Review

Cerebral Protection Strategies and Stroke in Surgery for Acute Type A Aortic Dissection

Leonard Pitts [1,2,*], Markus Kofler [1,2,3], Matteo Montagner [1,2], Roland Heck [1,2], Jasper Iske [1,2], Semih Buz [1,2,3], Stephan Dominik Kurz [1,2], Christoph Starck [1,2,3], Volkmar Falk [1,2,3,4] and Jörg Kempfert [1,2,3]

1   Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum der Charité (DHZC), 13353 Berlin, Germany
2   Charité—Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, 10117 Berlin, Germany
3   DZHK (German Centre for Cardiovascular Research), Partner Site Berlin, 10785 Berlin, Germany
4   Department of Health Sciences and Technology, ETH Zurich, 8092 Zurich, Switzerland
*   Correspondence: leonard.pitts@dhzc-charite.de; Tel.: +49-30-4593-2059

Abstract: Background: Perioperative stroke remains a devastating complication in the operative treatment of acute type A aortic dissection. To reduce the risk of perioperative stroke, different perfusion techniques can be applied. A consensus on the preferred cerebral protection strategy does not exist. Methods: To provide an overview about the different cerebral protection strategies, literature research on Medline/PubMed was performed. All available original articles reporting on cerebral protection in surgery for acute type A aortic dissection and neurologic outcomes since 2010 were included. Results: Antegrade and retrograde cerebral perfusion may provide similar neurological outcomes while outperforming deep hypothermic circulatory arrest. The choice of arterial cannulation site and chosen level of hypothermia are influencing factors for perioperative stroke. Conclusions: Deep hypothermic circulatory arrest is not recommended as the sole cerebral protection technique. Antegrade and retrograde cerebral perfusion are today's standard to provide cerebral protection during aortic surgery. Bilateral antegrade cerebral perfusion potentially leads to superior outcomes during prolonged circulatory arrest times between 30 and 50 min. Arterial cannulation sites with antegrade perfusion (axillary, central or carotid artery) in combination with moderate hypothermia seem to be advantageous. Every concept should be complemented by adequate intraoperative neuromonitoring.

Keywords: acute type A aortic dissection; cerebral protection; stroke; hypothermic circulatory arrest; cerebral perfusion; antegrade; retrograde

1. Introduction

Although acute type A aortic dissection (ATAAD) is rare, it is a possibly lethal event that presents cardiac surgeons with major challenges [1–3]. Even though ATAAD is still associated with high mortality and morbidity rates, thirty-day mortality has dropped to an average of 17% [4]. Instant surgical treatment remains the therapy of choice and should be performed irrespectively of time or day [5–8]. This includes the resection of the entry tear in combination with an open distal anastomosis to prevent aortic rupture, re-establish antegrade true lumen perfusion and resolve malperfusion [9]. Perioperative stroke represents a devastating complication and is influenced by multiple patient specific factors [10–12]. Female patients, particularly, may suffer from an impaired neurological outcome [13]. Compared to elective aortic arch surgery, the incidence of stroke is significantly higher in surgery for ATAAD and may adversely affect post-operative outcomes [14]. Preoperative neurological dysfunction and cerebral malperfusion frequently appear in the setting of ATAAD and are associated with an increased risk of perioperative stroke [12,15]. To prevent this severe complication, different cerebral protection strategies evolved in the

past. While systemic hypothermia prolongs the tolerance for cerebral ischemia, the use of a selective cerebral perfusion technique aims to meet the metabolic and oxygen demand of the brain in a direct matter. The aim of this narrative review is to provide an overview about cerebral protection strategies in ATAAD, discussing the most relevant topics in terms of cerebral protection based on the current scientific literature and give concrete clinical advice about how modern cerebral protection should be performed in surgery for ATAAD.

2. Materials and Methods

For this narrative review, the literature research was performed on Medline/PubMed using the following medical subject heading terms: "Cerebral Protection OR Cerebral Perfusion AND Acute Type A Aortic Dissection". Only original articles dealing with cerebral protection strategies and neurological outcomes in the treatment of ATAAD published in 2010 or later were considered for further investigation. Each topic had to show potential impact on neurological outcome in the current literature and is, furthermore, of relevant clinical interest, playing a concrete role in the perioperative and surgical management of ATAAD. Studies reporting about cerebral protection strategies including patient cohorts that were not applicable (e.g., elective aortic surgery) or lacked detailed information regarding the different cerebral protection techniques, were excluded. The research process is illustrated in Figure 1. This review is a narrative review. We do not claim the conduction of a fully systematic review according to the PRISMA guidelines.
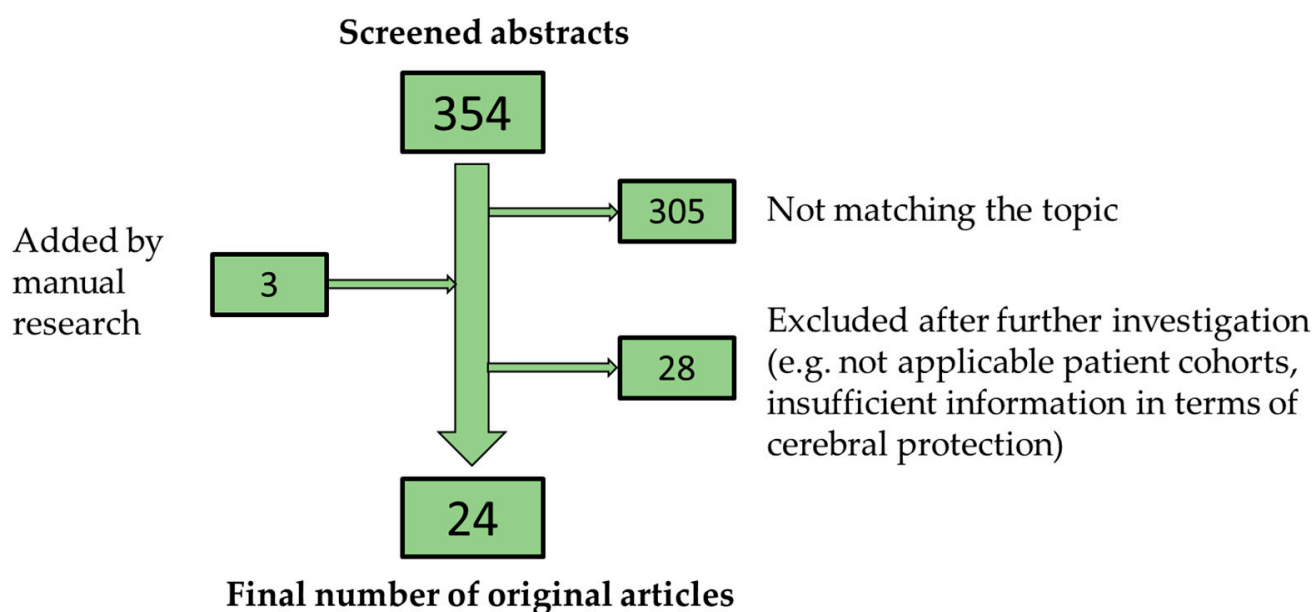

Figure 1. Process of the literature research.

3. Results

In total, 24 original articles were identified for further investigation. The selected articles were stratified according to the recruited cerebral protection technique and examined for the presence of preoperative cerebral malperfusion, the time of circulatory arrest, the level of hypothermia and the rate of perioperative strokes. The occurrence of perioperative stroke was furthermore subdivided according to the most common neurological endpoints monitored in studies investigating cerebral protection techniques for ATAAD. Thus, postoperative neurological deficits were defined as permanent neurological deficits (e.g., stroke) **and** transient neurological deficits (e.g., transient ischemic attack, delirium etc.) **or** solely new postoperative neurological deficits (e.g., stroke), which were defined through the absence of preoperative neurological dysfunction. Furthermore, influencing factors identified by regression analyses—if performed—were added. The complete results are shown in Appendix A in Table 1. The gathered information is embedded in the following

chapters, dealing with the most relevant aspects of neuroprotection in surgery for ATTAD with a specific focus on cerebral perfusion techniques.

3.1. Deep Hypothermic Circulatory Arrest

The use of deep hypothermic circulatory arrest (DHCA) was the first standardized approach of cerebral protection in aortic arch surgery. While the proximal anastomosis is made, the systemic temperature is usually lowered to between 16 and 19 °C. The use of DHCA offers the advantage to perform the open distal anastomosis in a bloodless and canula-free field without the use of clamps. Although this method leads to acceptable short-term results when a short circulatory arrest is needed, the risk for perioperative stroke and mortality may rise when circulatory arrest exceeds between 30 and 40 min [16–18]. Furthermore, Czerny et al. identified the use of isolated DHCA as an independent risk factor for permanent neurologic injury [19]. Additionally, the use of DHCA showed the poorest long-term survival compared to cerebral perfusion techniques according to Wiedemann et al. [20]. Based on these findings, isolated DHCA without selective cerebral perfusion is no longer recommended for cerebral protection in the operative treatment of ATAAD [9,21,22]. Especially in terms of more extensive, complex and time-consuming arch operations, the use of a selective cerebral perfusion technique as an adjunct to systemic hypothermia seems of upmost importance.

3.2. Retrograde Cerebral Perfusion

The idea of retrograde cerebral perfusion (RCP) is to complement DHCA by supplying additional oxygen to the brain through the venous and capillary system, thereby prolonging the tolerance of cerebral ischemia while flushing embolic material out of the brain vessels in a retrograde manner. For this purpose, a cannula is inserted into the superior vena cava through which oxygenated blood is applied during circulatory arrest with a flow rate of approximately 500 mL/min and a pressure of around 25 mmHg. A schematic example of RCP is shown in Figure 2. The use of RCP became popular after 1990 and was associated with a lower mortality, morbidity and perioperative stroke rate compared to DHCA alone [23,24]. Additionally, RCP enabled a prolongation of the safe cerebral ischemic time up to 40 min [17,25,26]. Although the use of RCP delivered excellent clinical results, doubts were cast about RCP regarding the true benefit of actual brain perfusion. Several studies demonstrating the superiority of RCP had been based on comparisons with historical cohorts treated with DHCA, potentially leading to bias in favor of RCP [23]. Notably, in a prospective clinical trial, Bonser et al. demonstrated no clinical or metabolic advantage of using DHCA in combination with RCP compared to DHCA alone [27]. Moreover, the potential effect of retrograde washout also remained questionable and is still lacking conclusive evidence [28,29]. Some have even tried to combine the flush effect of RCP with antegrade cerebral perfusion (ACP), but without any significant clinical advantage proven [30]. However, according to a recent meta-analysis, the additional use of RCP to DHCA is associated with a lower risk for perioperative stroke compared to DHCA alone, supporting the concept of an additional neuroprotective effect [31]. These results were also confirmed by a multicenter analysis by Ghoreishi et al. [32]. Mechanistically, the additional use of RCP may result in more homogenous cooling effects as well as an enhanced clearance of neurotoxic substances released due to latent cerebral ischemia. Nevertheless, the risk for a perioperative stroke during RCP may rise when circulatory arrest exceeds 60 min, which casts doubt about the use of RCP for longer circulatory arrest times [33,34]. Indeed, the implementation of RCP as a primary cerebral perfusion strategy is often performed under DHCA, which is associated with longer cardiopulmonary bypass times as well as hypothermia-related side effects [35,36]. The performance of RCP under higher temperatures in the range of moderate hypothermia has not been broadly established, but may be a valid option in cases of shorter circulatory arrest times not exceeding 30 min [37].
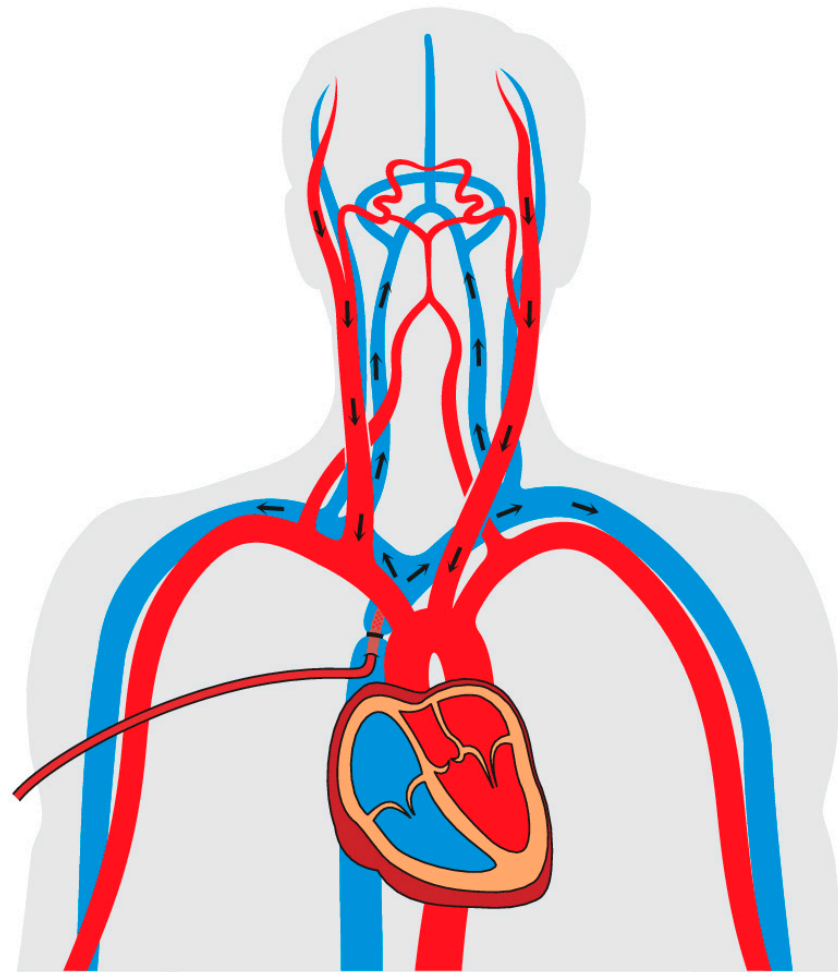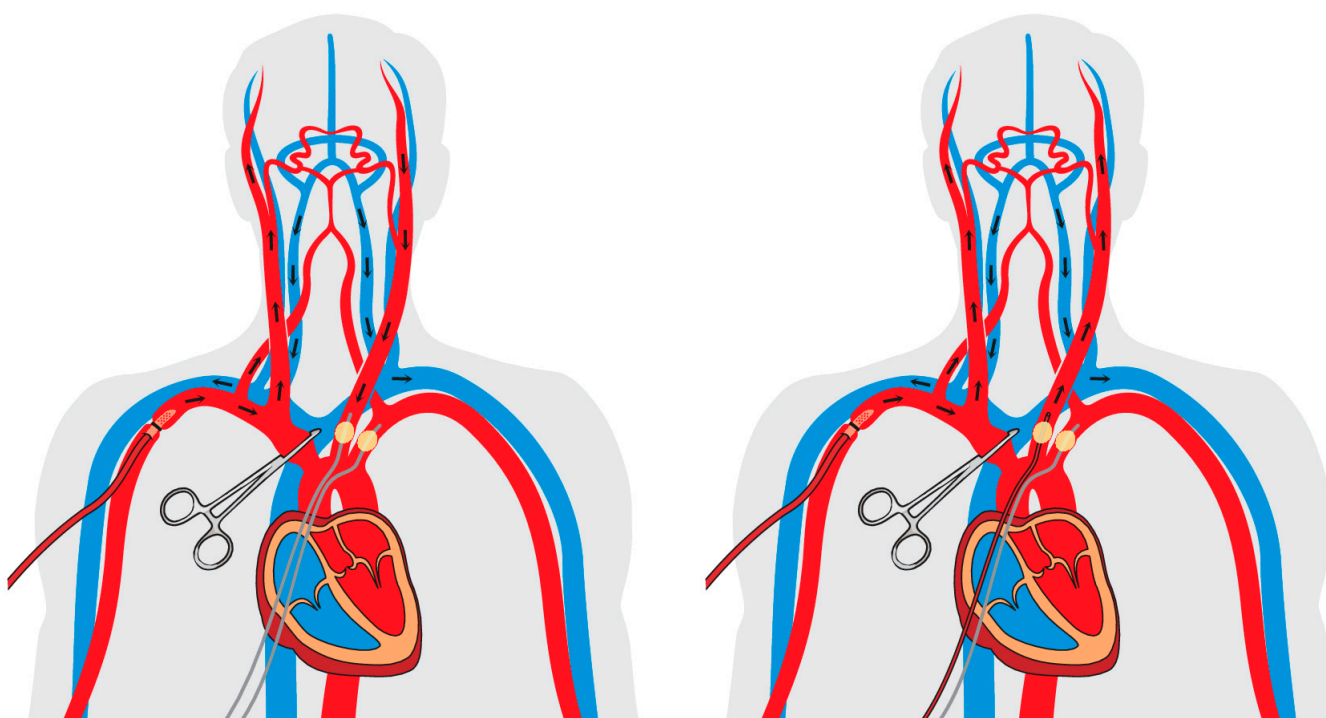
Figure 2. Performance of retrograde cerebral perfusion.

3.3. Antegrade Cerebral Perfusion

During antegrade cerebral perfusion (ACP), the brain is perfused in a physiological antegrade manner through the supra-aortic vessels. This allows to perform aortic arch surgery and treatment of ATAAD safely under moderate hypothermia from 26 °C to 28 °C, or even higher temperatures in selected cases, which leads to a lower cardiopulmonary bypass time and less hypothermia-related side effects [36]. For ACP, a target flow rate of 10 mL/kg bodyweight is applied, and the pressure is usually kept from around 40–70 mmHg. The cannulation of the right axillary artery constitutes the basis of ACP. In case of unilateral antegrade cerebral perfusion (uACP), the brachiocephalic trunk, the left common carotid artery and the left subclavian artery are clamped proximally to maintain sufficient perfusion pressure and to prevent a steal phenomenon. Furthermore, uACP can be expanded to bilateral antegrade cerebral perfusion (bACP) by additionally cannulating the left common carotid artery. Both techniques are illustrated in Figure 3. Another possibility for bACP is the cannulation of both common carotid arteries, offering the advantage of continuous cerebral blood flow without interruption. To get an overview, we identified all available studies since 2010 that investigated the neurological outcomes in ATAAD in terms of the applied selective cerebral perfusion techniques. So far, the majority of the studies have failed to detect a significant difference between RCP and ACP [14,21,38–44]. Moreover, prospective randomized trials are scarce, often limited due to small patients cohorts and have thus far not shown any significant difference regarding the risk for a perioperative stroke [45]. These findings suggest that similar neurological outcomes may be achieved using either RCP or ACP, justifying both techniques as legitimate and reproducible selective cerebral perfusion strategies, as recently recommended in the expert consensus of the

American Association for Thoracic Surgery [6]. Moreover, in a propensity score-matched analysis, Montagner et al. recently showed that all three cerebral perfusion strategies lead to similar results during open zone 0 arch anastomosis for the treatment of ATAAD in terms of neurologic outcomes [38]. This may allow for tailored approaches addressing specific patient needs in the surgical treatment of ATAAD and adapt the procedure to individual conditions, e.g., the ability to implement RCP if cannulation of the supra-aortic vessels is not feasible due to substantial atherosclerosis. However, considering the advantages of moderate instead of deep hypothermia as well as the potentially limited safety of RCP for longer circulatory arrest times, ACP has been established as the main selective cerebral perfusion strategy in European cardiac centers, providing a suitable approach in cases of prolonged circulatory arrest [46,47].

Figure 3. Performance of unilateral (**left**) and bilateral antegrade cerebral perfusion (**right**).

3.4. Unilateral or Bilateral?

Although the implementation of ACP is recommended by current guidelines, there is no consensus regarding the specific technique of ACP in the setting of ATAAD [9]. This decision is often made on the basis of institutional policies, expert consensus and the surgeon's preference. Due to its simplicity, uACP represents an attractive strategy for many surgeons, especially in cases of shorter circulatory arrest [48]. In contrast, bACP is currently the most frequently performed technique in Europe [46]. Assuming that uACP ensures an adequate perfusion of the whole brain, it is supported by several studies, which demonstrated equal results in terms of risk for perioperative stroke comparing uACP to bACP [18,49–54]. Norton et al. advocated the use of uACP on the basis of a similar incidence of right and left hemispheric strokes while avoiding the additional manipulation of supra-aortic vessels for bACP [53]. However, these findings also showed that bACP may not be associated with a higher risk for perioperative left hemispheric strokes. Interestingly, in a recent multicenter trial, Piperata et al. observed a higher incidence of perioperative as well as left hemispheric strokes in case of bACP compared to uACP [55]. So far, this is the only study reporting inferior neurological outcomes following bACP, highlighting the demand for further investigation. Regarding the potential time-consuming complexity of bACP, Tong and colleagues reported equal cardiopulmonary bypass and circulatory arrest

times in comparison with uACP [56]. Although the incidence of perioperative strokes was not significantly lower, bACP led to a reduction in permanent neurologic deficits by 50% when compared to uACP. Additionally, the performance of uACP presupposes an intact circle of Willis to ensure an adequate perfusion of the left hemisphere, which does not apply to all patients undergoing surgery for ATAAD [57]. In contrast, Urbanski et al. demonstrated that the circle of Willis' individual anatomical conditions do not correlate with potential contralateral hypoperfusion and that excellent neurological results can be achieved via uACP in elective aortic arch surgery [58,59]. A major limitation of most studies supporting the use of uACP is the fact that they often include a disproportionally higher number of hemiarch replacements and shorter circulatory arrest times (<40 min) when compared to complex aortic arch surgery [53,59]. This discrepancy was also highlighted by Preventza et al., leading to potential bias and possibly underestimating the efficacy of bACP because of its preferred use in extensive arch surgery [49]. Therefore, they suggested bACP as the perfusion strategy of choice if the estimated circulatory arrest time should extend >30 min. Notably, more recent studies have supported these suggestions with Angleitner et al. demonstrating superior long-term survival for bACP if the circulatory arrest time exceeded ≥50 min [52]. Consistently, a meta-analysis of Angeloni et al. revealed that longer circulatory arrest times were associated with increased mortality only among patients treated with uACP but not bACP [60]. The safety of uACP for shorter circulatory arrest times and the need of bACP for extended circulatory arrest was also confirmed by current results of the UK National Adult Cardiac Surgical Audit [22]. In case of total arch replacement in the setting of ATAAD, Liu et al. could even observe a significantly reduced risk for perioperative stroke in the group treated by bACP compared to uACP [61]. However, a clear recommendation for the limited safety time of circulatory arrest from which bACP should be applied has not been reliably described yet. The most recent guidelines suggest a time interval between 30 and 50 min of circulatory arrest, for which bACP may be advantageous [9]. The idea of performing trilateral cerebral perfusion via additional cannulation of the left axillary artery in selected cases represents a rather experimental approach with no available clinical evidence [62].

3.5. Arterial Cannulation and Neuroprotection

Femoral arterial cannulation has been used widely for the safe implementation of cardiopulmonary bypass. In recent years, increasing evidence suggests that femoral cannulation and consecutive retrograde perfusion may be inferior to antegrade perfusion techniques in terms of mortality and the risk for perioperative stroke [9,63,64]. Cannulation of the right axillary artery, particularly, in the setting of ATAAD may be associated with lower risk for perioperative stroke while being suitable for antegrade cerebral perfusion by clamping the innominate artery [65]. This may also be possible and safe in cases of innominate artery dissection [66]. Other approaches such as the direct central cannulation of the dissected aorta or bilateral cannulation of the common carotid arteries are possible cannulation strategies, but are only used at a few centers [9,67,68]. Double arterial cannulation strategies combining axillary and femoral cannulation are gaining interest with regards to potentially preventing and treating malperfusion syndromes, especially in cases of true lumen collapse and consecutive hypoperfusion [69]. Whether these techniques could also lower the risk of perioperative stroke is still under investigation.

3.6. Hypothermia and Neuroprotection

Because DHCA was the first established cerebral protection technique for aortic arch surgery during circulatory arrest, subsequently developed selective cerebral perfusion strategies were initially also performed during deep hypothermia. Then, especially in terms of ACP, the setting of deep hypothermia slowly switched to moderate hypothermia and reached average temperatures of approximately 28 °C [70,71]. Leshnower et al. compared the use of deep hypothermia in combination with ACP to moderate hypothermia with ACP in the treatment of ATAAD, showing no benefit in terms of mortality or perioperative

stroke in the group with deep hypothermia [72]. These findings underline that there is no significant effect of additional cerebral protection when performing ACP under lower temperatures, justifying the use of moderate or maybe even mild hypothermia in the treatment of ATAAD [73]. In support, a recent propensity-matched analysis of the International Registry of Acute Aortic Dissection showed satisfactory results under moderate hypothermia while avoiding extended cardio-pulmonary bypass times under deep hypothermia [74]. Although deeper levels of hypothermia do not seem to offer an additional significant effect of cerebral protection during ACP, the risk of ischemic damage to the spinal cord must be considered as having particular relevance during prolonged circulatory arrest under moderate hypothermia [75]. Indeed, Kamiya et al. showed that the incidence of postoperative paraplegia increased from 0 to 18% when circulatory arrest exceeded ≥60 min and only moderate instead of deep hypothermia was used [76]. Of note, different sites of perioperative body temperature assessment have been delineated to diverge from the actual cerebral temperature, which may affect study outcomes. While tympanic temperature measurements were tightly correlated with arterial blood monitoring, bladder and rectal measurements resulted in significantly divergent measurements [77]. The optimal location for cerebral temperature measurement thus remains to be defined, although a combination of two locations may increase reliability.

3.7. Monitoring for Neuroprotection

Using near infrared spectroscopy (NIRS) to constantly monitor brain tissue oxygen saturation seems to be indispensable during surgery for ATAAD and is, furthermore, the most frequently used neuromonitoring technique in Europe during aortic arch surgery [46]. According to the individual baseline levels of cerebral oxygen saturation, proportional alterations can be immediately detected. This offers the opportunity to identify the occurrence of a sudden cerebral malperfusion syndrome while providing positive feedbacks after the successful restoration of dissected supra-aortic vessels with recovered adequate cerebral perfusion. Furthermore, when applying uACP with asymmetric oxygen saturation reflected by decreases over the left hemisphere, NIRS can support the decision to switch to bACP, which, in turn, may lower the risk for developing a perioperative stroke [78]. Though NIRS represents an essential and useful tool during aortic arch surgery, its registration range is restricted to the frontal cortex when placed bilaterally on the forehead. Thus, local perioperative strokes in the frontal lobes or global oxygen declines in one or both hemispheres can be reliably detected, whereas strokes in the medial or vertebrobasilar area may not be recognized.

3.8. Neuroprotective Drugs

The perioperative application of drugs with potential neuroprotective effects, such as barbiturates, steroids or mannitol, is also frequently discussed in aortic arch surgery. An analysis of the German Registry for Acute Aortic Dissection Type A revealed that 50% of patients undergoing surgery for ATAAD received at least one neuroprotective drug, indicating a slight advantage for the use of steroids in terms of neurological outcomes [79]. However, further scientific evidence supporting the implementation of neuroprotective pharmacological treatment is low, while no significant benefit has been shown in larger clinical trials yet [80].

4. Conclusions

The chosen concept of cerebral protection in the surgical treatment of ATAAD has a great impact on patients' outcome in terms of mortality and the risk for a perioperative stroke. Whereas the use of DHCA alone seems to be outdated today, RCP and ACP have both been established as legitimate and reproducible selective cerebral perfusion strategies. Thereby, the use of ACP seems to be superior regarding the possibility to perform the operation safely under moderate hypothermia compared to RCP and deep hypothermia. Although there is no clear recommendation by current guidelines for the technique of

ACP, several studies suggest bACP as the most suitable cerebral perfusion strategy for prolonged circulatory arrest, while uACP is proven to be safe for shorter times of circulatory arrest. A well-described and evidence-based time threshold for this purpose is still missing, although a time interval from 30–50 min has recently been proposed. This issue demands a prospective, randomized and ideally multicenter trial to evaluate the true benefit of bACP. Arterial cannulation sites with consecutive antegrade body perfusion, especially right axillary cannulation, may lead to lower mortality and superior neurological outcome. Single arterial femoral cannulation leading to retrograde body perfusion should hereby be avoided, if possible. Regarding the level of hypothermia, moderate hypothermia at approximately 28 °C seems to be an effective and well-balanced strategy, offering adequate cerebral protection while avoiding the disadvantages of deep hypothermia. Additionally, precise temperature management and adequate neuromonitoring should complement the concept of cerebral protection. For this purpose, NIRS plays a major role in neuromonitoring during aortic arch surgery, possibly detecting and potentially lowering the risk for developing a perioperative stroke.

Author Contributions: Conceptualization: all authors; methodology: L.P., M.K., M.M. and J.K.; software: L.P.; validation: L.P. and M.K.; formal analysis: L.P., M.K. and J.K.; investigation: L.P., M.K. and J.K.; resources: L.P., J.K. and V.F.; data curation: L.P.; original draft preparation: L.P., M.K., M.M. and J.K.; writing—review and editing: all authors; visualization: L.P.; supervision: M.K., S.B., S.D.K., C.S., V.F. and J.K.; project administration: J.K.; funding acquisition: not required. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: Ethical review and approval were waived for this study due to the nature of a narrative review, involving no clinical data or animals.

Informed Consent Statement: Patient consent was waived due to the nature of a narrative review with no active enrollment of patients.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

ACP	Antegrade cerebral perfusion
ATAAD	Acute type A aortic dissection
bACP	Bilateral antegrade cerebral perfusion
DHCA	Deep hypothermic circulatory arrest
NIRS	Near infrared spectroscopy
RCP	Retrograde cerebral perfusion
uACP	Unilateral antegrade cerebral perfusion

Appendix A

Table 1. Recent Studies Investigating the Neurological Outcome after Surgery for ATAAD Taking into Account the Different Techniques of Cerebral Protection.

Author and Year	Number of Patients	Cerebral Protection Technique, *n* (%)	Preoperative Cerebral Malperfusion, *n* (%)	Mean Temperature, °C (±SD/Median)	Circulatory Arrest, Minutes (±SD/Median)	Neurological Outcome Defined as New Postoperative Neurological Deficit (*) or Permanent (PND) and Transient (TND) Neurological Deficit, *n* (%)	Identified Influencing Factors on Neurological Outcome
Montagner, 2022 [38]	*n* = 186	uACP: 62 (33.3) bACP: 62 (33.3) RCP: 62 (33.3)	uACP: 12 (19.4) bACP: 10 (16.1) RCP: 8 (12.9)	uACP: 25 ± 4 bACP: 28 ± 3 RCP: 17 ± 3	uACP: 33 ± 16 bACP: 38 ± 14 RCP: 35 ± 15	uACP: 8 (12.9) * bACP: 7 (11.3) * RCP: 8 (12.9) *	n.a.
Song, 2022 [50]	*n* = 188	uACP: 94 (50.0) bACP: 94 (50.0)	n.a.	uACP: 28 (27–28) bACP: 28 (27–28)	uACP: 41 (32–56) bACP: 43 (35–56)	uACP: PND 8 (8.5), TND 19 (20.2) bACP: 11 (11.8), TND 17 (18.1)	n.a.
Samanidis, 2021 [39]	*n* = 290	ACP: 117 (40.3) RCP: 173 (59.7)	ACP: 14 (12.0) RCP: 32 (18.5)	ACP: 22 (21–23) RCP: 18 (17–21)	ACP: 33 (26–48) RCP: 26 (21–33)	ACP: PND 12 (10.3), TND 15 (12.8) RCP: PND 12 (6.9), TND 22 (12.7)	n.a.
Piperata, 2021 [55]	*n* = 378	uACP: 189 (50.0) bACP: 189 (50.0)	uACP: 5 (3) bACP: 5 (3)	uACP: 28 (28–28) bACP: 28 (25–28)	uACP: 35 (28–44) bACP: 36 (28–44)	uACP: PND 8 (4.0), TND 21 (11.0) bACP: PND 26 (14.0), TND 23 (12.0)	Risk Factors: • bACP may be associated with a higher risk for perioperative as well as left hemispheric strokes
Benedetto, 2021 [22]	*n* = 1929	uACP: 117 (6.1) bACP: 760 (39.4) RCP: 222 (11.5) DHCA: 830 (43.0)	uACP: 10 (8.5) bACP: 76 (10.0) RCP: 22 (9.9) DHCA: 52 (6.3)	n.a.	uACP: 35 ± 21 bACP: 44 ± 36 RCP: 31 ± 19 DHCA: 33 ± 22	uACP: 11 (9.4) * bACP: 111 (14.6) * RCP: 29 (13.1) * DHCA: 118 (14.2) *	Risk Factors: • DHCA as the single technique for cerebral protection
Sun, 2021 [40]	*n* = 108	ACP: 54 (50.0) RCP: 54 (50.0)	ACP: 2 (3.7) RCP: 2 (3.7)	ACP: 25 (n.a.) RCP: 18 (n.a.)	ACP: 88 ± 5 RCP: 63 ± 10	ACP: PND 10 (18.5) RCP: PND 6 (11.1)	Risk Factors: • S/p stroke • Total arch replacement
Xue, 2021 [41]	*n* = 746	uACP: 617 (82.7) bACP: 13 (1.8) RCP: 51 (6.8) DHCA: 65 (8.7)	Total: 82 (11.0)	Total: 21 (14–30)	Total: 29 ± 12	Total: PND 35 (4.7)	Risk Factors: • Preoperative cerebral malperfusion • Preoperative peripheral malperfusion • End-Stage renal disease • Salvage surgery Protective Factors: • Conservative arch repair • Low-Flow-ACP

Table 1. *Cont.*

Author and Year	Number of Patients	Cerebral Protection Technique, *n* (%)	Preoperative Cerebral Malperfusion, *n* (%)	Mean Temperature, °C (±SD/Median)	Circulatory Arrest, Minutes (±SD/Median)	Neurological Outcome Defined as New Postoperative Neurological Deficit (*) or Permanent (PND) and Transient (TND) Neurological Deficit, *n* (%)	Identified Influencing Factors on Neurological Outcome
Angleitner, 2020 [52]	*n* = 184	uACP: 93 (50.5) bACP: 91 (49.5)	uACP: 21 (22.6) bACP: 15 (16.5)	n.a.	uACP: 30 (25–45) bACP: 38 (30–57)	uACP: PND 18 (19.4), TND 9 (9.7) bACP: PND 17 (18.7), TND 7 (7.7)	n.a.
Norton, 2020 [53]	*n* = 307	uACP: 140 (45.6) bACP: 167 (54.4)	uACP: 10 (7.1) bACP: 7 (4.2)	uACP: 20 (18–24) bACP: 17 (16–18)	uACP: 29 (23–38) bACP: 45 (38–55)	uACP: 9 (6.4) * bACP: 15 (9.0) *	n.a.
O'Hara, 2020 [21]	*n* = 6387	ACP: 2950 (46.2) RCP: 1445 (22.6) No Cerebral Perfusion: 1992 (31.2)	n.a.	ACP: 22 (18–25) RCP: 18 (19–22) No Cerebral Perfusion: 19 (18–21)	ACP: 35 (26–48) RCP: 33 (25–45) No Cerebral Perfusion: 26 (20-34)	ACP: PND 369 (12.5) RCP: PND 162 (11.2) No Cerebral Perfusion: PND 277 (13.9)	Risk Factors: • Prolonged circulatory arrest • Protective Factors: • Utilization of either ACP or RCP in combination with Deep or moderate hypothermic arrest vs. no cerebral perfusion
Liu, 2020 [61]	*n* = 321	uACP: 124 (38.6) bACP: 197 (61.4)	uACP: 5 (4.0) bACP: 11 (5.6)	uACP: 25 ± 0 bACP: 27 ± 1	uACP: 27 ± 7 bACP: 26 ± 6	uACP: PND 22 (17.7), TND 32 (25.8) bACP: PND 16 (8.1), TND 31 (15.7)	Risk Factors: • Preoperative neurological dysfunction • Prolonged CPB time • Type of cerebral perfusion
Dong, 2020 [51]	*n* = 61	uACP: 36 (59.0) bACP: 25 (41.0)	n.a.	uACP: 25 ± 1 bACP: 29 ± 1	uACP: 29 ± 5 bACP: 16 ± 4	uACP: PND 3 (8.3), TND 5 (13.9) bACP: PND 0 (0.0), TND 2 (8.0)	n.a.
Dumfarth, 2018 [14]	*n* = 303	ACP: 202 (66.7) RCP: 45 (14.9) DHCA: 46 (15.2) Without: 10 (3.2)	Total: 17 (5.6)	Total: 21 ± 4	Total: 45 ± 21	Total: PND: 48 (15.8)	Risk Factors: • Bovine aortic arch • Preoperative resuscitation • Preoperative malperfusion
Furukawa, 2017 [81]	*n* = 137	ACP: 137 (100.0)	Total: 12 (8.8)	Total: 22–28 (n.a.)	n.a.	Total: PND: 4 (2.9)	Risk Factors: • Preoperative neurological symptoms • Partial or complete thrombosis of supra-aortic branch vessels
Keeling, 2017 [48]	*n* = 342	uACP: 342 (100.0)	n.a.	Total: 26 ± 3	Total: 39 ± 19	Total: PND: 25 (7.3) TND: 20 (5.8)	n.a.

Table 1. *Cont.*

Author and Year	Number of Patients	Cerebral Protection Technique, *n* (%)	Preoperative Cerebral Malperfusion, *n* (%)	Mean Temperature, °C (±SD/Median)	Circulatory Arrest, Minutes (±SD/Median)	Neurological Outcome Defined as New Postoperative Neurological Deficit (*) or Permanent (PND) and Transient (TND) Neurological Deficit, *n* (%)	Identified Influencing Factors on Neurological Outcome
Zierer, 2017 [71]	*n* = 453	uACP: 298 (66.0) bACP: 155 (34)	Total: 33 (7.0)	Total: 29 ± 1	Total: 46 ± 23	Total: PND: 27 (6.0) TND: 31 (7.0)	n.a.
Tong, 2017 [56]	*n* = 203	uACP: 82 (40.4) bACP: 121 (59.6)	uACP: 4 (4.9) bACP: 5 (5.8)	uACP: 24 ± 1 bACP: 24 ± 1	uACP: 23 ± 9 bACP: 24 ± 8	uACP: PND 11 (16.9), TND 6 (9.2) bACP: PND 9 (8.4), TND 5 (4.7)	Risk Factors: • Prolonged CPB time • Prolonged circulatory arrest
Stamou, 2016 [42]	*n* = 324	ACP: 84 (25.9) RCP: 55 (17.0) DHCA: 184 (56.8)	n.a.	ACP: 19 (8–26) RCP: 17 (10–20) DHCA: 19 (10–32)	ACP: 31 (0–71) RCP: 36 (4–61) DHCA: 17 (0–146)	ACP: 12 (14.3) * RCP: 12 (21.8) * DHCA: 26 (14.1) *	n.a.
Preventza, 2015 [49]	*n* = 157	uACP: 90 (57.3) bACP: 63 (40.1)	uACP: 16 (18.6) bACP: 17 (27.9)	Total: 22–24 (n.a.)	uACP: 34 ± 11 bACP: 46 ± 27	uACP: PND 12 (13.6), TND 10 (11.4) bACP: PND 7 (11.3), TND 5 (8.2)	Risk Factors: • S/p coronary intervention or coronary artery bypass graft • Preoperative peripheral malperfusion
Tokuda, 2014 [43]	*n* = 4128	ACP: 2769 (67.1) RCP: 1359 (32.9)	n.a.	ACP: 25 ± 3 RCP: 23 ± 3	n.a.	ACP: PND 311 (11.2), TND 121 (4.4) RCP: PND 132 (9.7), TND 61 (4.5)	n.a.
Wiedemann, 2013 [20]	*n* = 329	ACP: 91 (27.7) RCP: 122 (37.0) DHCA: 116 (35.3)	ACP: 3 (3.3) RCP: 9 (7.4) DHCA: 8 (6.9)	ACP: 25 (n.a.) RCP: 18 (n.a.) DHCA: 18 (n.a.)	ACP: 30 (14–92) RCP: 30 (14–88) DHCA: 36 (12-88)	ACP: PND 11 (12) RCP: PND 15 (12) DHCA: PND 27 (23)	n.a.
Sugiura, 2012 [44]	*n* = 203	ACP: 94 (46.3) RCP: 109 (53.7)	ACP: 3 (3.2) RCP: 1 (0.9)	ACP: 26 ± 1 RCP: 24 ± 1	ACP:65 ± 15 RCP: 53 ± 16	ACP: PND 11 (12.0), TND 32 (34) RCP: PND 10 (9.2), TND 41 (38)	n.a.
Lu, 2012 [54]	*n* = 263	uACP: 135 (51.3) bACP: 128 (48.7)	n.a.	uACP: 16 ± 2 bACP: 18 ± 2	uACP: 35 ± 15 bACP: 32 ± 14	uACP: PND 14 (10.4), TND 9 (6.7) bACP: PND 16 (12.5), TND 7 (5.5)	n.a.
Krüger, 2011 [18]	*n* = 1558	uACP: 628 (40.3) bACP: 453 (29.1) RCP: 34 (2.2) DHCA: 355 (22.8) Without: 88 (5.6)	uACP: 107 (17.0) bACP: 106 (23.4) DHCA: 76 (21.4)	n.a.	uACP: 32 ± 18 bACP: 38 ± 24 DHCA: 23 ± 14	uACP: 79 (12.6) * bACP: 64 (14.1) * DHCA: 53 (15) *	n.a.

* ACP: Antegrade cerebral perfusion; ATAAD: Acute type A aortic dissection; bACP: Bilateral antegrade cerebral perfusion; CPB: Cardiopulmonary bypass; DHCA: Deep hypothermic circulatory arrest; n.a.: not available; PND: Permanent neurological deficit; RCP: Retrograde cerebral perfusion; SD: Standard deviation; S/p: Status post; TND: Transient neurological deficit.

References

1. Pitts, L.; Montagner, M.; Kofler, M.; Van Praet, K.; Heck, R.; Buz, S.; Kurz, S.; Sündermann, S.; Hommel, M.; Falk, V.; et al. State of the Art Review: Surgical Treatment of Acute Type A Aortic Dissection. *Surg. Technol. Int.* **2021**, *38*. [CrossRef]
2. Pitts, L.; Van Praet, K.M.; Montagner, M.; Kofler, M.; Falk, V.; Kempfert, J. David Procedure as Valve-Sparing Root Replacement. *Surg. Technol. Int.* **2022**, *41*. [CrossRef] [PubMed]
3. Kurz, S.; Falk, V.; Kempfert, J.; Gieb, M.; Ruschinski, T.; Kukucka, M.; Tsokos, M.; Grubitzsch, H.; Herbst, H.; Semmler, J.; et al. Insight into the incidence of acute aortic dissection in the German region of Berlin and Brandenburg. *Int. J. Cardiol.* **2017**, *241*, 326–329. [CrossRef]
4. Karck, M.; Conzelmann, L.; Easo, J.; Krüger, T.; Rylski, B.; Weigang, E.; Boening, A. German Registry for Acute Aortic Dissection Type A: Structure, Results, and Future Perspectives. *Thorac. Cardiovasc. Surg.* **2016**, *65*, 077–084. [CrossRef] [PubMed]
5. Gasser, S.; Stastny, L.; Kofler, M.; Krapf, C.; Bonaros, N.; Grimm, M.; Dumfarth, J. Rapid Response in Type A Aortic Dissection: Is There a Decisive Time Interval for Surgical Repair? *Thorac. Cardiovasc Surg.* **2021**, *69*, 49–56. [CrossRef] [PubMed]
6. Gasser, S.; Stastny, L.; Kofler, M.; Zujs, V.; Krapf, C.; Semsroth, S.; Ströhle, M.; Grimm, M.; Dumfarth, J. Surgery out of office hours for type A aortic dissection: Does night-time and weekend surgery worsen outcome? *Interact. Cardiovasc. Thorac. Surg.* **2020**, *31*, 806–812. [CrossRef] [PubMed]
7. Zaschke, L.; Habazettl, H.; Thurau, J.; Matschilles, C.; Göhlich, A.; Montagner, M.; Falk, V.; Kurz, S.D. Acute type A aortic dissection: Aortic Dissection Detection Risk Score in emergency care–surgical delay because of initial misdiagnosis. *Eur. Hear. J. Acute Cardiovasc. Care* **2020**, *9*, S40–S47. [CrossRef] [PubMed]
8. Matschilles, C.; Mochmann, H.-C.; Syrmas, G.; Zaschke, L.; Kurz, S. Interhospital transfer of patients suffering from acute aortic dissection by helicopter and ground-based emergency medical services. *Resuscitation* **2018**, *130*, e136. [CrossRef]
9. Isselbacher, E.M.; Preventza, O.; Black, I.J.H.; Augoustides, J.G.; Beck, A.W.; Bolen, M.A.; Braverman, A.C.; Bray, B.E.; Brown-Zimmerman, M.M.; Chen, E.P.; et al. 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* **2022**, *146*, e334–e482. [CrossRef]
10. Dumfarth, J.; Peterss, S.; Luehr, M.; Etz, C.D.; Schachner, T.; Kofler, M.; Ziganshin, B.A.; Ulmer, H.; Grimm, M.; Elefteriades, J.A.; et al. Acute type A dissection in octogenarians: Does emergency surgery impact in-hospital outcome or long-term survival? *Eur. J. Cardio. Surg.* **2017**, *51*, 472–477. [CrossRef]
11. Dumfarth, J.; Peterss, S.; Kofler, M.; Plaikner, M.; Ziganshin, B.A.; Schachner, T.; Tranquilli, M.; Grimm, M.; Elefteriades, J.A. In DeBakey Type I Aortic Dissection, Bovine Aortic Arch Is Associated With Arch Tears and Stroke. *Ann. Thorac. Surg.* **2017**, *104*, 2001–2008. [CrossRef] [PubMed]
12. Dumfarth, J.; Kofler, M.; Stastny, L.; Gasser, S.; Plaikner, M.; Semsroth, S.; Krapf, C.; Schachner, T.; Bonaros, N.; Grimm, M. Immediate surgery in acute type A dissection and neurologic dysfunction: Fighting the inevitable? *Ann. Thorac. Surg.* **2020**, *110*, 5–12. [CrossRef] [PubMed]
13. Gasser, S.; Stastny, L.; Kofler, M.; Krapf, C.; Bonaros, N.; Grimm, M.; Dumfarth, J. Type A aortic dissection is more aggressive in women. *Eur. J. Cardio-Thoracic Surg.* **2022**, *62*, ezac040. [CrossRef]
14. Dumfarth, J.; Kofler, M.; Stastny, L.; Plaikner, M.; Krapf, C.; Semsroth, S.; Grimm, M. Stroke after emergent surgery for acute type A aortic dissection: Predictors, outcome and neurological recovery. *Eur. J. Cardio-Thoracic Surg.* **2018**, *53*, 1013–1020. [CrossRef] [PubMed]
15. Weigang, E.; Czerny, M.; Zierer, A.; Khaladj, N.; Schoenhoff, F.; Carrel, T.P.; Blettner, M.; Hoffmann, I.; Etz, C.; Englberger, L. The Impact of Pre-Operative Malperfusion on Outcome in Acute Type A Aortic Dissection: Results From the GERAADA Registry. *J. Am. Coll. Cardiol.* **2015**, *65*, 2628–2635. [CrossRef]
16. Gega, A.; Rizzo, J.A.; Johnson, M.H.; Tranquilli, M.; Farkas, E.A.; Elefteriades, J.A. Straight Deep Hypothermic Arrest: Experience in 394 Patients Supports Its Effectiveness as a Sole Means of Brain Preservation. *Ann. Thorac. Surg.* **2007**, *84*, 759–767. [CrossRef]
17. Svensson, L.G.; Crawford, E.S.; Hess, K.R.; Coselli, J.S.; Raskin, S.; A Shenaq, S.; Safi, H.J. Deep hypothermia with circulatory arrest. Determinants of stroke and early mortality in 656 patients. *J. Thorac. Cardiovasc. Surg.* **1993**, *106*, 19–28. [CrossRef]
18. Kruger, T.; Weigang, E.; Hoffmann, I.; Blettner, M.; Aebert, H. Cerebral protection during surgery for acute aortic dissection type A: Results of the German Registry for Acute Aortic Dissection Type A (GERAADA). *Circulation* **2011**, *124*, 434–443. [CrossRef]
19. Czerny, M.; Fleck, T.; Zimpfer, D.; Dworschak, M.; Hofmann, W.; Hutschala, D.; Dunkler, D.; Ehrlich, M.; Wolner, E.; Grabenwoger, M. Risk factors of mortality and permanent neurologic injury in patients undergoing ascending aortic and arch repair. *J. Thorac. Cardiovasc. Surg.* **2003**, *126*, 1296–1301. [CrossRef]
20. Wiedemann, D.; Kocher, A.; Dorfmeister, M.; Vadehra, A.; Mahr, S.; Laufer, G.; Ehrlich, M. Effect of cerebral protection strategy on outcome of patients with Stanford type A aortic dissection. *J. Thorac. Cardiovasc. Surg.* **2013**, *146*, 647–655.e1. [CrossRef]
21. O'Hara, D.; McLarty, A.; Sun, E.; Itagaki, S.; Tannous, H.; Chu, D.; Egorova, N.; Chikwe, J. Type-A Aortic Dissection and Cerebral Perfusion: The Society of Thoracic Surgeons Database Analysis. *Ann. Thorac. Surg.* **2020**, *110*, 1461–1467. [CrossRef] [PubMed]
22. Benedetto, U.; Dimagli, A.; Cooper, G.; Uppal, R.; Mariscalco, G.; Krasopoulos, G.; Goodwin, A.; Trivedi, U.; Kendall, S.; Sinha, S.; et al. Neuroprotective strategies in acute aortic dissection: An analysis of the UK National Adult Cardiac Surgical Audit. *Eur. J. Cardio-Thoracic Surg.* **2021**, *60*, 1437–1444. [CrossRef] [PubMed]

23. Safi, H.J.; Letsou, G.V.; Iliopoulos, D.C.; Subramaniam, M.H.; Miller, C.C., 3rd; Hassoun, H.; Asimacopoulos, P.J.; Baldwin, J.C. Impact of retrograde cerebral perfusion on ascending aortic and arch aneurysm repair. *Ann. Thorac. Surg.* **1997**, *63*, 1601–1607. [CrossRef] [PubMed]

24. Estrera, A.L.; Miller, C.C.; 3rd Lee, T.Y.; Shah, P.; Safi, H.J. Ascending and transverse aortic arch repair: The impact of retrograde cerebral perfusion. *Circulation* **2008**, *118* (Suppl. 14), S160–S166. [CrossRef] [PubMed]

25. Okita, Y.; Takamoto, S.; Ando, M.; Morota, T.; Matsukawa, R.; Kawashima, Y. Mortality And Cerebral Outcome In Patients Who Underwent Aortic Arch Operations Using Deep Hypothermic Circulatory Arrest With Retrograde Cerebral Perfusion: No Relation Of Early Death, Stroke, And Delirium To The Duration Of Circulatory Arrest. *J. Thorac. Cardiovasc. Surg.* **1998**, *115*, 129–138. [CrossRef] [PubMed]

26. Ueda, Y.; Okita, Y.; Aomi, S.; Koyanagi, H.; Takamoto, S. Retrograde cerebral perfusion for aortic arch surgery: Analysis of risk factors. *Ann. Thorac. Surg.* **1999**, *67*, 1879–1882. [CrossRef]

27. Bonser, R.; Wong, C.; Harrington, D.; Pagano, D.; Wilkes, M.; Clutton-Brock, T.; Faroqui, M. Failure of retrograde cerebral perfusion to attenuate metabolic changes associated with hypothermic circulatory arrest. *J. Thorac. Cardiovasc. Surg.* **2002**, *123*, 943–950. [CrossRef]

28. Yerlioglu, M.; Wolfe, D.; Mezrow, C.K.; Weisz, D.J.; Midulla, P.S.; Zhang, N.; Shiand, H.H.; Bodian, C.; Griepp, R.B. The effect of retrograde cerebral perfusion after particulate embolization to the brain. *J. Thorac. Cardiovasc. Surg.* **1995**, *110*, 1470–1485. [CrossRef]

29. Mills, N.L.; Ochsner, J.L. Massive air embolism during cardiopulmonary bypass. Causes, prevention, and management. *J. Thorac. Cardiovasc. Surg.* **1980**, *80*, 708–717. [CrossRef]

30. Estrera, A.L.; Miller, C.C.; Lee, T.-Y.; Shah, P.; Irani, A.D.; Ganim, N.; Abdullah, S.; Safi, H.J. Integrated cerebral perfusion for hypothermic circulatory arrest during transverse aortic arch repairs☆. *Eur. J. Cardio-Thoracic Surg.* **2010**, *38*, 293–298. [CrossRef]

31. Tian, D.H.; Weller, J.; Hasmat, S.; Oo, A.; Forrest, P.; Kiat, H.; Yan, T.D. Adjunct retrograde cerebral perfusion provides superior outcomes compared with hypothermic circulatory arrest alone: A meta-analysis. *J. Thorac. Cardiovasc. Surg.* **2018**, *156*, 1339–1348.e7. [CrossRef] [PubMed]

32. Ghoreishi, M.; Sundt, T.M.; Cameron, D.E.; Holmes, S.D.; Roselli, E.E.; Pasrija, C.; Gammie, J.S.; Patel, H.J.; Bavaria, J.E.; Svensson, L.G.; et al. Factors associated with acute stroke after type A aortic dissection repair: An analysis of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database. *J. Thorac. Cardiovasc. Surg.* **2019**, *159*, 2143–2154.e3. [CrossRef] [PubMed]

33. Usui, A.; Abe, T.; Murase, M. Early clinical results of retrograde cerebral perfusion for aortic arch operations in Japan. *Ann. Thorac. Surg.* **1996**, *62*, 94–104. [CrossRef] [PubMed]

34. Tanaka, A.; Chehadi, M.; Smith, H.N.; Hassan, M.; Sandhu, H.K.; Miller, C.C., 3rd; Safi, H.J.; Estrera, A.L. Deep Hypothermic Circulatory Arrest With Retrograde Cerebral Perfusion: How Long Is Safe? *Ann. Thorac. Surg.* **2022**; *Online ahead of print*.

35. Filgueiras, C.L.; Ryner, L.; Ye, J.; Yang, L.; Ede, M.; Sun, J.; Kozlowski, P.; Summers, R.; Saunders, J.K.; Salerno, T.A.; et al. Cerebral protection during moderate hypothermic circulatory arrest: Histopathology and magnetic resonance spectroscopy of brain energetics and intracellular pH in pigs. *J. Thorac. Cardiovasc. Surg.* **1996**, *112*, 1073–1080. [CrossRef] [PubMed]

36. Zierer, A.; Aybek, T.; Risteski, P.; Dogan, S.; Wimmer-Greinecker, G.; Moritz, A. Moderate hypothermia (30 degrees C) for surgery of acute type A aortic dissection. *Thorac. Cardiovasc. Surg.* **2005**, *53*, 74–79. [CrossRef]

37. Nakahara, Y.; Tsukioka, Y.; Tateishi, R.; Ono, S.; Shioya, M.; Itoda, Y.; Kanemura, T. Safety of retrograde cerebral perfusion under moderate hypothermia for hemiarch replacement. *Gen. Thorac. Cardiovasc. Surg.* **2022**, *70*, 842–849. [CrossRef]

38. Montagner, M.; Kofler, M.; Pitts, L.; Heck, R.; Buz, S.; Kurz, S.; Falk, V.; Kempfert, J. Matched comparison of 3 cerebral perfusion strategies in open zone-0 anastomosis for acute type A aortic dissection. *Eur. J. Cardio-Thoracic. Surg.* **2022**, *62*, ezac214. [CrossRef]

39. Samanidis, G.; Kanakis, M.; Khoury, M.; Balanika, M.; Antoniou, T.; Giannopoulos, N.; Stavridis, G.; Perreas, K. Antegrade and Retrograde Cerebral Perfusion During Acute Type A Aortic Dissection Repair in 290 Patients. *Hear. Lung Circ.* **2021**, *30*, 1075–1083. [CrossRef]

40. Sun, S.; Chien, C.-Y.; Fan, Y.-F.; Wu, S.-J.; Li, J.-Y.; Tan, Y.-H.; Hsu, K.-H. Retrograde cerebral perfusion for surgery of type A aortic dissection. *Asian J. Surg.* **2021**, *44*, 1529–1534. [CrossRef]

41. Xue, Y.; Liu, C.; Mi, L.; Chen, Y.; Wang, D. Risk factors for cerebral complications after type A aortic dissection surgery: Single center's experience. *Ann. Palliat. Med.* **2021**, *10*, 7458–7467. [CrossRef]

42. Stamou, S.C.; Rausch, L.A.; Kouchoukos, N.T.; Lobdell, K.W.; Khabbaz, K.; Murphy, E.; Hagberg, R.C. Comparison between antegrade and retrograde cerebral perfusion or profound hypothermia as brain protection strategies during repair of type A aortic dissection. *Ann. Cardiothorac. Surg.* **2016**, *5*, 328–335. [CrossRef] [PubMed]

43. Tokuda, Y.; Miyata, H.; Motomura, N.; Oshima, H.; Usui, A.; Takamoto, S.; Japan Adult Cardiovascular Database Organization. Brain Protection During Ascending Aortic Repair for Stanford Type A Acute Aortic Dissection Surgery. *Circ. J.* **2014**, *78*, 2431–2438. [CrossRef] [PubMed]

44. Sugiura, T.; Imoto, K.; Uchida, K.; Minami, T.; Yasuda, S. Comparative study of brain protection in ascending aorta replacement for acute type A aortic dissection: Retrograde cerebral perfusion versus selective antegrade cerebral perfusion. *Gen. Thorac. Cardiovasc. Surg.* **2012**, *60*, 645–648. [CrossRef] [PubMed]

45. Svensson, L.G.; Blackstone, E.H.; Apperson-Hansen, C.; Ruggieri, P.M.; Ainkaran, P.; Naugle, R.I.; Lima, B.; Roselli, E.E.; Cooper, M.; Somogyi, D.; et al. Implications from neurologic assessment of brain protection for total arch replacement from a randomized trial. *J. Thorac. Cardiovasc. Surg.* **2015**, *150*, 1140–1147.e11. [CrossRef] [PubMed]

46. De Paulis, R.; Czerny, M.; Weltert, L.; Bavaria, J.; Borger, M.A.; Carrel, T.P.; Etz, C.D.; Grimm, M.; Loubani, M.; Pacini, D.; et al. Current trends in cannulation and neuroprotection during surgery of the aortic arch in Europe. *Eur. J. Cardiothorac. Surg.* **2015**, *47*, 917–923. [CrossRef] [PubMed]

47. El-Sayed Ahmad, A.; Papadopoulos, N.; Risteski, P.; Hack, T.; Ay, M.; Moritz, A.; Zierer, A. Is More than One Hour of Selective Antegrade Cerebral Perfusion in Moderate-to-Mild Systemic Hypothermic Circulatory Arrest for Surgery of Acute Type A Aortic Dissection Safe? *Thorac. Cardiovasc. Surg.* **2018**, *66*, 215–221.

48. Keeling, W.B.; Leshnower, B.G.; Hunting, J.C.; Binongo, J.; Chen, E.P. Hypothermia and Selective Antegrade Cerebral Perfusion Is Safe for Arch Repair in Type A Dissection. *Ann. Thorac. Surg.* **2017**, *104*, 767–772. [CrossRef]

49. Preventza, O.; Simpson, K.H.; Cooley, D.A.; Cornwell, L.; Bakaeen, F.G.; Omer, S.; Rodriguez, V.; de la Cruz, K.I.; Rosengart, T.; Coselli, J.S. Unilateral Versus Bilateral Cerebral Perfusion for Acute Type A Aortic Dissection. *Ann. Thorac. Surg.* **2015**, *99*, 80–87. [CrossRef]

50. Song, S.J.; Kim, W.K.; Kim, T.H.; Song, S.W. Unilateral versus bilateral antegrade cerebral perfusion during surgical repair for patients with acute type A aortic dissection. *JTCVS Open* **2022**, *11*, 37–48. [CrossRef]

51. Dong, S.-B.; Xiong, J.-X.; Zhang, K.; Zheng, J.; Xu, S.-D.; Liu, Y.-M.; Sun, L.-Z.; Pan, X.-D. Different hypothermic and cerebral perfusion strategies in extended arch replacement for acute type a aortic dissection: A retrospective comparative study. *J. Cardiothorac. Surg.* **2020**, *15*, 1–8. [CrossRef]

52. Angleitner, P.; Stelzmueller, M.-E.; Mahr, S.; Kaider, A.; Laufer, G.; Ehrlich, M. Bilateral or unilateral antegrade cerebral perfusion during surgery for acute type A dissection. *J. Thorac. Cardiovasc. Surg.* **2020**, *159*, 2159–2167.e2. [CrossRef] [PubMed]

53. Norton, E.L.; Wu, X.; Kim, K.M.; Patel, H.J.; Deeb, G.M.; Yang, B. Unilateral is comparable to bilateral antegrade cerebral perfusion in acute type A aortic dissection repair. *J. Thorac. Cardiovasc. Surg.* **2019**, *160*, 617–625.e5. [CrossRef] [PubMed]

54. Lu, S.; Sun, X.; Hong, T.; Yang, S.; Song, K.; Lai, H.; Hu, K.; Wang, C. Bilateral Versus Unilateral Antegrade Cerebral Perfusion in Arch Reconstruction for Aortic Dissection. *Ann. Thorac. Surg.* **2012**, *93*, 1917–1920. [CrossRef]

55. Piperata, A.; Watanabe, M.; Pernot, M.; Metras, A.; Kalscheuer, G.; Avesani, M.; Barandon, L.; Peltan, J.; Lorenzoni, G.; Jorgji, V.; et al. Unilateral versus bilateral cerebral perfusion during aortic surgery for acute type A aortic dissection: A multicentre study. *Eur. J. Cardio-Thoracic Surg.* **2021**, *61*, 828–835. [CrossRef] [PubMed]

56. Tong, G.; Zhang, B.; Zhou, X.; Tao, Y.; Yan, T.; Wang, X.; Lu, H.; Sun, Z.; Zhang, W. Bilateral versus unilateral antegrade cerebral perfusion in total arch replacement for type A aortic dissection. *J. Thorac. Cardiovasc. Surg.* **2017**, *154*, 767–775. [CrossRef] [PubMed]

57. Papantchev, V.; Stoinova, V.; Aleksandrov, A.; Todorova-Papantcheva, D.; Hristov, S.; Petkov, D.; Nachev, G.; Ovtscharoff, W. The role of Willis circle variations during unilateral selective cerebral perfusion: A study of 500 circles. *Eur. J. Cardio-Thoracic Surg.* **2013**, *44*, 743–753. [CrossRef] [PubMed]

58. Urbanski, P.P.; Lenos, A.; Blume, J.C.; Ziegler, V.; Griewing, B.; Schmitt, R.; Diegeler, A.; Dinkel, M. Does anatomical completeness of the circle of Willis correlate with sufficient cross-perfusion during unilateral cerebral perfusion? *Eur. J. Cardiothorac. Surg.* **2008**, *33*, 402–408. [CrossRef]

59. Urbanski, P.P.; Thamm, T.; Bougioukakis, P.; Irimie, V.; Prasad, P.; Diegeler, A.; Lenos, A. Efficacy of unilateral cerebral perfusion for brain protection in aortic arch surgery. *J. Thorac. Cardiovasc. Surg.* **2019**, *159*, 365–371.e1. [CrossRef]

60. Angeloni, E.; Melina, G.; Refice, S.K.; Roscitano, A.; Capuano, F.; Comito, C.; Sinatra, R. Unilateral Versus Bilateral Antegrade Cerebral Protection During Aortic Surgery: An Updated Meta-Analysis. *Ann. Thorac. Surg.* **2015**, *99*, 2024–2031. [CrossRef]

61. Liu, Z.; Wang, C.; Zhang, X.; Wu, S.; Fang, C.; Pang, X. Effect of different types of cerebral perfusion for acute type A aortic dissection undergoing aortic arch procedure, unilateral versus bilateral. *BMC Surg.* **2020**, *20*, 1–8. [CrossRef]

62. Berger, T.; Kreibich, M.; Mueller, F.; Breurer-Kellner, L.; Rylski, B.; Kondov, S.; Schröfel, H.; Pingpoh, C.; Beyersdorf, F.; Siepe, M.; et al. Risk factors for stroke after total aortic arch replacement using the frozen elephant trunk technique. *Interact. Cardiovasc. Thorac. Surg.* **2022**, *34*, 865–871. [CrossRef] [PubMed]

63. Etz, C.D.; von Aspern, K.; Silva, J.D.R.E.; Girrbach, F.F.; Leontyev, S.; Luehr, M.; Misfeld, M.; Borger, M.; Mohr, F.W. Impact of Perfusion Strategy on Outcome After Repair for Acute Type A Aortic Dissection. *Ann. Thorac. Surg.* **2014**, *97*, 78–85. [CrossRef] [PubMed]

64. Kim, J.-H.; Lee, S.H.; Lee, S.; Youn, Y.-N.; Yoo, K.-J.; Joo, H.-C. Axillary artery cannulation reduces early embolic stroke and mortality after open arch repair with circulatory arrest. *J. Thorac. Cardiovasc. Surg.* **2019**, *159*, 772–778.e4. [CrossRef] [PubMed]

65. Hussain, A.; Uzzaman, M.; Mohamed, S.; Khan, F.; Butt, S.; Khan, H. Femoral versus axillary cannulation in acute type A aortic dissections: A meta-analysis. *J. Card. Surg.* **2021**, *36*, 3761–3769. [CrossRef] [PubMed]

66. Rylski, B.; Czerny, M.; Beyersdorf, F.; Kari, F.A.; Siepe, M.; Adachi, H.; Yamaguchi, A.; Itagaki, R.; Kimura, N. Is right axillary artery cannulation safe in type A aortic dissection with involvement of the innominate artery? *J. Thorac. Cardiovasc. Surg.* **2016**, *152*, 801–807.e1. [CrossRef]

67. Khaladj, N.; Shrestha, M.; Peterss, S.; Strueber, M.; Karck, M.; Pichlmaier, M.; Haverich, A.; Hagl, C. Ascending aortic cannulation in acute aortic dissection type A: The Hannover experience☆☆☆. *Eur. J. Cardio-Thoracic Surg.* **2008**, *34*, 792–796. [CrossRef]

68. Sicim, H.; Demirdas, E.; Bolcal, C. Direct bilateral carotid artery cannulation can be better strategy for acute aortic dissection involving both carotid arteries. *J. Card. Surg.* **2021**, *36*, 3977–3980. [CrossRef]

69. Kusadokoro, S.; Kimura, N.; Hori, D.; Hattori, M.; Matsunaga, W.; Itagaki, R.; Yuri, K.; Mieno, M.; Nakamura, M.; Yamaguchi, A. Utility of double arterial cannulation for surgical repair of acute type A dissection. *Eur. J. Cardio-Thoracic Surg.* **2020**, *57*, 1068–1075. [CrossRef]

70. Zhu, Y.; Lingala, B.; Baiocchi, M.; Tao, J.J.; Toro Arana, V.; Khoo, J.W.; Williams, K.M.; Traboulsi, A. A-R.; Hammond, H.C.; Lee, A.M.; et al. Type A Aortic Dissection-Experience Over 5 Decades: JACC Historical Breakthroughs in Perspective. *J. Am. Coll. Cardiol.* **2020**, *76*, 1703–1713. [CrossRef]

71. Zierer, A.; Ahmad, A.E.-S.; Papadopoulos, N.; Detho, F.; Risteski, P.; Moritz, A.; Diegeler, A.; Urbanski, P.P. Fifteen years of surgery for acute type A aortic dissection in moderate-to-mild systemic hypothermia†. *Eur. J. Cardio-Thoracic Surg.* **2016**, *51*, 97–103. [CrossRef]

72. Leshnower, B.G.; Thourani, V.H.; Halkos, M.E.; Sarin, E.L.; Keeling, W.B.; Lamias, M.J.; Guyton, R.A.; Chen, E.P. Moderate Versus Deep Hypothermia With Unilateral Selective Antegrade Cerebral Perfusion for Acute Type A Dissection. *Ann. Thorac. Surg.* **2015**, *100*, 1563–1569. [CrossRef] [PubMed]

73. Leshnower, B.G.; Myung, R.J.; Thourani, V.H.; Halkos, M.E.; Kilgo, P.D.; Puskas, J.D.; Chen, E.P. Hemiarch Replacement at 28 °C: An Analysis of Mild and Moderate Hypothermia in 500 Patients. *Ann. Thorac. Surg.* **2012**, *93*, 1910–1916. [CrossRef]

74. Pupovac, S.S.; Hemli, J.M.; Bavaria, J.E.; Patel, H.J.; Trimarchi, S.; Pacini, D.; Bekeredjian, R.; Chen, E.P.; Myrmel, T.; Ouzounian, M.; et al. Moderate vs Deep Hypothermia in Type A Acute Aortic Dissection Repair: Insights from IRAD. *Ann. Thorac. Surg.* **2021**, *112*, 1893–1899. [CrossRef] [PubMed]

75. Etz, C.D.; Luehr, M.; Kari, F.A.; Lin, H.M.; Kleinman, G.; Zoli, S.; Plestis, K.A.; Griepp, R.B. Selective cerebral perfusion at 28 degrees C–is the spinal cord safe? *Eur. J. Cardiothorac. Surg.* **2009**, *36*, 946–955. [CrossRef]

76. Kamiya, H.; Hagl, C.; Kropivnitskaya, I.; Böthig, D.; Kallenbach, K.; Khaladj, N.; Martens, A.; Haverich, A.; Karck, M. The safety of moderate hypothermic lower body circulatory arrest with selective cerebral perfusion: A propensity score analysis. *J. Thorac. Cardiovasc. Surg.* **2007**, *133*, 501–509.e2. [CrossRef] [PubMed]

77. Göbölös, L.; Philipp, A.; Ugocsai, P.; Foltan, M.; Thrum, A.; Miskolczi, S.; Pousios, D.; Khawaja, S.; Budra, M.; Ohri, S. Reliability of different body temperature measurement sites during aortic surgery. *Perfusion* **2013**, *29*, 75–81. [CrossRef]

78. Montagner, M.; Kofler, M.; Seeber, F.; Pitts, L.; Starck, C.; Sündermann, S.H.; Kurz, S.; Grubitzsch, H.; Falk, V.; Kempfert, J. The arch remodelling stent for DeBakey I acute aortic dissection: Experience with 100 implantations. *Eur. J. Cardio-Thoracic Surg.* **2022**, *62*, ezac384. [CrossRef]

79. Krüger, T.; Hoffmann, I.; Blettner, M.; Borger, M.A.; Schlensak, C.; Weigang, E.; on behalf of the GERAADA Investigators. Intraoperative neuroprotective drugs without beneficial effects? Results of the German Registry for Acute Aortic Dissection Type A (GERAADA). *Eur. J. Cardio-Thoracic Surg.* **2013**, *44*, 939–946. [CrossRef]

80. Fernández Suárez, F.E.; Fernández Del Valle, D.; González Alvarez, A.; Pérez-Lozano, B. Intraoperative care for aortic surgery using circulatory arrest. *J. Thorac. Dis.* **2017**, *9*, S508–S520. [CrossRef]

81. Furukawa, T.; Uchida, N.; Takahashi, S.; Yamane, Y.; Mochizuki, S.; Yamada, K.; Mochizuki, T.; Sueda, T. Management of cerebral malperfusion in surgical repair of acute type A aortic dissection. *Eur. J. Cardio-Thoracic Surg.* **2017**, *52*, 327–332. [CrossRef]