



Endovascular repair of acute complicated type B aortic dissection – systematic review and meta-analysis of long-term survival and reintervention

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Background: Thoracic endovascular repair (TEVAR) is considered the first-line therapy in the repair of acute complicated type B aortic dissection (AC-BAD). Given the difficulty of designing randomized trials in this surgical cohort, long-term outcome data is limited. This systematic review and meta-analysis provide a complete aggregation of reported long-term survival and freedom from reintervention of AC-BAD patients based on the existing literature.

Methods: Three databases were searched from date of database inception to January 2021. The relevant references were identified and baseline cohort characteristics, survival and freedom from reintervention were extracted. The primary endpoints were survival and freedom from reintervention, whilst secondary endpoints were post-operative outcomes such as cord ischemia and endoleak. Kaplan-Meier curves were digitized and aggregated as per established procedure.

Results: A total of 2,812 references were identified in the literature search for review, with 46 selected for inclusion. A total of 2,565 patients were identified, of which 1,920 (75%) were male. The mean age of the cohort was 59.8±5.8. Actuarial survival at 2, 4, 6 and 10 years was 87.5%, 83.2%, 78.5% and 69.7%, respectively. Freedom from all secondary reintervention at 2, 4, 6, 8 and 10 years was 74.7%, 69.1%, 65.7%, 63.9% and 60.9%, respectively. When accounting for study quality, actuarial survival at 2, 4, 6 and 8 years was 85.4%, 79.1%, 69.8% and 63.1%, respectively. Freedom from all secondary reintervention at 2, 4, 6 and 8 years was 73.2%, 67.6%, 63.7% (maintained), respectively.

Conclusions: TEVAR is associated with promising long-term survival extended to 10 years, though rates of freedom from reintervention remain an ongoing point for improvement. Randomized controlled trials comparing endovascular with open repair in the setting of acute, complicated type B aortic dissection are needed.

Keywords: Endovascular; minimally invasive; thoracic endovascular aortic repair (TEVAR); aortic dissection



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Introduction

Thoracic endovascular aortic repair (TEVAR) is considered the first-line therapy in the repair of acute, complicated type B aortic dissection (AC-BAD), with favorable

outcomes over that of open repair and medical management in short-term analyses (1). Given the difficulty of designing randomized clinical trials to evaluate the effectiveness of endovascular and open repair, long-term outcome data on

this important surgical cohort, particularly with respect to prosthesis endurance, hemodynamic remodeling and survival outcomes, is limited. This systematic review and meta-analysis provide a complete aggregation of reported long-term survival and freedom from reintervention of AC-BAD patients based on the existing literature.

Methods

Literature search strategy

This review was performed in accordance with PRISMA recommendations and guidance (2). Electronic searches were performed on PubMed, Scopus, and EMBASE/Medline from dates of database inception to January 2021, using (“endovascular” OR “minimally invasive” OR “TEVAR” OR “thoracic endovascular aortic repair” OR “thoracic endovascular aneurysm repair”) AND (“type B” OR “Stanford type B” OR “DeBakey type III” OR “DeBakey III”) AND (“aortic dissection”) AND (“acute”) AND (“complicated”) as search terms. After removal of duplicate records, abstracts and titles were screened and the appropriate studies meeting the inclusion criteria detailed below were selected for full-text review. Four independent authors individually assessed the eligibility of the selected papers (AWS, HK, BM, CCH). A PRISMA diagram of the search strategy is presented in [Figure S1](#). Additional references for discussion were included via a reference list search or via targeted database searches. This was deemed appropriate if studies were poorly indexed and did not appear outside of targeted searches (i.e., as is the case with early 2000’s papers).

Inclusion and exclusion criteria

Studies were included for review if they had at least 20 patients in their study cohorts where TEVAR was explicitly utilized in the management of acute, complicated type B aortic dissection, with ‘complicated’ dissection defined as aortic rupture and/or the presence of organ malperfusion syndromes. Non-English studies, reviews, case series, conference and paper abstracts, editorials, letters and opinions were all excluded. Studies were also excluded if they failed to present baseline patient characteristics, dissection type, time course and definition of presentation (e.g., acute *vs.* chronic), clinical outcomes and/or endpoints between their cohorts. Reoperation cohorts, either treated via TEVAR or conventional open/hybrid approaches were

not included. Failure to state acuity (i.e., acute, subacute, chronic) or complexity (e.g., complicated *vs.* uncomplicated) resulted in exclusion. Studies analyzing physician-customized stent grafts were also not included given the increased probability of heterogeneity (i.e., variable graft hemodynamics, differing deployment strategies, etc.). If a study was a part of an institutional series, the most recent study was taken for analysis. If studies were not available for full-text review, they were excluded (n=0). Registry reviews were not included given the inability to preclude patient overlap.

Primary and secondary endpoints, study quality appraisal

The primary endpoints were mortality (all reported time intervals) and freedom from reintervention. The secondary endpoints were rates of postoperative complications (e.g., stroke, cord ischemia, endoleak, etc.). Study quality was assessed with the Delphi Study Quality Appraisal tool ([Table S1](#)) (3).

Statistics

Baseline cohort characteristics and postoperative details were extracted by three independent researchers (AWS, HK, BM). Discrepancies were reviewed by the senior researcher (AWS) until a consensus was reached. Statistical analysis was carried out using Review Manager (Version 5.3. The Cochrane Collaboration, 2014) and R (Version 4.1.1. R Core Team, Vienna, Austria) using meta-analysis of proportions and means with a random-effects model. Values were considered statistically significant at P values of less than 0.05. Kaplan-Meier survival curves were digitized where presented, and an algorithmic computational tool was utilized, as outlined by Guyot and colleagues, to derive individual patient data (4). Censoring was assumed to be constant, unless the curve had a long follow-up of only minimal patients, in which case, censoring was manually entered. Events and censoring data were compiled for the entire patient cohort and overall survival curves were produced as per the Kaplan-Meier method using IBM SPSS Statistics 26 (IBM Corp. Released 2017; IBM SPSS Statistics for Macintosh, Version 26.0. Armonk, NY, USA: IBM Corp). Where studies had broken their cohorts into subgroups (e.g., DeBakey Type IIIa and Type IIIb), individual KM curves were generated for these first and then subsequently merged, prior to being included in the whole cohort analysis. Studies that failed

Table 1 Cohort characteristics

Characteristics	Values
Cohort size (n) of type B aortic dissection*	2,565
Males	1,920 (75% of cohort)
Mean age (mean \pm SD; reporting frequency)	59.8 \pm 5.8 (100%)
Comorbidities (n + reporting frequency in studies)	
Hypertension	1,950 (89%)
Atherosclerosis/IHD	417 (70%)
T2DM	167 (63%)
Marfan	14 (20%)
Peripheral vascular disease	167 (30%)
Pre-existing renal disease	236 (54%)
COPD	202 (61%)
Smoking	644 (43%)
Previous cardiac surgery	102 (28%)
Previous stroke	72 (37%)
Indication for surgery (n + reporting frequency)	
Rupture	325 (65%)
Organ ischemia/malperfusion	634 (67%)

*, type B aortic dissection was defined as involving the descending thoracic aorta and distal sites only, with the diagnosis made within 14 days of symptom onset. SD, standard deviation; IHD, ischemic heart disease; T2DM, type 2 diabetes mellitus; COPD, chronic obstructive pulmonary disease.

to report numbers at risk, or had data points obscured by censoring brackets, were excluded. These measures were applied in order to reduce the heterogeneity of the population and increase the validity of the findings, as per the recommendations of Guyot *et al.* (4).

Results

Baseline study characteristics

A total of 2,812 references were identified in the literature search for review. Following application of the selection criteria and reference list searches, 46 papers were identified for inclusion [see Ref. (5-29) and Ref. (30-50) for details]. Twenty-six of those studies provided KM

Table 2 Operative outcomes

Operative outcomes	Values
Cohort size	2,565
Early morbidity outcomes (n + reporting frequency in studies)	
Stroke/CVA	70 (59%)
MI + ACS	12 (17%)
Cord ischemia	53 (61%)
Endoleak	110 (50%)
Retrograde dissection (type A)	26 (33%)
AKI (\pm dialysis)	121 (33%)
Reoperations (all-cause)	401 (72%)

CVA, cerebrovascular accident; MI + ACS, myocardial infarction + acute coronary syndrome; AKI, acute kidney injury.

curves for meta-analysis. Baseline cohort characteristics, including reporting frequency, are presented in *Table 1*. A total of 2,565 patients were identified, of whom 1,920 (75%) were male. The mean age of the cohort was 59.8 \pm 5.8 years. The median number of patients per study was 43 (interquartile range, 33–60). Patient comorbidities were variably reported, ranging from 20% to 89% (*Table 1*). The majority of reported studies were from North American centers (18/46), with the remainder drawn from single European (17/46) and Chinese (11/46) centers. 57 percent of studies (26/46) were rated as high quality according to the Delphi Quality Assessment Criteria, and the remainder were classified as either moderate quality (18/46) or low quality (2/46) (*Table S2*) (3). Early postoperative outcome reporting ranged from 17–72%, with reintervention being the most frequently cited (*Table 2*). Prosthesis type was reported in 70% (32/46) of studies with Medtronic, Gore Medical and Cook Medical variants being used most frequently.

Post-procedural survival and freedom from reintervention

Actuarial survival at 2, 4, 6 and 10 years was 87.5%, 83.2%, 78.5% and 69.7%, respectively (*Figure 1*). Freedom from all secondary reintervention at 2, 4, 6, 8 and 10 years was 74.7%, 69.1%, 65.7%, 63.9% and 60.9%, respectively (*Figure 2*). Initial technical success was achieved in 96.3 \pm 3.7% of total cases. When accounting for study

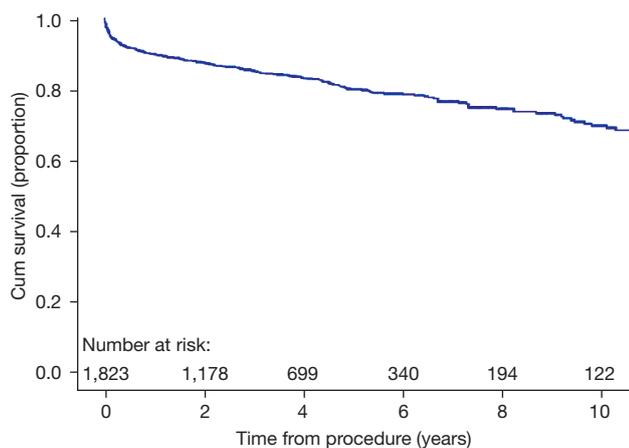


Figure 1 Post-operative survival in AC-BAD in endovascular repair. AC-BAD, acute complicated type B aortic dissection.

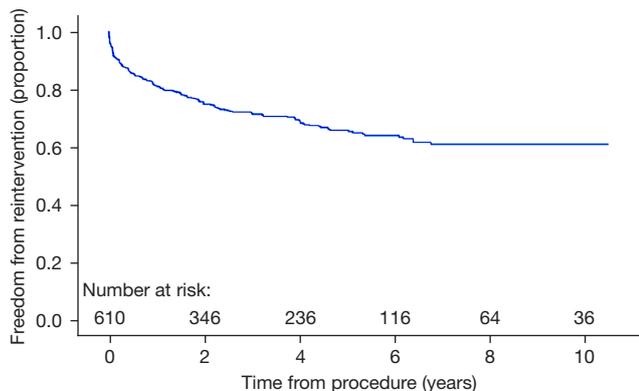


Figure 2 Freedom from reintervention in AC-BAD in endovascular repair. AC-BAD, acute complicated type B aortic dissection.

quality (i.e., high only), actuarial survival at 2, 4, 6 and 8 years was 85.4%, 79.1%, 69.8% and 63.1%, respectively (Figure S2). Freedom from all secondary reintervention at 2, 4, 6 and 8 years was 73.2%, 67.6%, 63.7% (maintained), respectively (Figure S3). All values were statistically significant.

Discussion

Since the adoption of endovascular repair in the management of patients with type B aortic dissection throughout the early 2000s, a number of studies have illustrated superior perioperative and short-term outcomes compared with traditional open surgical repair (51-53). In spite of these encouraging short- and mid-term results,

the long-term outcomes of endovascular repair have remained elusive, with variable mortality rates based on limited actuarial analyses. Additionally, the advantages of endovascular repair are often undermined in the literature by higher rates of reintervention compared to open surgical repair, primarily due to prosthesis endoleak, false lumen perfusion, aortic dilatation and retrograde dissection.

The present systematic review identified 46 studies encompassing 2,565 patients with acute, complicated type B aortic dissection who underwent endovascular repair and were assessed for early post-procedural complications, long-term survival and freedom from reintervention. Meta-analysis found encouraging long-term results, with a survival rate extended to 10 years of 69.7%. Significant incidence of reoperation is to be expected, however, with rates of freedom from reintervention at 10 years of 60.9%. When accounting for study quality, actuarial survival in the early years following the initial procedure remained comparable to whole-cohort rates, though rates of mortality increased modestly from 6 years onwards. This is likely to be reflective of reduced selection bias and lost-to-follow-up rates. Rates of freedom from secondary reintervention remained unchanged in the subgroup analysis throughout the follow-up period.

Excessive stent oversizing, along with bare-spring stent graft positioning in the proximal landing zone, large aortic dilatation and anticoagulant therapy were factors associated with reintervention in the most recent follow-up studies (54,55). Encouragingly, several reports have illustrated that reintervention is usually managed endovascularly, sparing patients from open surgical intervention (30). Neurologic complications and spinal cord ischemia remain some of the most devastating early adverse events of endovascular repair, though rates remain lower in comparison to surgical repair, as identified in previous meta-analyses (52). This study illustrated that the risk of stroke, cord ischemia, acute coronary syndromes and endoleak is similar to that reported in previous analyses from the early TEVAR era (52,56). Retrograde dissection fortunately remains an uncommon complication at 3%, consistent with the previous literature findings of 1-3% (57).

Limitations

Overall, the current literature and present analysis illustrate that TEVAR can be performed with encouraging long-term survival results. However, important questions remain to be answered with respect to long-term morbidity,

mortality and cost-effectiveness of TEVAR after secondary reintervention. Scant data exists surrounding mid- to late-term postoperative complications, which remains an ongoing issue with the literature more broadly. Additionally, thorough long-term morphologic follow-up studies remain lacking in elucidating the outcomes of this important surgical population. Data from 1- to 3-year follow-up illustrate favourable remodeling with total false lumen thrombosis and no difference in outcome between acute and chronic complicated type B aortic dissection, though past this time interval morphology data is limited (16,29,32).

Examining differences in type IIIa and type IIIb would also yield valuable data, with more favourable outcomes tending to be reported in IIIa cohorts, with better false lumen thrombosis versus IIIb cohorts (31). A considerable degree of heterogeneity should be expected given most studies did not delineate between these subtypes. Additionally, very few studies with substantive cohort sizes comparing endovascular repair with open surgery head-to-head exist, with most large registry studies suffering from a lack of pathology-specific reporting. Often, outcomes of type A and type B aortic dissection or acute and chronic acuity are aggregated, with no separate data presented for each of these disparate pathologies (58). A sizable proportion of patients (14%) also received previous cardiac surgery, which raises concern for patient selection bias. Other confounding variables, such as stent-graft make, generation, length of stent-graft coverage and adjunctive procedures could not be accounted for given limited reporting.

Future research and clinical direction

Following additional investigation into morbidity, mortality and cost-effectiveness of acute, complicated reintervention cohorts, examining endovascular repair in the context of acute uncomplicated aortic dissection has been raised as potentially fruitful by recent studies (20). The Investigation of Stent Grafts in Aortic Dissection (INSTEAD) trial illustrated endovascular repair in uncomplicated aortic dissection failed to improve 2-year survivability despite favourable aortic remodeling, findings reinforced by the more recent Acute Dissection: Stent Graft or Best Medical Therapy (ADSORB) trial (59,60). In recent years, this established boundary is beginning to shift, as long-term follow-up data comparing optimal medical therapy and TEVAR in uncomplicated cohorts is illustrating inferior outcomes in those managed with medical therapy alone (61).

Conclusions

This systematic review and meta-analysis involved the aggregation of survival outcomes and rates of freedom from reintervention in patients managed with TEVAR for acute, complicated type B aortic dissection. TEVAR is associated with promising long-term survival extended to 10 years, though rates of freedom from reintervention remain an ongoing point for improvement, and requires additional analysis in the way of morbidity, mortality and cost-effectiveness. To the authors' knowledge, this is the only study to have aggregated long-term mortality and freedom from reintervention in this important surgical cohort. In the absence of randomized controlled trials comparing endovascular with open repair in the setting of acute, complicated type B aortic dissection, the findings herein represent the highest level of clinical evidence on this issue.

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Footnote

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

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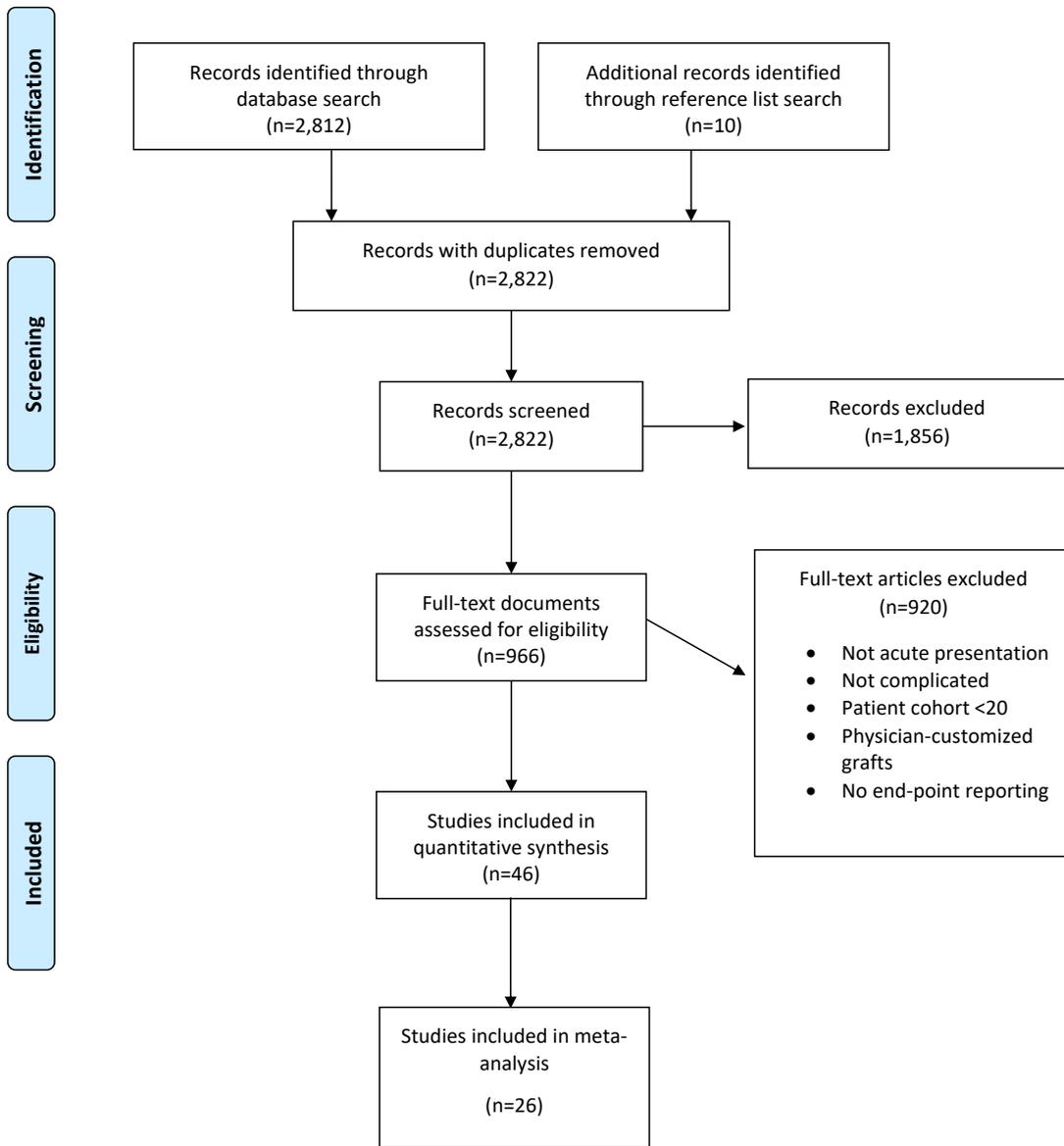


Figure S1 PRISMA search strategy.

Table S1 Delphi quality assessment tool

Criteria No.	Criterion definition
1	Is the hypothesis/aim/objective of the study stated in the abstract, introduction, or methods section?
2	Are the characteristics of the patients included in the study clearly described?
3	Were the cases collected in more than one center?
4	Are the eligibility criteria (inclusion and exclusion criteria) explicit and appropriate?
5	Were patients recruited consecutively?
6	Did patients enter the study at a similar point in the disease?
7	Did the authors describe the intervention?
8	In addition to intervention, did the patients receive any co-interventions?
9	Was loss to follow-up reported?
10	Are outcomes (primary, secondary) clearly defined in the introduction or methodology section?
11	Did the authors use accurate (standard, valid, reliable) objective methods to measure the outcomes?
12	Were outcomes assessed before and after intervention?
13	Was the length of follow-up clearly described/reported?
14	Were the statistical tests used to assess the primary outcomes appropriate?
15	Does the study provide estimates of the random variability in the data for the primary outcomes (e.g., standard error, standard deviation, confidence intervals)?
16	Was the analysis of outcomes based on intention to treat?
17	Are adverse events that may be a consequence of the intervention reported?
18	Are the conclusions of the study supported by results?
19	Is there a competing interest statement about the type and source of support received for the study or about the relationship of the author(s) or other contributors with the manufacturer of the technology?

Table S2 Study details and quality findings										
Author (year)	Cohort size (n)	Males (n)	Age (mean), years	Study quality (Delphi)	Country	Hospital	Years of patient enrollment	Graft type	Primary technical success (%)	30-day mortality
Schoder (2007)	24	23	57	H	Austria	Medical University of Vienna	2000–2005	Talent	100%	10.7%
Sayer (2008)	38	26	62.5	M	United Kingdom	St. George's Hospital	2000–2007	Valiant, Talent, Zenith, Excluder	NR	2.6%
Szeto (2008)	35	22	58.6	H	United States	Hospital of University of Pennsylvania	2004–2007	TAG, Zenith, Medtronic	97.1%	2.8%
Alves (2009)	73	56	56.4	M	Brazil	Hospital São Paulo–UNIFESP and Hospital do Coração da Associação do Sanatório Sírio	1997–2004	NR	99%	6.6%
Conrad (2009)	33	26	58	H	United States	Massachusetts General Hospital	2005–2007	TAG	NR	12%
Feezor (2009)	33	25	61	L	United States	UF Health Shands Hospital	2005–2007	TAG	NR	21%
Guangqi (2009)	72	65	72	H	China	The First Affiliated Hospital of Sun Yat-sen University	2001–2006	Talent, Zenith, Ankura, Aegis	88.9%	1.4%
Manning (2009)	45	35	66	H	Sweden	Malmö University Hospital UMAS	2001–2008	Zenith, TAG, Endofit, Relay	NR	12%
Patel (2009)	69	54	57.3	M	United States	University of Michigan Hospital	1997–2008	NR	95.7%	17.4%
Chemelli-Steingruber (2010)	38	29	64	M	Austria	University Hospital Innsbruck	1996–2008	Talent, Excluder, TAG	NR	23.7%
Ehrlich (2010)	32	25	56	M	Austria	Hospital Rudolfstiftung	2001–2010	Talent	87%	12%
Zeeshan (2010)	45	32	59.1	M	United States	University of Pennsylvania Medical Center	2002–2010	TAG, Talent, Zenith	NR	4%
Jing-Dong (2011)	30	23	64	M	China	TongJi Hospital	2007–2008	NR	100%	6.7%
Kim (2011)	41	31	67.6	H	United States	Harbor UCLA Medical Center	2002–2009	Talent, Valiant	92.5%	4.9%
Sfyroeras (2011)	23	20	60.9	H	United States	Arizona Heart Hospital	1998–2009	TAG, Talent, Endofit	91%	9%
Steuer (2011)	60	40	68	H	Sweden	Uppsala University	1999–2009	TAG, Relay	NR	3%
Ehrlich (2013)	29	22	61	H	Germany	University Hospital Vienna	1998–2004	Talent	100%	17%

Table S2 (continued)

Table S2 (continued)										
Author (year)	Cohort size (n)	Males (n)	Age (mean), years	Study quality (Delphi)	Country	Hospital	Years of patient enrollment	Graft type	Primary technical success (%)	30-day mortality
Eriksson (2013)	51	18	63.8	H	Sweden	Uppsala University Hospital	1999–2009	TAG, Talent, Valiant, TAG/Relay composite	100%	NR
Liu (2013)	33	27	47	M	China	First and Second Affiliated Hospital of Harbin Medical University	2009–2011	NR	100%	0%
Qin (2013)	152	137	63.61	H	United States	Mie University Hospital	1997–2017	NR	94.7%	2%
Wilkinson (2013)	49	28	70.1	M	United States	University of Michigan Cardiovascular Center	1995–2012	TAG, Talent, Valiant, Zenith	100%	12%
Xiong (2013)	26	3	52.8	H	China	Chines PLA General Hospital	2004–2010	Talent, Valiant, Zenith, Endofit, Hercules, Ankura	100%	15%
Hanna (2014)	50	36	59	M	United States	Duke University Medical Venter	2005–2012	TAG, Zenith, Talent, Valiant	98%	NR
Affi (2015)	37	25	61.3	L	United States	Memorial Hermann Hospital	2001–2014	NR	NR	7.6%
Bavaria (2015)	50	40	57.2	H	United States	The Heart Hospital	2010–2012	Valiant	100%	8%
Conrad (2015)	31	23	55	H	United States	Massachusetts General hospital	2005–2009	NR	NR	NR
He (2015)	113	92	43	H	China	The Third Xiangya Hospital of Central South University	2010–2013	Zenith, Relay, Talent, Hercules, Sinus-XL	95.9%	4.1%
Kische (2015)	35	27	63	M	Germany	Rostock University Medical Center	NR	Zenith, Valiant, Talent	NR	2.8%
Arafat (2016)	67	45	59.5	H	United States	Cleveland Clinic	2005–2013	Zenith, TAG, Talent	95.4%	4.4%
Du (2016)	264	201	58.3	M	China	General Hospital of Shenyang Military Region	2002–2013	Talent, Valiant, Zenith	NR	1%
Fanelli (2016)	32	21	68	H	Italy	University College Hospital Galway	2009–2011	TAG, Talent, Valiant, Zenith, Relay	93.1%	13.7%
Sobocinski (2016)	45	35	58.6	H	France	Lille University Hospital	2007–2013	Zenith	NR	5.5%
Leshnowar (2017)	51	34	55	H	United States	Emory Healthcare	2012–2015	Valiant, Zenith, TAG	NR	3.9%

Table S2 (continued)

Author (year)	Cohort size (n)	Males (n)	Age (mean), years	Study quality (Delphi)	Country	Hospital	Years of patient enrollment	Graft type	Primary technical success (%)	30-day mortality
Piffaretti (2017)	22	15	67	H	Italy	Circolo University Teaching Hospital	2001–2014	NR	91%	14%
Zhang (2017)	60	43	63.2	H	China	General Hospital of People's Liberation Army	2011–2013	NR	100%	2.4%
Chou (2018)	26	20	61	M	Taiwan	National Taiwan University Hospital	2008–2014	TAG, Zenith, Talent, Valiant, Relay	100%	4%
Faure (2018)	41	34	61	H	France	Georges Pompidou European Hospital	2011–2017	Zenith	NR	2%
Lou (2018)	80	51	63.8	M	United States	Emory University School of Medicine	2000–2016	NR	NR	5%
Sobocinski (2019)	41	32	60	H	France	Skane University Hospital	2005–2015	Zenith, TAG	NR	17.1%
Stelzmueller (2019)	55	40	52	M	Austria	Medical University of Vienna	2001–2016	NR	91%	9%
Zha (2019)	63	52	59.1	M	China	The First Affiliated Hospital of Anhui Medical University	2012–2016	Captiva, Zenith, Ankura, Grink	100%	4.3%
Zhou (2019)	45	43	50	M	China	Qingdao Municipal Hospital	2012–2016	NR	100%	NR
Eleshra (2020)	64	49	64.8	M	Germany	University Hospital Hamburg-Eppendorf	2010–2017	Zenith	97%	NR
Lou (2020)	39	24	52.1	H	United States	Emory University School of Medicine	2012–2018	Valiant, Medtronic, Zenith, TAG	90%	6%
Norton (2020)	182	139	55	H	United States	Michigan Medicine	1996–2018	NR	NR	7.7%
Sobocinski (2020)	41	32	58.8	H	France	Institut Coeur-Poumon, Chu Lille and Skane University Hospital	2005–2015	NR	NR	17.1%

Age w/ standard deviation was reported as age (mean) for readability. Where age was reported as age (range), this was converted according to the methods of Wan et al. H, high; M, medium; L, low; NR, not reported.

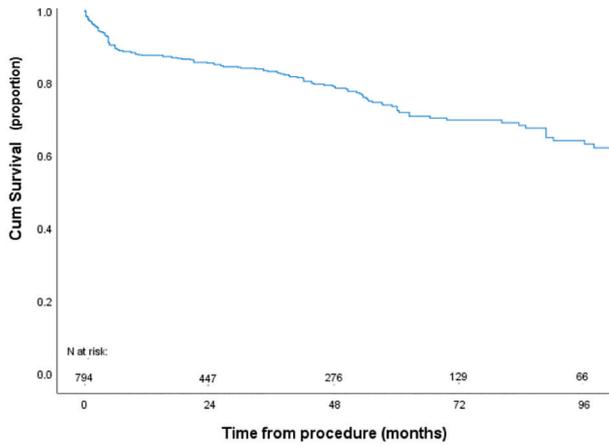


Figure S2 Post-operative survival in AC-BAD in endovascular repair (high-quality subgroup analysis).

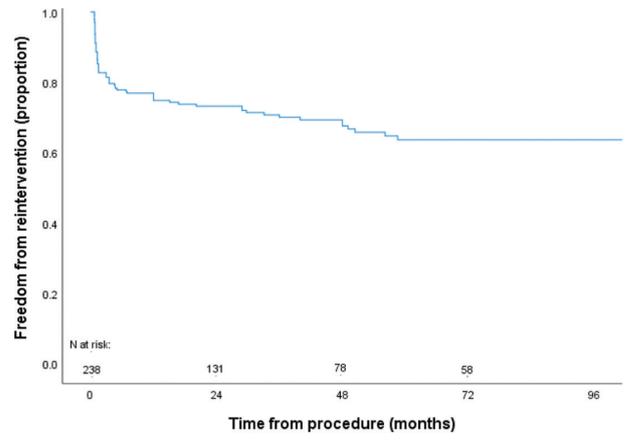


Figure S3 Freedom from reintervention in AC-BAD (high-quality subgroup analysis).