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Review Article

The Association of the Cerebral Protection Strategy with Early Mortality and Postoperative Stroke in Acute Type A Aortic Dissection: A Systematic Review and Meta-Analysis

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Objective. The optimal cerebral protection strategy in acute type A aortic dissection (ATAAD) is still without a clear consensus. The purpose of this meta-analysis was to compare the outcome of different cerebral protection strategies on ATAAD patients. *Materials and Methods*. We conducted a systematic review including all studies concerning surgically managed ATAAD patients between 1.1.2010 and 28.2.2022 and reporting the use of cerebral protection strategies in three large databases (Pubmed, Cochrane library, and Scopus). The main outcome events were 30-day mortality and a postoperative stroke rate. The pooled event rates adjusted by age, gender, CPB duration, circulatory arrest duration, and total arch reconstruction rate were calculated. *Results*. Overall, 39 articles were included covering a total of 16, 876 ATAAD patients. The estimated adjusted pooled early mortality rate was 10.1% (95% confidence interval [CI] 9.1–11.3%) in the ACP group, 15.9% (13.3–18.9%) in the RCP group, and 11.6% (9.2–14.5%) in the HCA group. Compared to the RCP group, ACP and HCA demonstrated lower early mortality (RCP vs. ACP odds-ratio 1.66 [1.28–2.15], $p < 0.001$; RCP vs. HCA odds-ratio 1.45 [1.02–2.07], $p = 0.039$). The adjusted pooled stroke rate was 9.0% (8.3–9.8%) in the ACP group, 10.5% (9.3–11.7%) in the RCP group, and 9.1% (8.1–10.2%) in the HCA group. *Conclusion*. Early mortality might be more common in ATAAD patients treated with RCP compared to ACP and HCA. With regards to postoperative stroke, the results were inconclusive despite the trending inferiority of RCP compared to the other strategies.

1. Introduction

Acute type A aortic dissection (ATAAD) is still associated with significant mortality and morbidity despite advances in diagnostics and surgical treatment. ATAAD requires emergency surgery and reconstruction of the diseased aortic section. Performing an open distal aortic anastomosis causes a substantial risk for ischemic cerebral events during the surgery. Cerebral protection strategies have evolved to mitigate cerebral ischemia during open distal anastomosis. The main cerebral protection approaches, antegrade cerebral perfusion (ACP), retrograde cerebral perfusion (RCP), and deep hypothermic circulatory arrest alone (HCA), each have specific advantages and pitfalls [1]. Thus far, institutional as well as surgeon preferences have guided the usage of neuroprotective strategies as evidence on the optimal cerebral protection strategy is scarce [2]. The current guidelines suggest that the addition of either ACP or RCP during the circulatory arrest is reasonable for ATAAD repair (IIa B) and that circulatory arrest with ACP and moderate or deep hypothermia is reasonable for ATAAD repair during extended arch reconstruction (IIa, C) [3].

Since 2010, only four RCTs focusing on cerebral protection in aortic arch surgery have been published, only one of which [4] focuses on ATAAD patients, while others solely encompass elective arch reconstructions [5–7]. Therefore, the evidence on neuroprotective strategies in ATAAD patients is almost exclusive from the retrospective studies and institutional series as well as from meta-analysis. Most of these studies have heterogeneous patient samples involving patients with acute dissections, chronic dissections, and degenerative aneurysms, even though mortality and stroke rates have been shown to differ substantially between these patient groups [8–12]. Therefore, we conducted a meta-analysis comparing the outcomes of ACP, RCP, and HCA in surgically treated ATAAD patients during the past and current decades.

2. Methods

We conducted a systematic review and meta-analysis of studies reporting the rates of early mortality and postoperative stroke after surgery for ATAAD. This review has been reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (PRISMA checklist available in Supplementary 1).

2.1. Search Strategy. We searched PubMed, Cochrane library, and Scopus on March 1st, 2022 using search phrases presented in detail in Table 1. The publication year was limited to 2010 or later.

2.2. Inclusion Criteria. All original studies reporting outcomes after surgical treatment for ATAAD with explicitly reported cerebral protection strategies and early mortality and postoperative stroke rates were included. We excluded studies in which ATAAD patients and other patients were pooled and studies in which patients with different cerebral protection strategies were pooled, and studies in which only pooled outcomes were there were reported. In addition, non-English studies were excluded.

2.3. Main Outcome Measures. The main outcome measures were early mortality and postoperative stroke. Early mortality was defined as death within 30 days from surgery or death during the primary in-hospital period after surgery. If both were reported in a study article, the one indicating a higher event rate was selected for analysis. Postoperative stroke was defined as a new permanent neurological deficit occurring after the surgery.

2.4. Screening and Data Extraction. Each article was screened, and the data of included studies were extracted by a single author. The following information was gathered: author, number of patients, mean age, the proportion of males, cerebral protection strategy, postoperative stroke rate, early mortality rate, cannulation site, hypothermia temperature, mean cardiopulmonary bypass time, mean circulatory arrest time, and proportion of total aortic arch reconstruction. The cerebral protection strategy was stratified into the following three categories: antegrade cerebral perfusion (ACP), retrograde cerebral perfusion (RCP), and hypothermic circulatory arrest only (HCA).

2.5. Definitions of Cerebral Protection Strategies. The definition of ACP was that cerebral perfusion was used with an arterial perfusion line located at the aorta, brachiocephalic trunk, right subclavian/axillary artery, right common carotid artery, left common carotid artery, or left subclavian/axillary artery. In RCP, cerebral perfusion was used via the superior vena cava. In HCA only, no selective cerebral perfusion was used during systemic circulatory arrest. ACP was further stratified into unilateral (one-sided cerebral perfusion line) and bilateral (two-sided cerebral perfusion via both right and left-sided arteries) ACP.

2.6. Statistical Methods. A statistical analysis was performed using R statistical software version 4.1.2 (R Project for Statistical Computing). Crude and adjusted pooled event rates were calculated. Adjusted event rate per study was estimated using Poisson regression with the observed event rate set as a dependent variable and mean age (or median age if mean not reported), the proportion of males, mean cardiopulmonary bypass time (or median age if mean not reported), mean circulatory arrest time (or median age if mean not reported), and proportion of total aortic arch reconstruction set as independent variables. Function "glm" from "stats" package version 4.1.2 was used. To calculate adjusted event rates, missing covariate values were replaced using multiple imputations by chained equations using the "mice" function from "mice" package version 3.14.0 [13].

A meta-analysis using a random intercept logistic regression model was conducted, and pooled crude and adjusted outcome event rates and 95% confidence intervals (CI) were calculated. The random effects model was used due to the high heterogeneity between the studies ($I^2 > 40\%$). Inverse variance with a logit transformation was used as a meta-analysis method. Odds ratios and 95% CIs for outcome events between different cerebral protection strategies were calculated. The pooled outcome event rates were calculated using the function "metaprop" from "meta" package version 5.1 – 1. Lastly, a sensitivity analysis was conducted by systematically removing each study from the meta-analysis one at a time to examine their potential influence on the overall effect size estimate.

The quality of the included studies was assessed using the Newcastle-Ottawa scale. This review has been registered with PROSPERO (ID: CRD42022359545) and can be accessed via https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=359545.

3. Results

The initial search retrieved a total of 2,110 articles. After removing the duplicates, 1,817 articles were screened and 91 articles were selected for full-text assessment. Ultimately, 39 articles were included in the analysis (Figure 1). The study characteristics are presented in Supplementary 2. The quality of the included studies is presented in Supplementary 3. The included studies reported outcomes of 16,876 patients, of which 11,355 were operated on patients using ACP, 2,549 using RCP, and 2,972 using HCA (Table 2). Three of the studies were prospective, while the others were retrospective studies. Only one of the included studies was a randomized controlled trial. In the ACP group, the mean age was lower

Table 1: Search strategy.

PubMed	Aortic dissection [Title] AND (circulatory arrest [Title] OR hypotherm* [Title] OR retrograde [Title] OR antegrade [Title] OR selective [Title]) OR (cerebral perfusion [Title] OR cerebral protection [Title] OR brain protection [Title]) Filter year 2010–2022
Cochrane library	Aortic dissection AND (circulatory arrest OR hypotherm* OR retrograde OR antegrade OR selective) OR (cerebral perfusion OR cerebral protection OR brain protection) in record title - (word variations have been searched) Filter year 2010–2022
Scopus	TITLE (“aortic dissection” AND (“circulatory arrest” OR hypotherm* OR retrograde OR antegrade OR selective) OR (“cerebral perfusion” OR “cerebral protection” OR “brain protection”)) AND (LIMIT-TO (PUBYEAR, 2022) OR LIMIT-TO (PUBYEAR, 2021) OR LIMIT-TO (PUBYEAR, 2020) OR LIMIT-TO (PUBYEAR, 2019) OR LIMIT-TO (PUBYEAR, 2018) OR LIMIT-TO (PUBYEAR, 2017) OR LIMIT-TO (PUBYEAR, 2016) OR LIMIT-TO (PUBYEAR, 2015) OR LIMIT-TO (PUBYEAR, 2014) OR LIMIT-TO (PUBYEAR, 2013) OR LIMIT-TO (PUBYEAR, 2012) OR LIMIT-TO (PUBYEAR, 2011) OR LIMIT-TO (PUBYEAR, 2010))

The search was performed 1st March, 2022.

and the proportion of males was higher than in the other groups. The circulatory arrest time was shorter in the HCA group when compared to the others. The proportion of total arch replacement was highest in the ACP group.

3.1. Early Mortality. The pooled data contained a total of 2,212 early deaths (13.1% of all patients). According to I^2 values (≥75%) and the funnel plot of crude early mortality rates (Figure 2), heterogeneity was high between studies. The estimated crude pooled early mortality rate was 10.7% (95% CI 9.1–12.4%) in the whole population. A meta-analysis of the crude early mortality rate did not reveal eligible evidence between cerebral protection strategies (Figure 3 and Table 3). The sensitivity analysis indicated that no single study had a substantial influence on the effect size estimate, as removing any individual study led to only small changes in the overall estimate (crude early mortality rate estimate range of 10.5–11.1%, tau range of 0.54–0.60, and I^2 range of 83.2–84.9%).

After correcting for the confounders, heterogeneity between the studies decreased although residual heterogeneity was still high ($I^2 \geq 58\%$, Figure 2). According to the adjusted early mortality rates, RCP (early mortality rate 15.9%, 95% CI 13.3–18.9%) was inferior to the other groups (early mortality rate in ACP 10.1%, 95% CI 9.1–11.3%, and $p < 0.001$ and in HCA 11.6%, 95% CI 9.2–14.5%, and $p = 0.039$; Figure 4 and Table 3). The sensitivity showed no major influence on estimates after removing any single study (adjusted early mortality rate estimate range of 10.2–10.6%, tau range of 0.307–0.356, and I^2 range of 58.1–67.1%).

3.2. Postoperative Stroke. A total of 1,695 (10.0% of all patients) postoperative strokes were observed in the pooled data. High heterogeneity was observed between studies ($I^2 \geq 64\%$, Figure 2). The pooled postoperative stroke rate estimate was 8.5% (7.0–10.2%) in the whole population, and estimates calculated separately in the cerebral protection strategy groups did not indicate clear differences between the groups (Figure 5 and Table 3). The sensitivity analysis indicated that the changes in the estimate ranged from negligible to small (crude stroke rate estimate range of 8.3–8.8%, tau range of 0.651–0.698, and I^2 range of 83.6–86.1%).

Heterogeneity diminished after correcting for covariates in postoperative stroke rate calculations ($I^2 \leq 25\%$, Figure 2). A meta-analysis of the adjusted postoperative stroke rates showed a trending superiority of ACP (postoperative stroke rate 9.0%, 95% CI 8.3–9.8%) in relation to RCP (10.5%, 95% CI 9.3–11.7%; $p = 0.057$) (Figure 6 and Table 3). In the sensitivity analysis, removing any single study had only a minor effect on the overall estimate (adjusted stroke rate estimate range of 9.0–9.3%, tau range of 0.192–0.226, and I^2 range of 26.1–38.0%).

4. Discussion

The present systematic review and meta-analysis of three main cerebral protection strategies demonstrate the outcomes of the two major complications after ATAAD surgery, 30-day mortality, and postoperative stroke. To the best of our knowledge, this is the first meta-analysis focusing solely on ATAAD patients, and it is the first to exclude older studies published before the year 2010. A summary of the previous meta-analyses can be founded in Supplementary 4.

In this meta-analysis, the observed early mortality and postoperative stroke rates were 13.1% and 10.0%, respectively, which were slightly lower compared to the early mortality rate of 17% and postoperative stroke rate of 10–20% previously reported in the three large multicenter retrospective ATAAD patient registers (IRAD, NORCAAD, and GERAADA) [10–12, 14–16]. One explanation may be the inclusion of single-arm studies from highly specialized high-volume centers.

In the present meta-analysis, an eligible piece of evidence of a difference between the cerebral protection strategies in the crude early mortality or postoperative stroke rate was not found. However, the comparison of the adjusted early

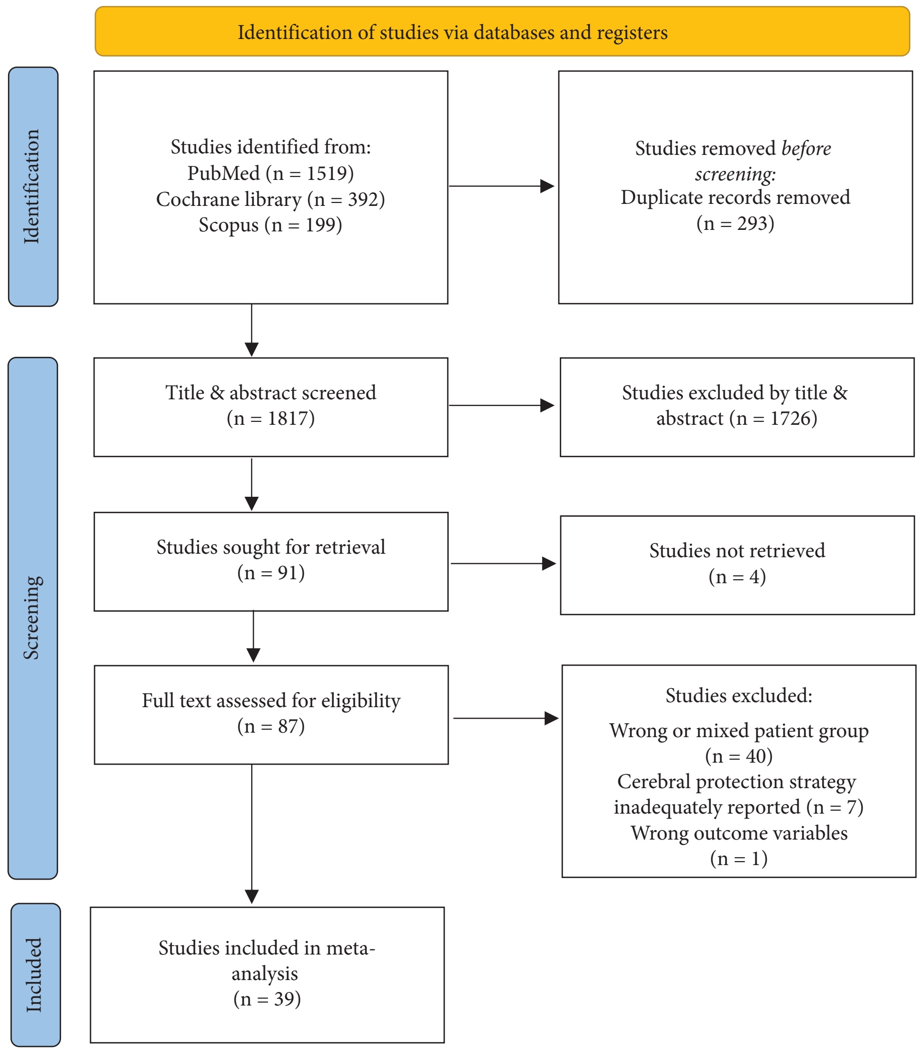

Figure 1: PRISMA flow chart of study screening.

mortality rates revealed that RCP might be inferior to ACP and HCA. In the light of two recent meta-analyses of aortic arch surgery patients, this was rather unexpected, as contradictory to our findings, those concluded that HCA may be associated with higher early mortality and postoperative stroke rates than ACP or RCP [17, 18]. The discrepancy may relate to the inclusion of elective patients in those previous meta-analyses. Compared to ATAAD surgery, cerebral perfusion (either antegrade or retrograde) is more regularly utilized in elective aortic arch reconstructions and the complication rate is also substantially lower in elective degenerative aneurysms and chronic dissections [8, 9]. Therefore, including elective patients with presumably higher rates of cerebral perfusion and concurrently lower complication risks potentially leads to erroneous disfavoring of HCA when considering ATAAD patients.

Indeed, according to the results of this meta-analysis, HCA resulted in closely equal rates of early mortality and postoperative stroke as ACP in both crude and adjusted analyses. Nonetheless, the use of HCA in ATAAD surgery has been diminishing similarly during the last two decades as in elective aortic surgery, probably due to the meta-analyses showing the superiority of cerebral perfusion over HCA [2]. Currently, only a few actively publishing centers utilize HCA as their main cerebral protection strategy and their results seem to be in line with the current data [8, 19]. In ATAAD surgery, ACP and HCA have been shown to produce equal results regarding early mortality and postoperative stroke with circulatory arrest durations under 25–30 minutes [20]. This duration is considered sufficient for hemiarch replacement, which accounts for approximately 80% of primary surgeries. More complex arch surgeries require longer arrest time, and therefore, the use of cerebral perfusion is a necessity. This was also seen in the present meta-analysis as the rate of total arch replacement was 48% in the ACP group and 15% in the HCA group.

RCP was the least used cerebral protection strategy in this meta-analysis. Unexpectedly, it had the longest mean durations in both cardiopulmonary bypass and circulatory arrest (35 minutes) as well as the lowest circulatory arrest temperatures (20°C) and the lowest frequency of total arch reconstructions (6%). The combination of a low frequency of

Table 2: Patient characteristics.

	Antegrade cerebral perfusion ($n = 11, 355$)	Retrograde cerebral perfusion ($n = 2, 549$)	Hypothermic circulatory arrest only ($n = 2, 972$)
Age, mean*	56	61	61
Male, n (%)	7, 845 (69)	1, 647 (65)	1, 915 (64)
Cardiopulmonary bypass time, minutes, mean*	190	201	185
Circulatory arrest time, minutes, mean*	32	35	24
Hypothermia temperature, mean*	24	20	25
Total arch reconstructed, n (%)	5, 551 (49)	153 (6)	447 (15)

*Estimated as a patient count weighted mean of reported mean/median values of included studies.

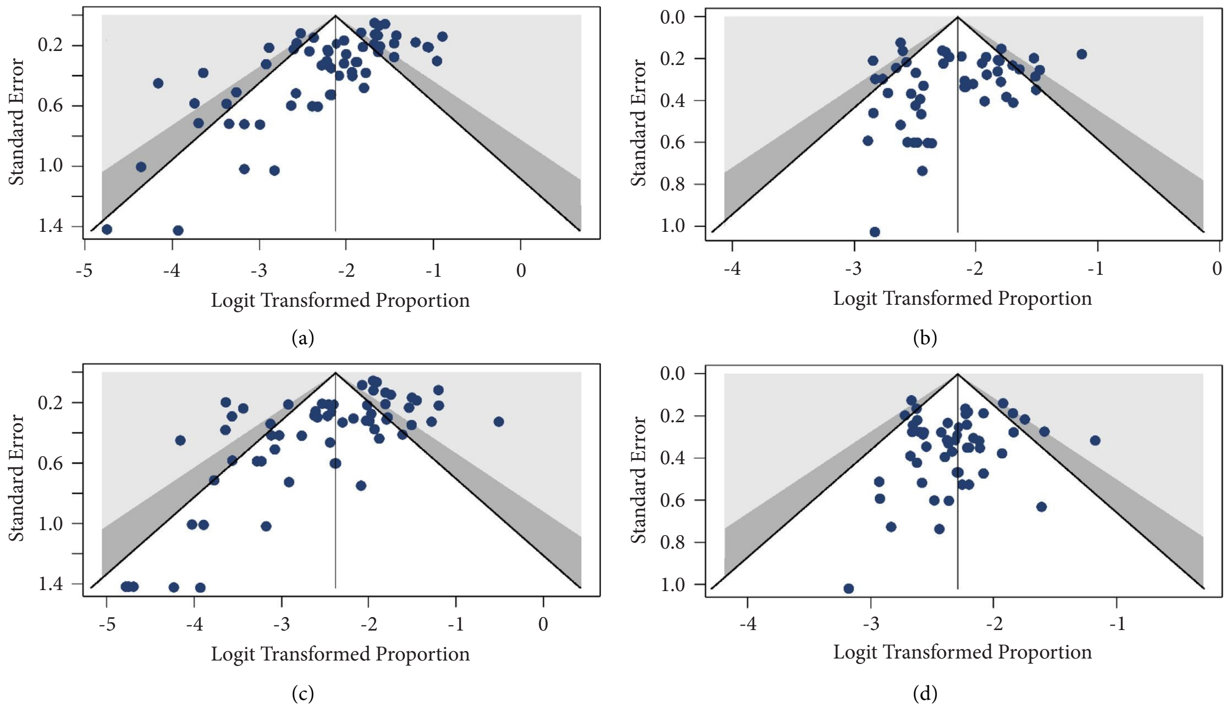

FIGURE 2: Funnel plots to assess the risk for publication bias and systematic heterogeneity of proportions of outcome events. Black diagonal lines show 95% confidence interval, and the dark grey area shows 99% confidence interval. (a) = Crude early mortality rate, (b) = adjusted early mortality rate, (c) = crude stroke rate, and (d) = adjusted stroke rate.

Cerebral protection strategy	Observed early deaths	Patients	Pooled estimate for early mortality	Estimate [95% CI]
Antegrade cerebral perfusion Heterogeneity: $I^2 = 85\%$, $p < 0.01$	**1346**	**11355**		**0.103 [0.086; 0.122]**
Hypothermic circulatory arrest only Heterogeneity: $I^2 = 83\%$, $p < 0.01$	**491**	**2972**		**0.095 [0.046; 0.185]**
Retrograde cerebral perfusion Heterogeneity: $I^2 = 75\%$, $p < 0.01$	**375**	**2549**		**0.128 [0.096; 0.168]**
Overall	**2212**	**16876**		**0.107 [0.091; 0.124]**

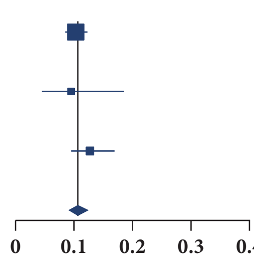

FIGURE 3: Comparison of crude pooled early mortality by using the cerebral protection strategy.

TABLE 3: Pairwise comparisons between cerebral protection strategies.

	HCA vs. ACP OR (95% CI)	p	RCP vs. ACP OR (95% CI)	p	RCP vs. HCA OR (95% CI)	p
Early mortality						
Crude	1.17 (0.68–1.99)	0.574	1.20 (0.75–1.92)	0.440	1.03 (0.54–1.97)	0.928
Adjusted	1.14 (0.85–1.54)	0.377	1.66 (1.28–2.15)	<0.001	1.45 (1.02–2.07)	0.039
Postoperative stroke						
Crude	1.22 (0.67–2.21)	0.515	1.02 (0.59–1.75)	0.956	0.83 (0.40–1.73)	0.625
Adjusted	0.99 (0.81–1.20)	0.894	1.20 (1.00–1.44)	0.057	1.21 (0.95–1.55)	0.122

ACP = antegrade cerebral perfusion, HCA = hypothermic circulatory arrest, RCP = retrograde cerebral perfusion, OR = odds-ratio, and CI = confidence interval.

Cerebral protection strategy	Adjusted early deaths	Patients	Pooled estimate for early mortality	Estimate [95% CI]
Antegrade cerebral perfusion Heterogeneity: $I^2 = 71\%$, $p < 0.01$	1268	11355		0.102 [0.091; 0.114]
Hypothermic circulatory arrest only Heterogeneity: $I^2 = 64\%$, $p < 0.01$	409	2972		0.113 [0.089; 0.142]
Retrograde cerebral perfusion Heterogeneity: $I^2 = 62\%$, $p < 0.01$	406	2549		0.156 [0.128; 0.187]
Overall	2083	16876		0.111 [0.100; 0.122]

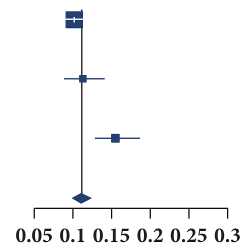

Figure 4: Comparison of adjusted pooled early mortality by using the cerebral protection strategy.

Cerebral protection strategy	Observed postoperative strokes	Patients	Pooled estimate for postoperative strokes	Estimate [95% CI]
Antegrade cerebral perfusion Heterogeneity: $I^2 = 88\%$, $p < 0.01$	1067	11355		0.082 [0.064; 0.103]
Hypothermic circulatory arrest only Heterogeneity: $I^2 = 77\%$, $p < 0.01$	379	2972		0.102 [0.065; 0.156]
Retrograde cerebral perfusion Heterogeneity: $I^2 = 64\%$, $p < 0.01$	249	2549		0.090 [0.069; 0.117]
Overall	1695	16876		0.085 [0.070; 0.102]

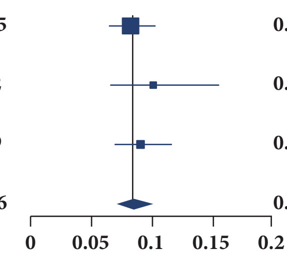

Figure 5: Comparison of crude pooled postoperative stroke by using the cerebral protection strategy.

Cerebral protection strategy	Adjusted postoperative strokes	Patients	Pooled estimate for postoperative strokes	Estimate [95% CI]
Antegrade cerebral perfusion Heterogeneity: $I^2 = 29\%$, $p = 0.04$	1024	11355		0.090 [0.083; 0.098]
Hypothermic circulatory arrest only Heterogeneity: $I^2 = 0\%$, $p = 0.89$	275	2972		0.093 [0.083; 0.104]
Retrograde cerebral perfusion Heterogeneity: $I^2 = 0\%$, $p = 0.77$	271	2549		0.107 [0.096; 0.120]
Overall	1570	16876		0.093 [0.087; 0.100]

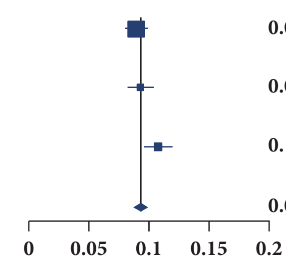

Figure 6: Comparison of adjusted pooled postoperative stroke by using the cerebral protection strategy.

total arch operations and relatively long average durations of circulatory arrest for hemiarch surgeries may indicate that it was used in less experienced aortic centers although this hypothesis could not be further assessed in this meta-analysis. However, it has been shown that the cerebral capillary oxygen supply using RCP is insufficient which may also contribute to the inferior outcomes of RCP [21].

The newly founded guidelines on ATAAD surgery advocate using cerebral perfusion in ATAAD patients [3]. However, these recommendations are based on studies that include, besides the ATAAD patients, a significant proportion of patients with degenerative aneurysms and chronic dissections even though the emergency status and therefore the possibility to plan the operation in advance as well as risk status of the patients have substantial differences. The differences in patient groups reflect in the outcomes of surgery as early mortality and postoperative stroke rate located around 17% and 10–20% in ATAAD [10–12, 14–16] compared to 1–5% early mortality and 1–5% stroke rate of degenerative aneurysms and chronic dissections [8, 9, 22]. With such fundamental issues, the validity of these guidelines should be critically assessed. To patch this flaw, well-designed randomized controlled studies with sufficient statistical power focusing solely on ATAAD patients are still needed before recommending against the usage of HCA as a sole cerebral protection strategy in ATAAD surgery.

4.1. Strengths and Limitations. The main strength of this meta-analysis was the focus on ATAAD patients, which provided a more accurate estimation of outcomes in these patients when compared to the previous meta-analyses with heterogeneous patient samples. All studies reporting early mortality and postoperative stroke rates after surgery for ATAAD between 2010 and 2022 were included, and no study was excluded by design or study setting. This provided a high number of patients in each cerebral protection strategy group with an urge for a pragmatic approach and modern treatment practices. As a counterpart, the inclusion of both observational and experimental studies may cause bias in the outcome event estimates due to selection bias and other artificial determinants of surgical decision-making in experimental studies. However, the inclusion of all studies enables catching the whole spectrum of various clinical conditions related to different cerebral protection strategies during the surgery for ATAAD patients. Furthermore, along with the crude estimation, the covariate-corrected estimation of outcome event rates provided further insight into outcomes related to cerebral protection strategies. To the best of the authors' knowledge, no such adjustments have been made in the previous meta-analyses on the field. With the more or less inevitable differences in patient characteristics and surgical techniques used, correction for known covariates related to the outcomes improves the precision of estimation and thereby improves the usability of the findings. This was also seen in the decreased heterogeneity between the studies after correcting the outcome event rates for the covariates. However, it should be acknowledged that in addition to the covariates used in the adjustments, there are also other factors that may have affected the outcomes. Since the raw data of the included studies were not available and the data on the covariates were gathered from the study articles, other confounding variables than those we controlled could not be accounted for in the adjusted analysis, leading to residual confounding within the estimates. Therefore, the analyses are mostly exploratory in nature.

5. Conclusions

Early mortality might be more common in ATAAD patients treated with RCP compared to ACP and HCA. With regards to postoperative stroke, the results were inconclusive despite the trending inferiority of RCP compared to the other strategies. A well-designed randomized controlled trial with high statistical power or largely registered studies solely with ATAAD patients is still needed before declaring the superiority or inferiority of cerebral protection strategies.

Data Availability

The data underlying this article are included in the supplementary materials.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Caius Mustonen and Mikko Uimonen were responsible for the conceptualization, methodology, project administration, data curation, roles or writing the original draft, reviewing, and editing. Mikko Uimonen was also responsible for formal analysis and visualization.

Supplementary Materials

Supplementary 1: the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist. Supplementary 2: characteristics of the included studies. Supplementary 3: quality of the included studies by using the Newcastle-Ottawa scale. Supplementary 4: published prior meta-analyses on cerebral protection with HCA, ACP, and RCP. (*Supplementary Materials*)

References

[1] M. P. Falasa, G. J. Arnaoutakis, G. M. Janelle, and T. M. Beaver, "Neuromonitoring and neuroprotection advances for aortic arch surgery," *JTCVS Techniques*, vol. 7, p. 11, 2021.

[2] R. De Paulis, M. Czerny, L. Weltert et al., "Current trends in cannulation and neuroprotection during surgery of the aortic arch in Europe," *European Journal of Cardio-Thoracic Surgery*, vol. 47, no. 5, pp. 917–923, 2015.

[3] S. C. Malaisrie, W. Y. Szeto, M. Halas et al., "2021 the American Association for Thoracic Surgery expert consensus document: surgical treatment of acute type A aortic dissection," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 162, no. 3, pp. 735–758.e2, 2021.

[4] X. Sun, H. Yang, X. Li et al., "Randomized controlled trial of moderate hypothermia versus deep hypothermia anesthesia on brain injury during Stanford A aortic dissection surgery," *Heart and Vessels*, vol. 33, no. 1, pp. 66–71, 2018.

[5] L. G. Svensson, E. H. Blackstone, C. Apperson-Hansen et al., "Implications from neurologic assessment of brain protection for total arch replacement from a randomized trial," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 150, no. 5, pp. 1140–1147.e11, 2015.

[6] O. V. Kamenskaya, A. S. Klinkova, A. M. Chernyavsky, V. V. Lomivorotov, I. O. Meshkov, and A. M. Karaskov, "Deep hypothermic circulatory arrest vs. Antegrade cerebral perfusion in cerebral protection during the surgical treatment of chronic dissection of the ascending and arch aorta," *Journal of Extra-Corporeal Technology*, vol. 49, no. 1, p. 16, 2017.

[7] B. G. Leshnower, S. Rangaraju, J. W. Allen, A. Y. Stringer, T. G. Gleason, and E. P. Chen, "Deep hypothermia with retrograde cerebral perfusion versus moderate hypothermia with antegrade cerebral perfusion for arch surgery," *The Annals of Thoracic Surgery*, vol. 107, no. 4, pp. 1104–1110, 2019.

[8] B. A. Ziganshin, B. G. Rajbanshi, M. Tranquilli, H. Fang, J. A. Rizzo, and J. A. Elefteriades, "Straight deep hypothermic circulatory arrest for cerebral protection during aortic arch

surgery: safe and effective," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 148, no. 3, pp. 888–900, 2014.

[9] O. Preventza, J. S. Coselli, A. Garcia et al., "Moderate hypothermia at warmer temperatures is safe in elective proximal and total arch surgery: results in 665 patients," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 153, no. 5, pp. 1011–1018, 2017.

[10] L. O. Conzelmann, E. Weigang, U. Mehlhorn et al., "Mortality in patients with acute aortic dissection type A: analysis of pre- and intraoperative risk factors from the German Registry for Acute Aortic Dissection Type A (GERAADA)," *European Journal of Cardio-Thoracic Surgery*, vol. 49, no. 2, pp. e44–e52, 2016.

[11] R. A. Chemtob, S. Fuglsang, A. Geirsson et al., "Stroke in acute type A aortic dissection: the nordic consortium for acute type A aortic dissection (NORCAAD)," *European Journal of Cardio-Thoracic Surgery*, vol. 58, no. 5, pp. 1027–1034, 2020.

[12] A. Evangelista, E. M. Isselbacher, E. Bossone et al., "Insights from the international registry of acute aortic dissection: a 20-year experience of collaborative clinical research," *Circulation*, vol. 137, no. 17, pp. 1846–1860, 2018.

[13] S. van Buuren and K. Groothuis-Oudshoorn, "Mice: multivariate imputation by chained equations in R," *Journal of Statistical Software*, vol. 45, no. 3, pp. 1–67, 2011.

[14] L. O. Conzelmann, I. Hoffmann, M. Blettner et al., "Analysis of risk factors for neurological dysfunction in patients with acute aortic dissection type A: data from the German Registry for Acute Aortic Dissection Type A (GERAADA)," *European Journal of Cardio-Thoracic Surgery*, vol. 42, no. 3, pp. 557–565, 2012.

[15] A. Geirsson, K. Shioda, C. Olsson et al., "Differential outcomes of open and clamp-on distal anastomosis techniques in acute type A aortic dissection," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 157, no. 5, pp. 1750–1758, 2019.

[16] M. Di Eusanio, H. J. Patel, C. A. Nienaber et al., "Patients with type A acute aortic dissection presenting with major brain injury: should we operate on them?" *The Journal of Thoracic and Cardiovascular Surgery*, vol. 145, no. 3, pp. S213–S221.e1, 2013.

[17] I. Hameed, M. Rahouma, F. M. Khan et al., "Cerebral protection strategies in aortic arch surgery: a network meta-analysis," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 159, no. 1, pp. 18–31, 2020.

[18] D. Abjigitova, K. M. Veen, G. van Tussenbroek et al., "Cerebral protection in aortic arch surgery: systematic review and meta-analysis," *Interactive Cardiovascular and Thoracic Surgery*, vol. 35, no. 3, 2022.

[19] M. Jormalainen, P. Raivio, C. Mustonen et al., "Direct aortic versus peripheral arterial cannulation in surgery for type A aortic dissection," *The Annals of Thoracic Surgery*, vol. 110, no. 4, pp. 1251–1258, 2020.

[20] T. Krüger, E. Weigang, I. Hoffmann, M. Blettner, and H. Aebert, "Cerebral protection during surgery for acute aortic dissection type A," *Circulation*, vol. 124, no. 4, pp. 434–443, 2011.

[21] M. P. Ehrlich, C. Hagl, J. N. McCullough et al., "Retrograde cerebral perfusion provides negligible flow through brain capillaries in the pig," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 122, no. 2, pp. 331–338, 2001.

[22] Y. Iba, K. Minatoya, H. Matsuda et al., "Contemporary open aortic arch repair with selective cerebral perfusion in the era of endovascular aortic repair," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 145, no. 3, pp. S72–S77, 2013.