohort size, n	Males, n	Age (years), mean	Study quality (Delphi)	Country	Hospital	Years of patient enrolment	Crawford TAAA type†, n			Overall mortality, n	SCI (any), n	Paraplegia, n
								Type I	Type II	Type III			
Bertoglio, 2022	122	95	72.3	Medium	Italy	Italian Multicentre Fenestrated Branched Endografting Study	2008–2019	20	46	47	11	19	4
Coselli, 2022	27	15	58.9	Medium	USA	Baylor	1994–2017	NR	NR	NR	15	0	0
Di Marco, 2018	15	14	58.9	Medium	Italy	Bologna	2011–2016	6	10	1	2	0	0
Etz, 2010	35	20	62	Medium	USA	Mount Sinai	1994–2007	NR	NR	NR	4	0	0
Gallitto, 2022	64	48	–	High	Italy	Bologna	2010–2020	NR	NR	NR	6	7	2
Gombert, 2022	32	20	45	High	Germany/Netherlands	Aachen/Maastricht	2006–2019	0	28	4	6	2	1
Haensig, 2020	10	5	65.7	Medium	Germany	Leipzig	2014–2018	3	4	0	1	0	0
Hawkins, 2017	25	16	53	Medium	USA	Ohio	2005–2015	0	25	0	1	2	0
Hughes, 2012	25	8	67.7	High	USA	Duke	2005–2012	2	12	11	3	0	0
Iannacone, 2022	38	24	65.8	Medium	USA	Weill Cornell Medicine	1997–2020	30	8	0	2	3	1
Kawajiri, 2021	10	8	71	High	USA	Minnesota/Texas	2014–2018	3	7	0	2	1	0
King, 2022	116	68	72	Medium	USA	Vascular Quality Initiative	2014–2019	NR	NR	NR	NR	8	3
LeMaire, 2006	76	35	64.9	High	USA	Baylor	1990–2005	35	25	0	3	2	2
O'Callaghan, 2015	27	12	69.9	Medium	USA	Cleveland Clinic	2008–2013	0	27	0	0	3	0
Orrico, 2019	32	24	69.9	High	Italy	San Camillo Forlanini Hospital	2015–2017	5	6	16	0	2	0
Safi, 2007	115	59	59.75	High	USA	Texas-Houston	1991–2005	47	28	1	11	1	0
Spinella, 2020	11	10	74.5	Medium	Italy	Genoa/Pavia	2017–2019	0	8	3	0	3	0
Thompson, 2022	92	63	58	High	USA	Cleveland Clinic	2006–2021	0	92	0	7	6	6
Tsilimparis, 2020a	10	6	69.8	High	Germany/Sweden/France	Hamburg/Munich/Malmo/Paris	2012–2017	NR	NR	NR	6	1	1
Tsilimparis, 2020b	20	14	64.8	High	Germany/Sweden/France	Hamburg/Munich/Malmo/Paris	2012–2017	NR	NR	NR	6	3	3
Vivacqua, 2016	22	17	56	Medium	USA	Cleveland Clinic	2001–2013	NR	NR	NR	2	1	1

†, some studies included a small proportion of extent IV/V or non-TAAA patients. TAAA, thoraco-abdominal aortic aneurysm; SCI, spinal cord ischemia; NR, not reported.

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