Systematic Review

Prophylactic cerebrospinal fluid drainage and spinal cord ischemia in thoracic and thoracoabdominal endovascular procedures: a systematic review and meta-analysis

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Background: Spinal cord ischemia (SCI) is one of the most devastating complications of thoracic endovascular aortic repair (TEVAR). Prophylactic cerebrospinal fluid drainage (CSFD) has been shown to decrease the risk of SCI in open thoracic aortic procedures; however, its utility in TEVAR remains uncertain. This systematic review and meta-analysis aim to determine the role of prophylactic CSFD in preventing SCI in TEVAR.

Methods: A literature search of five databases was performed and all studies published before September 2022 that reported SCI rates in TEVAR patients undergoing prophylactic CSFD were included. A random effects meta-analysis of means or proportions was performed for single-arm data. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported for comparisons between groups.

Results: A total of 4,793 patients undergoing TEVAR from 40 studies were included. The mean age was 68.8 years and 70.9% of patients were male. The overall SCI rate was 3.5%, with a 1.3% rate of immediate SCI and a 1.9% rate of delayed SCI. There were no significant differences in SCI rates between prophylactic CSFD patients and non-drained patients. Routine CSFD did not have a significant impact on SCI rates compared to non-drained patients. There was an increased rate of transient SCI with selective CSFD compared to non-drained patients (OR 2.08; 95% CI: 1.06–4.08; P=0.03). The most common drain-related complication was spinal headache (4.3%). The major complication rate was 1.6%, of which epidural or spinal hematoma (0.9%) was the most common, followed by intracranial or subdural hemorrhage (0.8%) and paraparesis or paraplegia (0.8%).

Conclusions: This study found no significant difference in SCI rates between prophylactic CSFD patients and their non-drained counterparts. CSFD is associated with a small but non-negligible risk of serious complications. Multi-center randomized controlled trials (RCTs) are warranted to help stratify the risk of both SCI and CSFD-related complications in patients undergoing endovascular aortic procedures.

Keywords: Cerebrospinal fluid drainage (CSFD); thoracic endovascular aortic repair (TEVAR); spinal cord ischemia (SCI); systematic review; meta-analysis

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Introduction

Spinal cord ischemia (SCI) is one of the most devastating complications of thoracic aortic procedures. The traditional standard of open thoracic aortic repair sees SCI rates reported between 5–21% (1). Thoracic endovascular aortic repair (TEVAR) sees lower SCI rates reported between 0–17%, with procedures on thoracoabdominal aortic aneurysms (TAAA) carrying the highest risk (2-4).

Such procedures carry an inherent risk of spinal cord injury as thoracic aortic pathologies often involve branches of the aorta directly involved in the vascular supply of the spinal cord. The artery of Adamkiewicz had been traditionally thought to be the major culprit of such malperfusion but empirical experience has shown that occlusion of collateral supply (intercostal, lumbar, subclavian arteries) may contribute a larger factor to SCI, and incidence of SCI increases with extent of aortic coverage (5,6).

The perfusion of these critical arteries is termed spinal cord perfusion pressure (SCPP), and many any neuroprotective techniques have since been employed to maintain SCPP and reduce the risk of paraplegia. Effective surgical techniques include left subclavian artery revascularization and the use of fenestrated and branched endografts (7,8). Similarly, anesthesiology techniques include mean arterial pressure (MAP) maintenance, cardiac index maintenance, and monitoring of motor and sensory evoked potentials throughout the procedure (9). One debated method of maintaining SCPP is through cerebrospinal fluid drainage (CSFD), for which the body of literature remains divided. Various studies have reported reduced risks of SCI following CSFD, and patients who receive routine prophylactic CSFD may receive the greatest benefit (10-13). Other studies suggest that SCI rates remain similar between drained and non-drained patients (14,15). As such, the use of CSFD has remained stable around 30% over the past decade (16).

Furthermore, CSFD is not a benign procedure, and carries complications including that of paraplegia itself. Such complications have been reported up to rates of 10% and multiple centers have abandoned the neuroprotective procedure following severe adverse outcomes, leading to many clinicians warning against overuse of the procedure (17-20).

This systematic review and meta-analysis address the various CSFD indications implemented in TEVAR procedures for different aortic pathologies to provide more insight to the global experience of CSFD and its efficacy in protecting against SCI.

Methods

Literature search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (*Figure 1*) recommendations (21). Scopus, Embase, Medline, Cochrane and Evidence-Based Medicine (EBM) Reviews databases were searched by two independent authors (CHJ Chen, H Jiang) for the following electronic keyword and medical subject heading (MeSH) terms: ("TEVAR" OR "EVAR" OR "endovascular") AND ("aneurysm" OR "aortic dissection" OR "TAA" OR "TAAA" OR "thoracic" OR "thoracoabdominal") AND (("spinal cord ischemia" OR "spinal cord injury" OR "SCI" OR "paraplegia" OR "weakness" OR "paresis") OR ("cerebrospinal fluid" OR "CSF" OR "CSFD" OR "drain" OR "drainage")). Studies published between the inception of the database to September 2022 containing the search terms in the title and abstract were included for screening following removal of duplicate studies. Published systematic reviews and references were manually screened for eligible studies.

Eligibility criteria

The inclusion criteria for the systematic review and meta-analysis include (I) studies with more than ten adult (>18 years of age) patients undergoing CSFD; (II) studies reporting SCI rates; and (III) English studies. Studies were excluded from analysis if it met any of the following exclusion criteria: (I) studies reporting open surgical procedures*; (II) studies focusing on redo endovascular procedures; and (III) editorials, reviews, conference abstracts and case reports. Studies were screened independently by two authors (CHJ Chen, VDD Nguyen) for inclusion in the meta-analysis and discrepancies were discussed with the

* Studies reporting both open and endovascular procedures were included if data on patients undergoing endovascular procedures could be extracted independently.

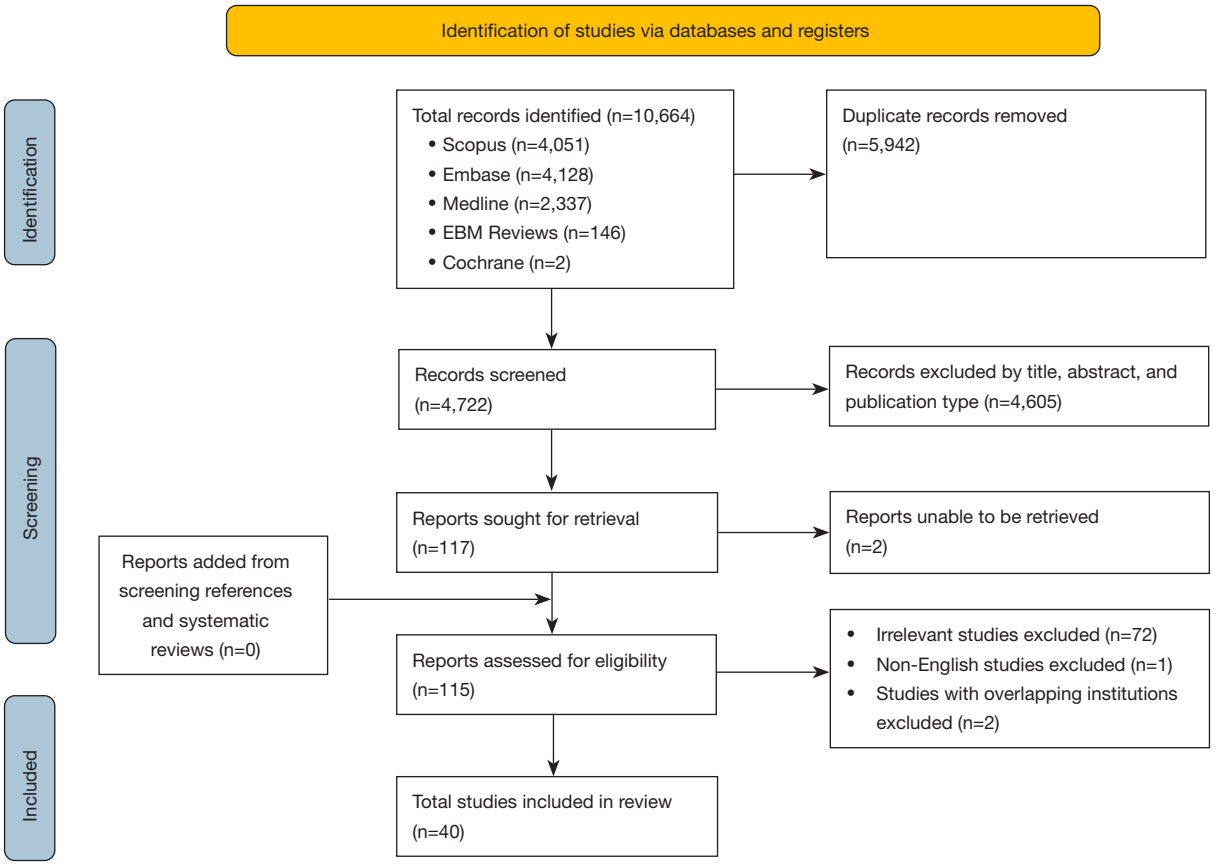

Figure 1 PRISMA search strategy. EBM, Evidence-Based Medicine; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

third author (H Jiang).

Data extraction and critical appraisal

Data was extracted by three authors (CHJ Chen, H Jiang, VDD Nguyen) independently. Primary outcomes for this study included immediate, delayed, transient and permanent SCI. Secondary outcomes included CSFD complications, procedural complications, and mortality. Quality assessment was completed using a modified schema from the Institute of Health Economics (Alberta, Canada) (Table S1) (22). Studies were classified as low quality, moderate quality and high quality if it satisfied fewer than 10 criteria, 10–12 criteria and more than 12 criteria, respectively.

Statistical analysis

Pooled means and proportions were calculated using OpenMeta[Analyst] (Center for Evidence-based Medicine, Brown University, USA) (23). Continuous and binary Dersimonian-Laird random effects models were used for meta-analyses of means and proportions, respectively. Pooled means are presented as mean [95% confidence interval (CI)] and pooled proportions are presented as rate (95% CI). The Box-Cox method described by McGrath *et al.* was used to convert median and interquartile range to mean and standard deviation to facilitate pooling (24). Odds ratios (ORs) and 95% CI were calculated for data comparing CSFD and non-CSFD patients using Review Manager (RevMan) (Version 5.4, The Cochrane Collaboration, 2020) (25). Heterogeneity between studies was calculated using the I^2 statistic, with I^2 values of 0–49%, 50–74% and 75–100% representing low, moderate and high heterogeneity, respectively. P values <0.05 were considered statistically significant. Publication bias was assessed by visual inspection of funnel plots by two authors (CHJ Chen and H

Jiang) independently. Significant asymmetry in funnel plots suggested publication bias for the outcome.

Results

Study details

A total of 10,664 records were identified following an extensive literature search, of which 40 studies (4,793 patients) were included following exclusion (*Table 1*). The earliest study was published in 2005. The majority of the data was sourced from the United States (16 studies), followed by Japan (5 studies), Germany (4 studies), and Italy (4 studies) (*Table 1*). Seventeen studies were found to be of low quality, 21 of medium quality, and two studies were of high quality. There was a total of 14 comparative studies and 26 single arm studies included (*Table 2*).

Procedures

All studies included in the meta-analysis targeted thoracic aortic pathologies. Most studies analyzed multiple aortic pathologies, with the most common pathology being thoracic and thoracoabdominal aneurysmal disease. Standard TEVAR was studied in 34 studies, with 11 studies exclusively or simultaneously addressing fenestrated or branched endograft procedures (Table S1). Elective, urgent,

Table 1 Study details

First author, publication year	Data type	Data source	Country
Acher (26), 2016	Single center	University of Wisconsin School of Medicine and Public Health	United States
Adams (27), 2019	Single center	Carilion Roanoke Memorial Hospital	United States
Addas (28), 2022	Single center	University Health Network Research Centre, Toronto	Canada
Angiletta (29), 2021	Multicenter	University of Bari School of Medicine; University of Insubria School of Medicine; Bolzano Hospital; University of Padua School of Medicine	Italy
Arnaoutakis (30), 2014	Single center	Johns Hopkins Hospital	United States
Banno (31), 2021	Single center	Nagoya University Graduate School of Medicine	Japan
Bisdas (18), 2015	Single center	St. Franziskus Hospital	Germany
Bobadilla (32), 2013	Single center	St. Claire Health Centre, Kentucky	United States
Chaudhary (33), 2021	Single center	Beth Israel Deaconess Medical Center, Harvard Medical School	United States
Cheung (34), 2005	Single center	University of Pennsylvania	United States
Chuter (35), 2008	Single center	University of California, San Francisco	United States
D'Oria (36), 2019	Single center	University Hospital of Cattinara ASUITs, Trieste	Italy
D'Souza (37), 2009	Single center	Mayo Clinic, Rochester, Minnesota	United States
Desart (38), 2013	Single center	University of Florida, Gainesville	United States
Fossaceca (39), 2013	Single center	Maggiore Della Carita Hospital, A. Avogadro University, Novara	Italy
Hiraoka (40), 2018	Single center	Kurashiki Central Hospital, Kurashiki, Okayama	Japan
Hnath (41), 2008	Single center	Albany Medical Center, New York	United States
Iafrancesco (42), 2014	Single center	Queen Elizabeth University Hospital	United Kingdom
Iyer (43), 2006	Single center	McGill University	Canada
Juszczak (19), 2019	Single center	Heartlands Hospital, Birmingham	United Kingdom
Kato (44), 2015	Single center	Morinomiya Hospital	Japan
Khoynezhad (45), 2013	Multicenter	20 different centers (RESCUE trial)*	United States

Table 1 (*continued*)

Table 1 (*continued*)

First author, publication year	Data type	Data source	Country
Kitpanit (46), 2021	Single center	New York Presbytarian Hospital	United States
Kotelis (47), 2015	Single center	Heidelberg University Hospital	Germany
Maier (48), 2019	Single center	University Heart Center Freiburg	Germany
Maurel (49), 2015	Single center	CHRU de Lille	France
Mazzeffi (50), 2018	Single center	University of Maryland	United States
Nathan (51), 2015	Single center	University of Washington	United States
Pasqualucci (52), 2020	Multicenter	Santa Maria della Misericordia University Hospital, Italy; Rashid Hospital, DHA, Dubai	Italy; United Arab Emirates
Preventza (53), 2009	Single center	Arizona Heart Institute	United States
Rizk (54), 2021	Single center	Ain Shams University, Cairo	Egypt
Schurink (55), 2007	Single center	University Hospital Maastricht	Netherlands
Seike (15), 2022	Single center	National Cerebral and Cardiovascular Center	Japan
Song (12), 2017	Single center	Gangnam Severance Hospital, Yonsei University College of Medicine	South Korea
Sugiyama (56), 2022	Single center	Shinshu University Hospital	Japan
Sulzinski (57), 2022	Single center	Medstar Hospital, Washington	United States
Verma (58), 2022	Single center	All India Institute of Medical Sciences	India
Verzini (59), 2020	Single center	AOU Citta della Salute e della Scienza, University of Turin; S Giovanni-Addolorata Hospital, Rome; A.O. Perugia, Perugia	Italy
Yang (60), 2019	Single center	University of British Columbia	Canada
Zipfel (61), 2013	Single center	Deutsches Herzzentrum Berlin	Germany

*, the individual centers in the RESCUE trial in the study by Khoynezhad *et al.* 2013 were examined and found to not overlap with the other studies in the included.

Table 2 Study details

First author, publication year	Patient recruitment	Data source type	Data type (comparison)	Years of recruitment	Patients (n)	Quality of evidence
Acher (26), 2016	Retrospective	Single center	Single arm	2005–2014	155	Low
Adams (27), 2019	Retrospective	Single center	Multi-arm (Gore TAG endoprosthesis post-FDA approval *vs.* phase II trial)	2005–2006	50	Medium
Addas (28), 2022	Retrospective	Single center	Single arm	2017–2020	17	Medium
Angiletta (29), 2021	Retrospective	Multicenter	Single arm	2018–2019	14	High
Arnaoutakis (30), 2014	Retrospective	Single center	Multi-arm (adjunctive procedure *vs.* no adjunctive procedure for TEVAR)	2005–2012	90	Low
Banno (31), 2021	Retrospective	Single center	Multi-arm (SCI *vs.* no SCI)	2008–2018	212	Medium
Bisdas (18), 2015	Retrospective	Single center	Multi-arm (SCI *vs.* no SCI)	2010–2014	142	Medium
Bobadilla (32), 2013	Retrospective	Single center	Single arm	2005–2012	94	Low

Table 2 (*continued*)

Table 2 (*continued*)

First author, publication year	Patient recruitment	Data source type	Data type (comparison)	Years of recruitment	Patients (n)	Quality of evidence
Chaudhary (33), 2021	Retrospective	Single center	Multi-arm (CSFD *vs.* no CSFD)	2014–2019	235	Low
Cheung (34), 2005	Prospective	Single center	Single arm	1999–2004	75	Medium
Chuter (35), 2008	Prospective	Single center	Single arm	2006–2007	22	Medium
D'Oria (36), 2019	Retrospective	Single center	Single arm	2015–2017	24	Medium
D'Souza (37), 2009	Retrospective	Single center	Single arm	2001–2007	20	Low
Desart (38), 2013	Retrospective	Single center	Multi-arm (SCI *vs.* no SCI)	2000–2011	607	Medium
Fossaceca (39), 2013	Retrospective	Single center	Single arm	2005–2011	53	Low
Hiraoka (40), 2018	Retrospective	Single center	Multi-arm (SCI *vs.* no SCI)	2008–2014	175	Medium
Hnath (41), 2008	Prospective	Single center	Multi-arm (CSFD *vs.* no CSFD)	2004–2006	121	Medium
Iafrancesco (42), 2014	Retrospective	Single center	Single arm	2007–2012	62	Low
Iyer (43), 2006	Retrospective	Single center	Multi-arm (elective *vs.* emergent)	1999–2005	70	Low
Juszczak (19), 2019	Retrospective	Single center	Single arm	2008–2017	270	Medium
Kato (44), 2015	Retrospective	Single center	Single arm	2007–2014	54	Low
Khoynezhad (45), 2013	Prospective	Multicenter	Single arm	2010–2012	59	Medium
Kitpanit (46), 2021	Prospective	Single center	Multi-arm (SCI *vs.* no SCI)	2014–2019	106	Medium
Kotelis (47), 2015	Prospective	Single center	Single arm	2012–2013	30	Medium
Maier (48), 2019	Retrospective	Single center	Multi-arm (CSFD *vs.* no CSFD)	1998–2014	223	Low
Maurel (49), 2015	Retrospective	Single center	Multi-arm (before *vs.* after implantation of modified peri-operative protocol)	2004–2013	204	Medium
Mazzeffi (50), 2018	Retrospective	Single center	Single arm	2011–2015	102	Low
Nathan (51), 2015	Retrospective	Single center	Single arm	2006–2013	47	Medium
Pasqualucci (52), 2020	Prospective	Multicenter	Single arm	2016–2018	47	Low
Preventza (53), 2009	Prospective	Single center	Single arm	2000–2008	346	Low
Rizk (54), 2021	Retrospective	Single center	Single arm	2014–2020	23	Low
Schurink (55), 2007	Retrospective	Single center	Single Arm	2000–2005	13	Low
Seike (15), 2022	Retrospective	Single center	Multi-arm (CSFD *vs.* no CSFD)	2009–2020	204	Medium
Song (12), 2017	Prospective	Single center	Single arm	2012–2014	81	Medium
Sugiyama (56), 2022	Retrospective	Single center	Single arm	2011–2019	31	Medium
Sulzinski (57), 2022	Retrospective	Single center	Single arm	2017–2018	130	Low
Verma (58), 2022	Retrospective	Single center	Multi-arm (stent graft length ≤200 mm *vs.* stent graft length >200 mm)	2014–2020	38	Medium
Verzini (59), 2020	Retrospective	Single center	Single arm	2012–2018	21	High
Yang (60), 2019	Retrospective	Single center	Single arm	2007–2016	130	Medium
Zipfel (61), 2013	Retrospective	Single center	Single arm	2000–2010	406	Low

n, number; FDA, Food and Drug Association; TEVAR, thoracic endovascular aortic repair; SCI, spinal cord ischemia; CSFD, cerebrospinal fluid drainage.

and emergent procedures were all included in the study. Selective CSFD protocols were utilized in 23 studies and routine in 17 studies. Where reported, brief details about the selective indication of each study are included in Table S2.

Baseline characteristics

A total of 4,793 patients undergoing thoracic endovascular aortic procedures from 40 studies were included in the meta-analysis. The mean age was 68.8 years (95% CI: 67.3–70.3; I^2=99%). Of these patients, 70.9% were male (95% CI: 66.7–75.0%; I^2=90%). The left subclavian artery (LSA) was covered in 42.7% of patients (95% CI: 32.3–53.2%; I^2=98%), and 18.7% (95% CI: 14.2–23.1%; I^2=94%) of the total number of patients underwent a LSA revascularization procedure prior to their operation; 30.6% (95% CI: 23.5–37.7%; I^2=98%) of patients had prior aortic repair, with 19.3% (95% CI: 14.0–24.6%; I^2=97%) having had prior abdominal aortic repair, and 18.8% (95% CI: 12.9–24.8%; I^2=97%) having had prior thoracic aortic repair (*Table 3*). Further patient comorbidities and vascular risk factors are detailed in *Table 3*. Baseline characteristics were highly heterogeneous throughout the various patient cohorts, attributable to the variety of conditions requiring TEVAR and their associated risk factors. There was a mixture of studies focusing on a single disease process, such as aneurysmal disease or blunt aortic injury, and also studies which covered multiple disease processes (Table S1).

SCI rates

The incidence of SCI in this study was 232, translating to a rate of 3.5% (95% CI: 2.6–4.4%; I^2=67%) (*Figure 2*). The immediate SCI rate, defined as presence at the emergence of anesthesia, was 1.3% (95% CI: 0.7–1.8%; I^2=60%), and the delayed SCI rate was 1.9% (95% CI: 1.2–2.5%; I^2=53%). Compared to non-drained patients, CSFD patients demonstrated no significant difference in rates of any SCI (OR 1.34; 95% CI: 0.88–2.04; P=0.17), transient SCI (OR 1.84; 95% CI: 0.95–3.54; P=0.07) or permanent SCI (OR 1.25; 95% CI: 0.47–3.30; P=0.66). Routine CSFD also did not produce any significant difference in rates of any SCI (OR 0.54; 95% CI: 0.14–2.03; P=0.36), transient SCI (OR 0.16; 95% CI: 0.01–3.13; P=0.23) and permanent SCI (OR 0.27; 95% CI: 0.03–2.40; P=0.24). Selective CSFD produced comparable results for rates of any SCI (OR 1.48; 95% CI: 0.98–2.24; P=0.06) and permanent SCI (OR 1.51; 95% CI: 0.52–4.36; P=0.44), but this population was associated with an increased rate of transient SCI (OR 2.08; 95% CI: 1.06–4.08; P=0.03). CSFD failed to produce any significant effect on SCI rate in the population with aneurysmal disease (OR 1.39; 95% CI: 0.81–2.37; P=0.23) or dissection related disease (OR 1.31; 95% CI: 0.17–9.87; P=0.79). There was a trend towards an increased rate of SCI in drained elective patients (OR 2.51; 95% CI: 0.97–6.52; P=0.06), but this result did not reach significance (*Table 4*; *Figures 3-6*).

Publication bias was assessed for data comparing CSFD and non-CSFD patients. There was no convincing evidence of funnel plot asymmetry on visual inspection for any SCI, permanent SCI or transient SCI in patients undergoing CSFD versus non-CSFD patients (Figures S1-S3).

CSFD complication rates

A spinal headache was reported in 4.3% (95% CI: 1.8–6.9%; I^2=73%) of patients undergoing CSFD procedures. Major complications were reported in 1.6% (95% CI: 0.8–2.4%; I^2=22%) of CSFD procedures. These complications included meningitis in 0.6% (95% CI: 0.2–1.1%; I^2=0) of patients, a CSF leak requiring reintervention in 0.7% (95% CI: 0.2–1.1%; I^2=0), frank insertion site bleeding in 0.7% (95% CI: 0.2–1.1%; I^2=0), a retained catheter tip in 0.7% (95% CI: 0.2–1.2%; I^2=0), epidural or spinal hematoma in 0.9% (95% CI: 0.4–1.4%; I^2=0), intracranial or subdural hemorrhage in 0.8% (95% CI: 0.3–1.3%; I^2=0), significant paraparesis or paraplegia independent to the operation in 0.8% (95% CI: 0.3–1.3%; I^2=0), and death in 0.6% (95% CI: 0.2–1.0%; I^2=0) (*Table 5*).

Operative outcomes

In-hospital or perioperative mortality occurred at a rate of 1.7% (95% CI: 1.1–2.3%; I^2=53%). Mid-term mortality, reported as mortality within a year, occurred at a rate of 4.5% (95% CI: 3.2–5.8%; I^2=70%). Endoleaks of any type were reported at a rate of 12.9% (95% CI: 9.0–16.9%; I^2=90%). Cerebrovascular accidents, defined as either stroke or transient ischemic attacks, occurred at a rate of 2.0% (95% CI: 1.3–2.7%; I^2=38%). The mean reported total operation time was 180 minutes (range, 63–373 minutes), and the mean reported estimated blood loss was 187 mL (range, 50–714 mL) (*Table 6*).

Table 3 Baseline characteristics

Characteristic	Patients (n) [studies]	Weighted pooled estimate (95% CI)	Heterogeneity I^2 (%)
Age (years)*	4,624 [37]	68.8 (67.3, 70.3)	99
Male (%)	3,256 [38]	70.9 (66.7, 75.0)	90
LSA coverage (%)	1,234 [22]	42.7 (32.3, 53.2)	98
LSA revascularization (%)	566 [24]	18.7 (14.2, 23.1)	94
Prior aortic repair			
Any prior aortic repair (%)	1,047 [26]	30.6 (23.5, 37.7)	98
Prior AAA repair (%)	644 [22]	19.3 (14.0, 24.6)	97
Prior thoracic aneurysm repair (%)	295 [13]	18.8 (12.9, 24.8)	97
Chronic renal insufficiency			
GFR >15 and not on hemodialysis* (%)	598 [21]	19.6 (14.6, 24.5)	94
GFR <15 or on hemodialysis (%)	66 [13]	3.7 (2.1, 5.3)	60
Hypertension (%)	2,791 [30]	79.0 (72.1, 85.8)	97
Dyslipidemia (%)	825 [14]	49.1 (35.5, 62.7)	98
Smoking history			
Any smoking history (%)	1,035 [19]	51.3 (38.9, 63.7)	98
Current smoker (%)	272 [10]	27.3 (19.0, 35.5)	92
History of COPD (%)	888 [27]	26.5 (21.2, 31.9)	94
History of CAD (%)	911 [28]	28.8 (22.9, 34.6)	96
History of CHF (%)	79 [10]	5.4 (3.0, 7.9)	79
History of PAD (%)	180 [10]	15.4 (9.9, 20.9)	94
History of DM (%)	398 [25]	14.2 (10.8, 17.6)	89
History of stroke or CVD (%)	243 [14]	11.2 (7.5, 14.9)	90

*, Khoynezhad *et al.* 2013 was excluded following sensitivity analysis. Chronic renal insufficiency was defined as a GFR less than 60 mL/min or a creatinine greater than 1.5 mg/dL. Khoynezhad *et al.* 2013 was excluded from sensitivity analysis as its young patient cohort significantly skewed the mean age. This may be attributable to the mode of injury (BAI) leading to TEVAR in his patient population. n, number of patients; CI, confidence interval; LSA, left subclavian artery; AAA, abdominal aortic aneurysm; GFR, glomerular filtration rate; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; CHF, congestive heart failure; PAD, peripheral artery disease; DM, diabetes mellitus, CVD, cerebrovascular disease; BAI, blunt aortic injury.

Discussion

SCI is a major complication of aortic procedures that predisposes patients to notable life-long morbidity. While SCI rates have decreased following the widespread use of TEVAR in place of open aortic surgery, it continues to pose a significant threat to patients, occurring in 0–18% of patients (35,44). The current systematic review reported an overall SCI rate of 3.5%, including both transient and permanent SCI. TEVAR operators worldwide have adopted protocols aimed at monitoring and maintaining spinal cord perfusion during TEVAR, including neuromonitoring, intraoperative MAP maintenance and LSA revascularization (33,48,50,60). CSFD is a treatment adjunct that has been shown to reduce the risk of SCI in open aortic procedures. A randomized controlled trial (RCT) published in 2002 by Coselli and colleagues showed a significant decrease in paraplegia rates in CSFD patients undergoing open TAAA repair compared to their non-drained counterparts (62). Similarly, a systematic review and meta-analysis of RCTs

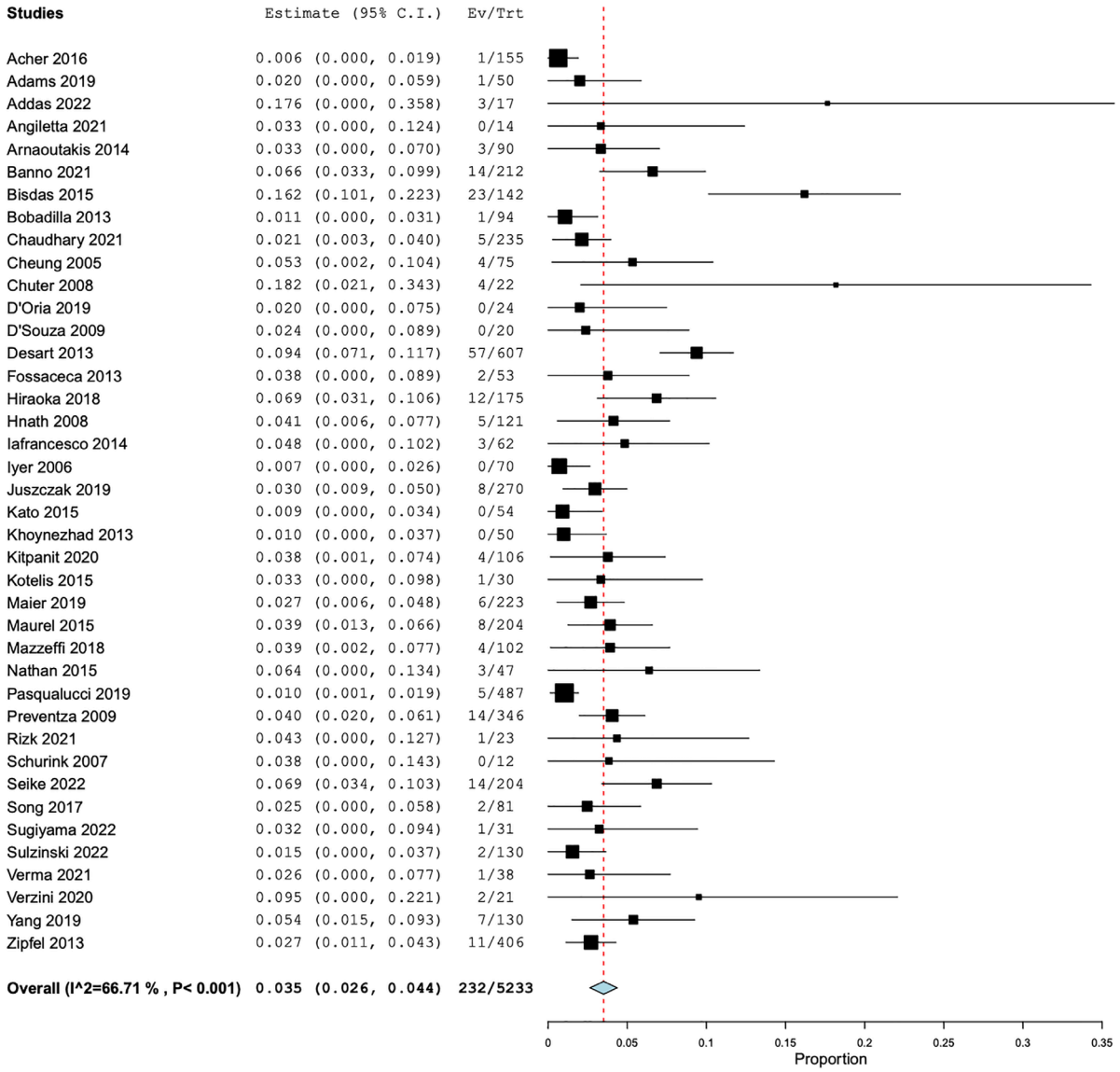

Figure 2 The rate of spinal cord injury across all studies. C.I., confidence interval.

and cohort studies showed significantly lower rates of paraplegia and paraparesis following CSFD in open aortic surgery (63).

The utility of CSFD in endovascular aortic procedures has been debated in the literature. Currently, there are no RCTs to the authors' knowledge that investigates the benefit of CSFD in patients undergoing TEVAR. The current systematic review found no significant difference in either transient or permanent SCI rates between prophylactic CSFD and non-CSFD patients undergoing TEVAR for aortic aneurysms or dissections. This is consistent with a systematic review and meta-analysis by Wong *et al.*, and we add that neither routine nor selective CSFD significantly reduced the risk of SCI (14). This contrasts the findings of a systematic review by Zhang *et al.*, which found that routine CSFD is superior to selective CSFD in reducing the risk of SCI (11). However, no direct comparison was made between drained and non-drained patients in that study. Several cohort studies have reported a significant decrease in SCI rates with prophylactic CSFD. Maier *et al.*

Table 4 Spinal cord ischemia rates

Outcome	Patients* (n) [studies]	Odds ratio (95% CI)	P value	Heterogeneity I^2 (%)
CSFD *vs.* non-CSFD				
Any SCI	102 [40]	1.34 (0.88, 2.04)	0.17	21
Transient SCI	33 [32]	1.84 (0.95, 3.54)	0.07	0
Permanent SCI	36 [32]	1.25 (0.47, 3.30)	0.66	62
Routine CSFD *vs.* non-CSFD				
Any SCI	28 [19]	0.54 (0.14, 2.03)	0.36	28
Transient SCI	12 [14]	0.16 (0.01, 3.13)	0.23	–
Permanent SCI	5 [14]	0.27 (0.03, 2.40)	0.24	0
Selective CSFD *vs.* non-CSFD				
Any SCI	78 [23]	1.48 (0.98, 2.24)	0.06	16
Transient SCI	21 [19]	2.08 (1.06, 4.08)	0.03	0
Permanent SCI	31 [19]	1.51 (0.52, 4.36)	0.44	66
TAA and TAAA only (CSFD *vs.* non-CSFD)				
Any SCI	33 [8]	1.39 (0.81, 2.37)	0.23	0
Elective procedures only (CSFD *vs.* non-CSFD)				
Any SCI	26 [5]	2.51 (0.97, 6.52)	0.06	46

*, refers to patients of each category who received CSFD prior to TEVAR and experienced SCI. n, number of patients; CI, confidence interval; CSFD, cerebrospinal fluid drainage; SCI, spinal cord ischemia; TAA, thoracic aortic aneurysm; TAAA, thoracoabdominal aortic aneurysm.

found a 3.9% decrease in SCI rates in patients undergoing CSFD compared to their non-drained counterparts, and Hnath *et al.* found an 8% decrease in SCI rates for the same comparison in 121 patients (41,48). Interestingly, we found an increased risk of transient SCI in patients who underwent selective CSFD compared to those who were not prophylactically drained. This may be due to the presence of preoperative risk factors for SCI in patients who are selected to undergo CSFD, such as extensive aortic coverage, prior aortic repair and distal descending aortic coverage (33,50,53).

Currently, CSFD protocols vary greatly between centers, and institutions report different CSF pressure targets and maximum drainage rates. As SCPP increases with lower spinal fluid pressures, lower CSF target pressures may decrease the incidence of SCI (32). In the current study, CSF pressure targets largely fall between 8 mmHg and 15 mmHg. Kato *et al.* and Maurel *et al.* adopted the most aggressive pressure targets of 7.3 mmHg (10 cmH_2O) in their patient population (44,49). Previous studies have also found that greater drainage volumes were associated with more drain-related complications, requiring operators to set maximum drainage volumes or rates (64-66). Drainage rates generally range from 10 to 20 mL/hour in studies included in this systematic review. Kotelis *et al.* reported the highest mean drainage amount (714 mL) and the highest rate of drain-related complications (23%) of studies included in this meta-analysis (47). Further studies are required to determine the ideal pressure targets and drainage rates that strike a balance between optimal spinal cord protection with the least drain-related complications.

CSFD is associated with potential complications that may lead to significant long-term morbidity. A systematic review and meta-analysis of over 30 studies published by Rong *et al.* found an overall complication rate of 6.5% for patients undergoing CSFD for open and endovascular aortic procedures (67). The same study also reported a 2.5% rate of major complications, including epidural hematoma,

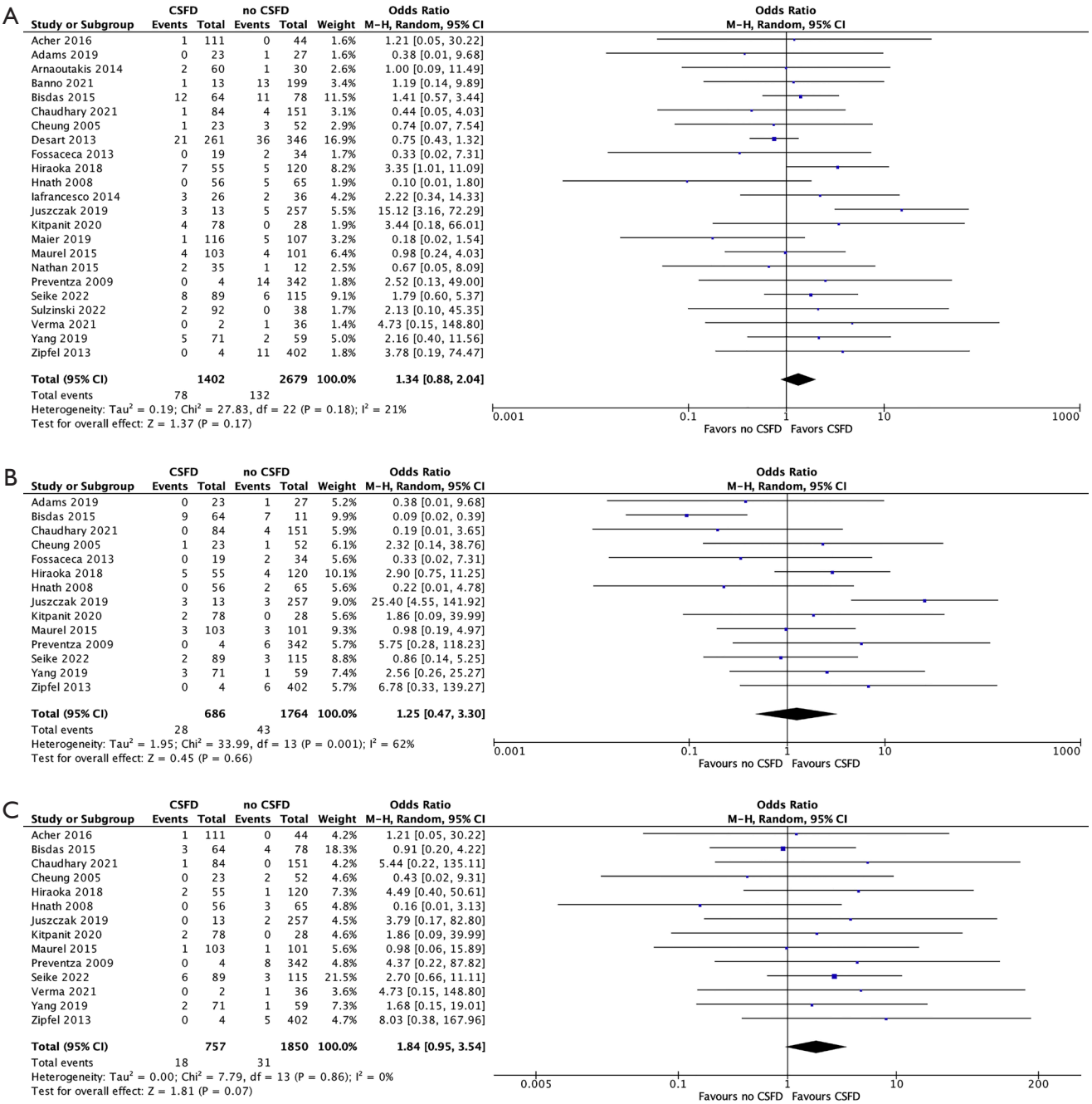

Figure 3 Forest plots comparing SCI rates in patients undergoing CSFD versus no CSFD. (A) Any SCI; (B) permanent SCI; (C) transient SCI. CSFD, cerebrospinal fluid drain; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom; SCI, spinal cord ischemia.

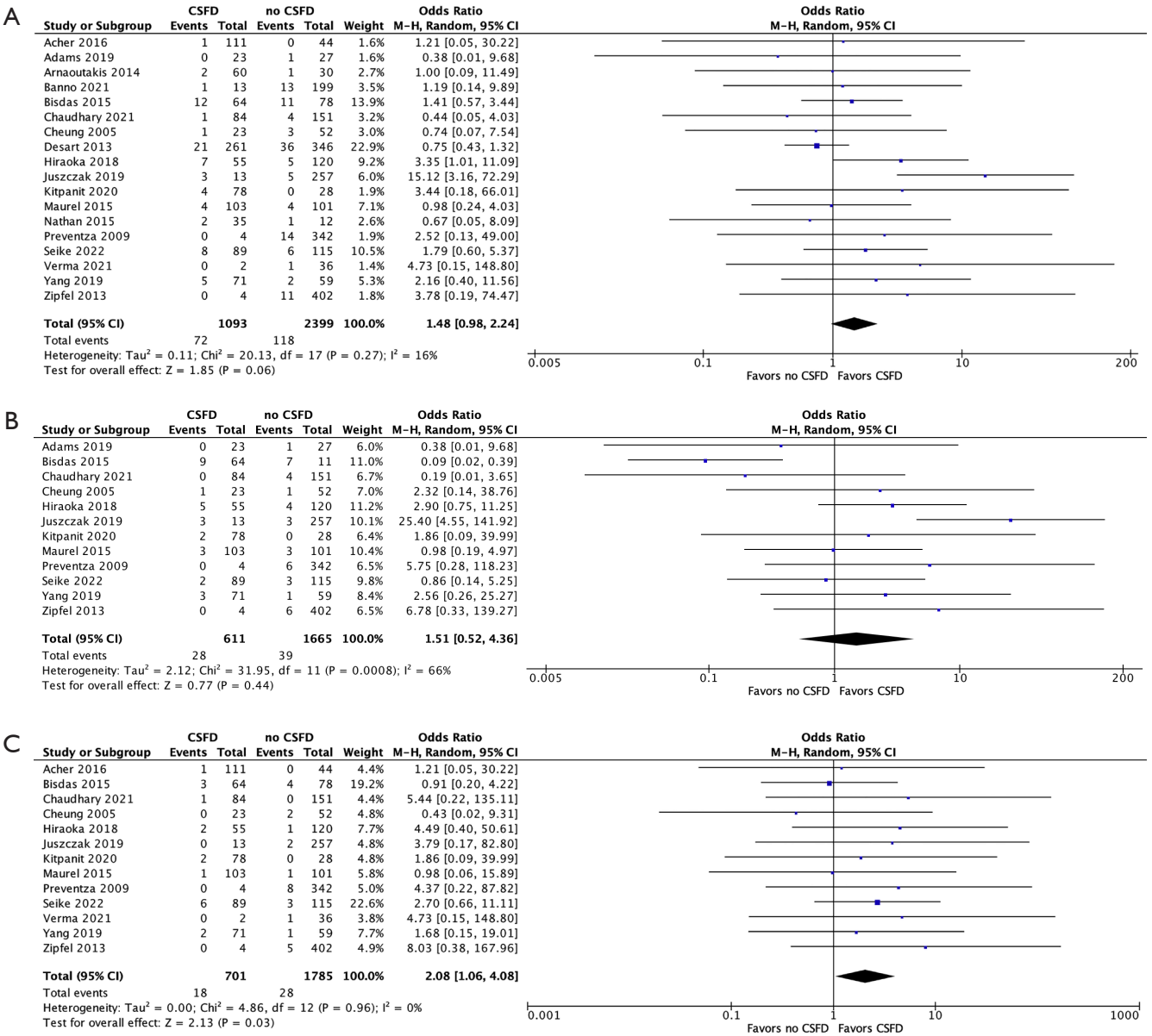

Figure 4 Forest plots comparing SCI rates in patients undergoing selective CSFD versus no CSFD. (A) Any SCI; (B) permanent SCI; (C) transient SCI. CSFD, cerebrospinal fluid drain; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom; SCI, spinal cord ischemia.

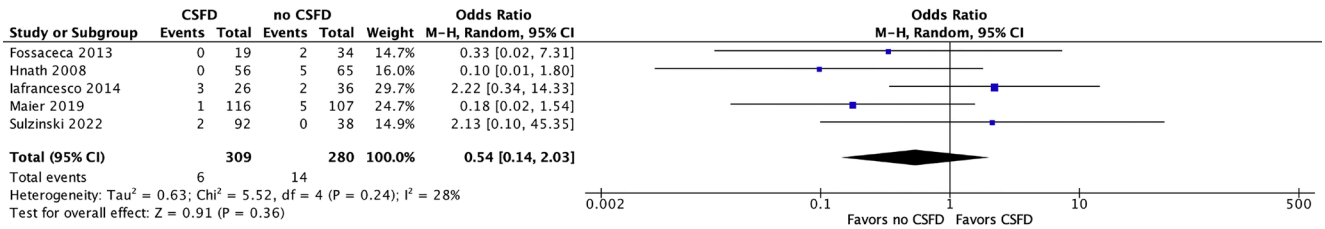

Figure 5 Forest plots comparing overall SCI rates in patients undergoing routine CSFD versus no CSFD. CSFD, cerebrospinal fluid drain; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom; SCI, spinal cord ischemia.

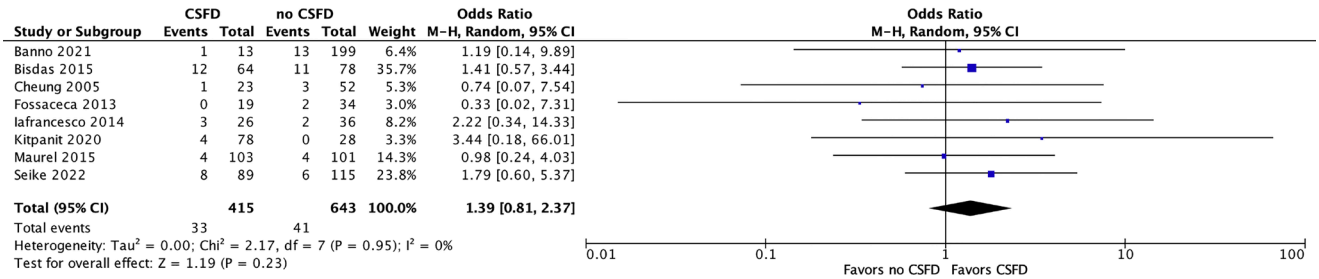

Figure 6 Forest plots comparing SCI rates in patients undergoing CSFD versus no CSFD in aneurysmal disease only. CSFD, cerebrospinal fluid drain; M-H, Mantel-Haenszel; CI, confidence interval; df, degrees of freedom; SCI, spinal cord ischemia.

Table 5 CSFD related complications

CSFD related complication	Patients (n) [studies]	Weighted pooled estimate (95% CI), (%)	Heterogeneity I^2 (%)
Common complications			
Spinal headache	38 [10]	4.3 (1.8, 6.9)	73
Major complications*			
Any major complication	35 [19]	1.6 (0.8, 2.4)	22
Meningitis	1 [18]	0.6 (0.2, 1.1)	0.0
CSF leak requiring intervention	7 [17]	0.7 (0.2, 1.1)	0.0
Frank insertion site bleeding	6 [18]	0.7 (0.2, 1.1)	0.0
Retained catheter tip	3 [18]	0.7 (0.2, 1.2)	0.0
Epidural or spinal hematoma	8 [18]	0.9 (0.4, 1.4)	0.0
Intracranial or subdural hemorrhage	10 [19]	0.8 (0.3, 1.3)	0.0
Significant paraparesis or paraplegia**	6 [20]	0.8 (0.3, 1.3)	0.0
Death	2 [24]	0.6 (0.2, 1.0)	0.0

*, major complications are defined by events that may cause significant morbidity or that require repeat intervention. The major complications investigated in this study are meningitis, CSF leak requiring re-intervention, frank insertion site bleeding, retained catheter tip, epidural or spinal hematoma, intracranial or subdural hemorrhage, significant paraparesis or paraplegia and death. Spinal headaches and minor insertion site bleeding or bloody CSF are not accounted for in major complications. These complications are reported as directly related to the CSFD process, not as a result of the operation. **, significant paraparesis or paraplegia is defined as sensory change or weakness of the lower limbs that is prolonged or permanent. CSFD, cerebrospinal fluid drainage; n, number of patients; CI, confidence interval; CSF, cerebrospinal fluid.

Table 6 Operative outcomes

Operative outcome	Patients (n) [studies]	Weighted pooled estimate (95% CI), (%)	Heterogeneity I^2 (%)
In-hospital or perioperative mortality	88 [31]	1.7 (1.1, 2.3)	53
30-day to 1-year mortality*	176 [29]	4.5 (3.2, 5.8)	70
Endoleak (of any type)	246 [21]	12.9 (9.0, 16.9)	90
Cerebrovascular accident (stroke or TIA)	73 [26]	2.0 (1.3, 2.7)	38

*, Angiletta *et al.* 2021 was excluded following sensitivity analysis. Angiletta *et al.* was excluded from analysis following sensitivity analysis due to their high 30D-1Y mortality rate. n, number of patients; CI, confidence interval; TIA, transient ischemic attack; 30D-1Y, 30 days to 1 year.

intracranial hemorrhage, meningitis, and drain-related neurological deficit (67). This is similar to the current study, which reported a 1.6% risk of major complications following CSFD. The most common major complication in this systematic review was epidural or spinal hematoma (weighted pooled estimate of 0.9%), followed by intracranial or subdural hemorrhage (weighted pooled estimate of 0.8%) and significant paraparesis or paraplegia (weighted pooled estimate of 0.8%). Of these, intracranial hemorrhage is undoubtedly the most dangerous complication, which may lead to permanent neurological damage and even death despite immediate management. In the current study, both-drain-related deaths occurred following large intracranial bleeds, one intraoperatively and the other following drain removal (19,47). Several studies have found that a larger total volume drained was a significant risk factor for intracranial hemorrhage, thus requiring CSFD operators to take extra caution in monitoring total CSF drainage volume both intraoperatively and postoperatively (64-66). Such risks, in conjunction with debatable benefit of CSFD, should warn operators that CSFD prior to TEVAR should be a judicious decision and may vary patient to patient.

Limitations and future directions

Several limitations were present in the current study. The meta-analysis did not account for confounding variables that influence SCI risk, including procedural risk factors like increased thoracic aorta coverage and patient risk factors like previous abdominal aortic aneurysm (AAA) repair, peripheral artery disease, and renal insufficiency (46,68,69). Similarly, there was high heterogeneity in the baseline characteristics of patients included in this study which may have contributed to the overall SCI risk (*Table 3*). The CSFD protocol and other methods of reducing SCI risk varied greatly between studies, preventing an accurate comparison of the true impact of CSFD on SCI risk. Lastly, following quality analysis of the studies included, only two of 41 studies were deemed to be of high quality. Large, multicenter RCTs are required to further assess the utility of routine and selective CSFD in preventing SCI and to investigate true indications for selective prophylactic CSFD.

Conclusions

This study found no significant reduction in SCI rates in patients undergoing TEVAR with prophylactic CSFD. TEVAR teams need to stratify both the risk of SCI and CSFD complications when planning for endovascular intervention with prophylactic CSFD. Large RCTs are required to accurately assess the utility of routine and selective prophylactic CSFD in reducing SCI risk of TEVAR patients.

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Footnote

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

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