Cerebral protection strategies in aortic arch surgery: a review of techniques and outcomes

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Background: Cerebral protection is a key determinant of perioperative outcomes in aortic arch surgery. Despite significant advances, optimal strategies regarding temperature, perfusion modality, and cannulation site remain controversial, with heterogeneous evidence and lack of standardized protocols.

Methods: This narrative review summarizes experimental and clinical evidence from the last 15 years, focusing on the main determinants of cerebral protection: cerebral blood flow (CBF), autoregulation, perfusion pressure, temperature management, cannulation strategies, and antegrade (ACP) versus retrograde cerebral perfusion (RCP).

Results: Available evidence consistently shows that any form of cerebral perfusion is superior to no perfusion during circulatory arrest (CA). Selective antegrade cerebral perfusion (SACP) has progressively emerged as the most widely adopted strategy worldwide, supported by its more physiological flow pattern and encouraging clinical outcomes. Axillary artery cannulation is currently the preferred approach and is associated with a lower stroke risk compared to femoral access, although femoral cannulation remains a valid alternative in unstable patients requiring rapid cardiopulmonary bypass (CPB) initiation. Comparative studies between ACP and RCP demonstrate no clear superiority in terms of mortality or permanent neurological dysfunction (PND), particularly for short CA times. However, SACP may reduce temporary neurological deficits (TNDs). A global shift towards moderate-to-mild hypothermia combined with cerebral perfusion has been observed, with favorable outcomes. Nonetheless, substantial variability persists in perfusion parameters, including flow, pressure, and the choice between unilateral and bilateral cerebral perfusion.

Conclusions: Contemporary practice is moving toward strategies that better replicate physiological cerebral perfusion, favoring antegrade flow with moderate hypothermia. However, the lack of high-quality randomized evidence and persistent heterogeneity limit definitive recommendations, highlighting the need for standardized protocols and individualized approaches.

Keywords: Cerebral protection; aortic surgery; aortic arch; cannulation

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Introduction

Cerebral protection in aortic arch surgery remains a key determinant of perioperative outcomes. The intrinsic vulnerability of nervous tissue to ischemia, combined with the challenges of circulatory arrest (CA), necessitates advanced and multimodal strategies. Over recent decades, surgical practice has evolved from the use of deep hypothermic circulatory arrest (DHCA) alone to integrated approaches that combine temperature and metabolic modulation, selective cerebral perfusion, technological advancements, and real-time neuromonitoring.

Despite these advances, there is still no consensus on several critical aspects, including the optimal degree of hypothermia, cannulation sites, perfusion strategies, and perfusion parameters. Consequently, the available evidence remains heterogeneous and, at times, inconclusive, limiting the development of standardized guidelines and robust protocols.

This review aims to provide a comprehensive overview of current cerebral protection techniques, analyzing available evidence, contemporary trends, and reported outcomes of the strategies currently in use.

Methods

Both experimental and clinical studies, including animal models, were considered to outline the physiological foundations and key innovations that have shaped current practice. Given the complexity of the topic and the multiple interacting variables involved, this review is structured around the main pillars of cerebral protection, offering a focused overview of current trends for each component. A structured literature search was conducted using PubMed, Scopus, and Web of Science databases. Studies published between January 2009 and February 2025 were considered. The search strategy included combinations of the following keywords: *aortic arch surgery*, *cerebral protection*, *antegrade cerebral perfusion*, *retrograde cerebral perfusion*, *hypothermic circulatory arrest*, *cannulation strategy*, and *neurological outcomes*.

Both experimental and clinical studies were included, with particular attention to observational studies, meta-analyses, and randomized trials evaluating cerebral protection strategies during aortic arch surgery. Case reports and studies not reporting neurological outcomes were excluded.

The selected literature was reviewed to summarize current evidence regarding the main determinants of cerebral protection, including cerebral blood flow (CBF) physiology, temperature management, perfusion pressure, cannulation strategies, and perfusion techniques.

Results

Neurophysiological basis of cerebral protection

CBF

The human brain is a high-energy demanding organ. Although representing only 2% of total body mass, it accounts for 15–20% of total energy consumption at rest. The neurons' vitality depends mostly on aerobic metabolism, so constant CBF has to be guaranteed for brain function and viability (1-5).

CBF is defined as the blood volume that flows per unit mass per unit time in brain tissue and amounts to approximately 50 mL/100 g/min at rest (4,6).

Electroencephalography (EEG) changes occur when CBF decreases below 20 mL/100 g/min, and neuronal dysfunction results. At flows below 10 mL/100 g/min, electrolyte release and neuronal death ensue (7), but hypothermia can reduce the brain metabolic demand, extending the ischemic tolerance (8,9). In fact, McCullough *et al.* (8) showed that cerebral metabolism decreases 6–7% for every 1 ℃ below 37 ℃; but between 15 and 10 ℃ there is only 5% decrease in the cerebral metabolic rate.

At normal body temperature, the cerebral metabolic rate of oxygen ($CMRO_2$, calculated as CBF × cerebral arteriovenous oxygen content difference / 100) is 2.9 mL/100 g/min. At 25 ℃, the demand reduces to 0.9 mL/100 g/min, and, at 20 ℃, to 0.2 mL/100 g/min (8,10,11).

Cerebral autoregulation (CAR)

Lassen *et al.* (12) in 1959 first described the central nervous system capacity to maintain a constant CBF, referred to as autoregulation. The CAR maintains a constant CBF across changes in cerebral perfusion pressure (CPP), despite variations in mean arterial pressure (MAP). CAR is mediated by a very complex interplay of myogenic, neurogenic, endothelial, and metabolic stimuli whose description goes beyond the purpose of this review (13,14).

The range of CAR is traditionally considered to be between 50 and 150 mmHg. Below the mentioned limits, CBF becomes pressure-dependent, risking hypoperfusion, and thus ischemia, in the former, or hyperperfusion with consequent cerebral edema and hemorrhage in the latter

(13-15). Although CAR has traditionally been considered a "static" mechanism, a dynamic relationship between MAP and CBF has been reported in more recent data: in fact, CBF shows variability according to the severity and direction of change in perfusion pressure (13,16).

Studies demonstrate that CAR is a strong predictor of post-operative complications in patients undergoing on-pump cardiac surgery (17). Impaired CAR can result from primary central nervous system disease or from CPP falling outside the CAR limits (18,19).

How CAR varies during cardiopulmonary bypass (CPB) remains unclear, since many physiological factors are modified simultaneously, such as pulsatile or continuous flow, temperature, hemoglobin concentration, inflammatory response to the circuit, and medications. Although earlier experiments (20-24) showed a preserved CAR with MAP >50 mmHg at both normothermia and hypothermia and even for MAP of 40 mmHg under deep hypothermia (20 ℃), more recent studies suggest that CAR may be impaired during hypothermia (25,26).

CPP

During CPB, MAP is the principal determinant of organ perfusion in the absence of cardiac output; however, defining an optimal MAP value remains controversial, as no universally accepted target exists.

Studies comparing higher versus lower MAP during CPB have reported conflicting results (27-33), although MAP values <65 mmHg appear to be associated with increased risk of stroke, acute kidney injury, and mortality, depending on the severity and duration of hypotension (34,35). Conversely, higher MAP targets have not consistently demonstrated additional benefit (36).

Accordingly, the current European guidelines recommend maintaining MAP between 50 and 80 mmHg during CPB, measured at the right radial artery and ideally tailored to the patient's CAR range under normocapnic conditions before CPB (37). Data by Haldenwang *et al.* showed that increasing perfusion pressure from 40 to 80 mmHg during antegrade cerebral perfusion (ACP) did not significantly enhance CBF, while prolonged exposure (>25 minutes) to higher pressures may increase cerebrovascular resistance and promote cerebral edema (38). Consequently, current guidelines recommend a pressure target between 40–80 mmHg (37), consistent with earlier, slightly more restrictive ranges proposed by Spielvogel (39,40).

The role of temperature as a modulator of cerebral protection

Temperature is the cornerstone of cerebral protection during aortic arch surgery. Experimental and clinical evidence consistently demonstrates that hypothermia increases cerebral tolerance to ischemia by reducing the $CMRO_2$, attenuating excitatory neurotransmitter release, and limiting inflammatory responses (8). The degree of neuroprotection is primarily related to the patient's core body temperature, which reflects cerebral metabolic suppression, whereas the arterial perfusate temperature is adjusted intraoperatively to achieve and maintain the desired core temperature during CPB. At normothermia, the safe cerebral ischemic time is limited to approximately 5 minutes, beyond which the risk of temporary and permanent neurological dysfunction (TND and PND) rises significantly. Cooling markedly extends this tolerance, with every 10 ℃ reduction in temperature resulting in an approximately 50–60% decrease in $CMRO_2$ and a corresponding increase in the duration of safe CA (8,41).

Traditionally, hypothermia has been classified into four temperature ranges associated with progressively longer safe CA times: mild (28.1–34 ℃, 6–10 minutes), moderate (20.1–28 ℃, 11–21 minutes), deep (14.1–20 ℃, 21–33 minutes), and profound (<14 ℃, >33 minutes) (8,42,43).

Based on these physiological principles, deep hypothermic circulatory arrest (DHCA), introduced by Griepp in the 1970s (44), became the cornerstone of cerebral protection during complex aortic arch surgery. DHCA provides satisfactory survival and neurological outcomes by allowing temporary interruption of CBF while markedly suppressing cerebral metabolism. However, its clinical application is limited by the finite duration of safe CA and by the systemic adverse effects associated with profound hypothermia, including coagulopathy, microcirculatory dysfunction, increased blood viscosity, hyperglycemia, and cerebral edema (45-48).

To minimize these limitations while preserving adequate neuroprotection, contemporary surgical strategies have progressively adopted warmer levels of hypothermia in combination with adjunctive cerebral perfusion techniques (49,50). This evolution was initiated by Leshnower *et al.* (51), who demonstrated comparable outcomes using warmer temperatures. Subsequently, Weidemann *et al.* (52) reported lower mortality and PND with moderate hypothermic CA combined with selective antegrade cerebral perfusion (MHCA + SACP) compared with DHCA in patients with

acute type A aortic dissection, although potential sources of bias should be acknowledged. Similar findings were reported by Leshnower *et al.* (53) and Gong *et al.* (54), who demonstrated non-inferiority of MHCA with SACP compared with DHCA regarding mortality and neurological outcomes.

Additional evidence supporting warmer strategies derives from the large multicenter Canadian propensity-matched study by Hage *et al.* (55), in which nadir core temperatures above 24 ℃ were associated with lower mortality, stroke, and major morbidity. More recent studies have explored even warmer temperature management. Urbanski (56), Zierer (57), El-Sayed Ahmad (58), and Jabagi (59) reported encouraging results using moderate-to-mild hypothermia (approximately 28–29 ℃) and mild hypothermia (approximately 32 ℃). Likewise, analysis of the Society of Thoracic Surgeons database by Seese *et al.* (60) demonstrated that mild hypothermia (>27.5 ℃) achieved mortality and TND rates comparable to moderate hypothermia while significantly reducing the incidence of PND.

Despite these promising findings, important concerns remain regarding adequate protection of the visceral organs during CA at higher temperatures (61). Moreover, current evidence is limited by the predominance of retrospective studies, heterogeneity in patient populations and operative techniques, differences in CA duration, and variability in perfusion strategies.

Overall, hypothermia remains the fundamental biological basis of all currently adopted cerebral protection strategies, irrespective of the adjunctive perfusion technique employed. While the traditional literature has used heterogeneous definitions of mild, moderate, deep, and profound hypothermia, current clinical guidelines (62) have introduced a more standardized classification, distinguishing mild, high-moderate, low-moderate, and deep hypothermia, thereby facilitating more consistent interpretation and comparison of contemporary studies.

Surgical strategies for cerebral protection

Cannulation sites

When discussing cannulation sites, it is important to recognize that the literature includes highly diverse patient populations. Differences in clinical setting (elective *vs.* emergency), as well as underlying pathology (acute aortic dissection *vs.* chronic aneurysm), strongly influence both the choice of cannulation site and surgical strategy. This heterogeneity represents the main limitation in building robust, standardized randomized trials comparing different cannulation approaches.

Axillary artery

Axillary artery cannulation is widely utilized in aortic arch surgery. Svensson *et al.* (50), in a cohort of 1,336 patients, showed that axillary perfusion via an interposition graft significantly reduced stroke risk compared with other cannulation sites. The main advantage is that, by simply clamping the innominate artery, it is possible to smoothly switch from standard CPB to unilateral ACP, thereby minimizing the risks associated with vessel manipulation, cannulation, and air embolism.

More recent data by Kim *et al.* (2019, n=468) confirm lower stroke rates compared with femoral or central cannulation (63). However, axillary artery cannulation carries specific risks, particularly iatrogenic dissection with possible retrograde extension (64), and may be time-consuming in unstable patients (65). Puiu *et al.* (n=688) reported higher complication rates in small-caliber arteries and emergency settings, with improved outcomes when using an 8-mm Dacron graft instead of direct cannulation, also reducing stroke incidence (66).

A large multicenter study (67) involving 772 centers and a total of 7,353 patients demonstrated the superiority of axillary over femoral artery cannulation in reducing stroke incidence. This represents further evidence of the paradigm shift observed over recent decades, with a progressive increase in the use of the right axillary artery.

Overall, the axillary artery is currently the most used cannulation site in aortic arch surgery including both elective and acute settings (62).

Innominate artery

Innominate artery cannulation can be performed either by direct arterial cannulation or through an 8-mm Dacron side graft, both providing antegrade perfusion to the brain and systemic circulation while maintaining a low risk of cerebral embolization. Direct cannulation is rapid and avoids the need for graft anastomosis, making it particularly attractive in the emergency settings. Conversely, graft-mediated cannulation may facilitate arterial access, reduce vessel manipulation during CPB, and simplify decannulation and vascular repair at the end of the procedure. However, when using a side graft, careful attention should be paid to arterial flow and perfusion pressure, as excessive CBF may theoretically increase the risk of hyperperfusion syndrome, although this complication remains uncommon with appropriate flow management. The large vessel diameter

and its easy accessibility through median sternotomy represent additional practical advantages that have contributed to the increasing adoption of innominate artery cannulation, with an expected uptake comparable to axillary cannulation (68).

Preventza *et al.* [2015] demonstrated the safety of this approach, reporting a low neurological event rate (3.4%) in 263 patients (69). In a larger subsequent series (n=938), the same group showed that both axillary and innominate cannulation were not independent predictors of adverse outcomes, including stroke, and could be used interchangeably (70). These findings were reinforced by a meta-analysis by Harky *et al.* (68), which found no significant differences between the two techniques in perioperative outcomes or neurological complications.

Moreover, a multicenter randomized trial (71) conducted across six Canadian centers (n=111) confirmed that innominate cannulation provides comparable neuroprotection to axillary access, as assessed by new ischemic lesions on magnetic resonance imaging.

Ascending aorta

This approach enables rapid CPB via median sternotomy, making it useful in unstable patients, but carries risks such as false lumen perfusion in cases of aortic dissection, aortic rupture, and the need for intraoperative conversion or adjunct cerebral perfusion (72).

Technical refinements, including direct true-lumen ("Samurai") cannulation and echocardiography-guided Seldinger techniques, have improved safety by reducing aortic injury and malperfusion (73,74). Earlier reports showed relatively high stroke rates ranging from 3.8% to 21% compared with axillary access (75), possibly due to embolization from aortic wall manipulation (63). However, more recent data show favorable results: Chung *et al.* (n=764) reported neurological outcomes comparable to axillary cannulation (72), and a meta-analysis by Ma *et al.* (3,022 patients) found lower TND versus femoral access, with no differences compared to axillary cannulation (65).

Despite these findings, ascending aortic cannulation remains underutilized in current practice (76) during aortic arch surgery.

Femoral artery

Femoral artery cannulation has historically been widely used in aortic arch surgery due to its rapid accessibility and technical simplicity, particularly in emergency settings. However, its use has declined in recent years because of limitations related to retrograde perfusion. These include the need for additional cannulation to ensure adequate cerebral perfusion, as well as risks of retrograde cerebral embolization, false lumen perfusion, end-organ malperfusion, and retrograde dissection. These concerns were first highlighted by Di Eusanio *et al.* in 2003 (77) and later confirmed by Benedetto *et al.* (78) in a 2015 meta-analysis of eight comparative studies (793 acute type A aortic dissection patients), which demonstrated lower mortality and fewer permanent neurological deficits with axillary versus femoral cannulation, even after adjustment for procedural variables such as hemiarch or total arch replacement, SACP time, and DHCA duration.

More recent studies have reported comparable stroke rates between axillary and femoral approaches. Tong *et al.* (79) [2021] and Elbatarny *et al.* (80) [2024], analyzing 646 and 2,145 patients with acute type A aortic dissection, respectively, found no significant difference in stroke risk. However, these findings should be interpreted with caution due to the higher proportion of total arch procedures in the axillary groups.

Currently, femoral cannulation is considered an acceptable alternative when axillary access is not feasible (79) or in hemodynamically unstable patients requiring rapid initiation of CPB (81).

With the exception of the small randomized trial by Peterson *et al.* (71), robust comparative evidence remains limited. Consequently, current practice relies largely on retrospective data. Future large-scale randomized trials are needed, while maintaining an individualized, patient-centered approach to clinical decision-making.

DHCA, ACP and retrograde cerebral perfusion (RCP)

DHCA

Because the integrity of the aortic arch is crucial for brain and lower body perfusion during extracorporeal circulation, aortic arch procedures must be performed under CA. Owing to the brain's low tolerance to ischemia, cerebral protection is of the utmost importance. Hypothermia is an effective way of prolonging ischemic tolerance. During CPB, the body is cooled down. After reaching the desired temperature, CPB is stopped, the arch is opened under DHCA and the aorta is replaced, generally by a Dacron graft. The risk-benefit balance is between efficient organ protection and risks of coagulation disorders, systemic inflammatory response syndrome, and longer CPB times.

RCP

In order to prolong the safe period for aortic arch repair, several cerebral perfusion strategies have been developed.

RCP via the superior vena cava was initially introduced as an emergency treatment for massive air embolism during CPB (82) and was later extended to aortic arch surgery (83). RCP is feasible due to the absence of valves in the superior venous system, allowing retrograde perfusion of the cerebral circulation through the superior vena cava at flows of 100–500 mL/min and pressures of approximately 20 mmHg (37). This approach avoids manipulation of the aortic arch and supra-aortic vessels while providing cerebral cooling, de-airing, and washout of ischemic metabolites (84).

SACP

Since the early 1990s, following the pioneering work of Kazui (85), the concept of SACP combined with moderate hypothermia has been introduced and progressively adopted.

Regardless of the primary cannulation site, bilateral cerebral perfusion can be achieved by cannulating the innominate and left common carotid arteries using balloon-tip cannulae. While this approach ensures adequate perfusion of both hemispheres, it may increase the risk of air embolism and embolization of debris due to manipulation of the supra-aortic vessels.

Alternatively, when the right axillary artery is used for arterial inflow, a different strategy can be employed. After cooling to the target temperature, pump flow is reduced and the brachiocephalic artery is clamped, allowing selective unilateral cerebral perfusion through the right carotid and vertebral arteries.

Regardless of the perfusion strategy, CBF is typically maintained at approximately 10 mL/kg/min at 25 ℃ (39,76).

Intraoperative neuromonitoring

Intraoperative neuromonitoring has become an integral component of cerebral protection strategies in aortic arch surgery, complementing perfusion and temperature management by providing real-time assessment of cerebral function and oxygenation. The most widely used modalities include near-infrared spectroscopy (NIRS), EEG, transcranial Doppler (TCD), somatosensory evoked potentials (SSEPs), and motor evoked potentials (MEPs) (86).

NIRS-based cerebral oximetry, typically measured bilaterally over the frontal cortex, allows continuous non-invasive monitoring of regional cerebral oxygen saturation (rSO_2). A reduction greater than 20% from baseline or an absolute value below 50% has been associated with adverse neurological outcomes and is used to guide perfusion adjustments during CA (87). During SACP, neuromonitoring should be integrated with continuous assessment of perfusion pressure and arterial flow, as these parameters are essential to ensure adequate cerebral blood supply while avoiding both hypoperfusion and excessive cerebral perfusion. Several studies have demonstrated that NIRS-guided protocols reduce the incidence of postoperative cognitive dysfunction and stroke in cardiac surgery, although robust randomized evidence specifically in aortic arch surgery remains limited (86,88,89).

EEG, either in its full multi-channel form or processed as a compressed spectral array (CSA), provides direct electrocortical monitoring and is used to detect cerebral ischemia and verify electrocerebral silence at deep hypothermia before initiating CA. Processed EEG indices allow titration of anesthetic depth and identification of critical reductions in cerebral perfusion. TCD of the middle cerebral arteries provides beat-to-beat assessment of CBF velocity and embolic load and may be particularly useful during cannulation and de-airing maneuvers. However, its routine use is limited by its marked operator dependency, the need for an adequate acoustic window, and limited availability in many institutions. In contrast, NIRS has become the standard neuromonitoring modality in most contemporary aortic centers owing to its simplicity, continuous monitoring capability, and ease of integration into routine clinical practice. SSEPs monitor posterior cortical and subcortical pathways, whereas MEPs provide functional assessment of the corticospinal tracts and may facilitate early detection of spinal cord ischemia, particularly during procedures involving the descending thoracic aorta.

In contemporary practice, multimodal neuromonitoring combining at least two complementary techniques is increasingly adopted, as no single modality provides complete information about all aspects of cerebral function. NIRS is commonly used as the primary monitoring tool and may be complemented by EEG, TCD, and evoked potentials according to institutional expertise and the complexity of the procedure. Despite the growing adoption of these tools, standardization of monitoring protocols, alarm thresholds, and intervention criteria remains lacking, and evidence from large prospective trials are still needed to define the optimal neuromonitoring strategy in aortic arch surgery (5,86).

Global trends and clinical outcomes in contemporary practice

Available contemporary evidence highlights substantial

international variability in the selection and use of cerebral protection strategies, with significant changes observed over recent decades.

In 2015, De Paulis (76) reported results from a European survey showing that SACP was used in approximately 90% of cases, whereas RCP was employed in only 3%. The use of DHCA ranged from 2% to 6%, depending on whether patients had chronic aortic disease or acute syndromes. Similar findings were reported by the GERAADA registry in 2011, where SACP was used in about two-thirds of patients, DHCA in approximately 30%, and RCP in only 2.2% (90).

Comparable trends have been observed in Japanese registries, as reported by Okita (91) [2025], where SACP is used in 70–80% of acute aortic dissection cases, with the remaining 20–30% managed with DHCA, with or without adjunctive RCP.

In contrast, North American data show more heterogeneous patterns. Koprivanac *et al.* (92), analyzing approximately 48,000 patients from 2011 to 2023, reported a stable use of RCP at around 22%. Over the same period, DHCA use declined significantly from 52% to 23%, while SACP increased markedly from 22% to 52%.

These findings are supported by another North American registry (2018–2024, 42 centers), in which 52% of patients received SACP, 24.5% RCP, and 23.6% DHCA (93).

Discussion

Clinical outcomes

PND

When comparing RCP and ACP, most studies do not demonstrate clear superiority of either strategy in preventing PND. Usui *et al.* (94), in a large retrospective analysis, found no significant difference in stroke incidence between RCP and ACP, both before and after propensity matching. Similarly, other studies (95) such as Keeling *et al.* (96) reported a lower stroke risk with RCP plus DHCA in elective hemiarch replacement, although this association lost significance after matching despite persisting in univariate analysis [adjusted odds ratio (aOR) 4.05; 95% confidence interval (CI): 1.17–14.03; P=0.028].

A clearer pattern emerges when cerebral perfusion is compared with no cerebral perfusion (NCP). In a multicenter study of 2,520 patients, Hage *et al.* (55) showed that ACP significantly reduced stroke risk versus NCP [odds ratio (OR) 0.55; 95% CI: 0.37–0.81; P=0.006]. Similarly, Makarem *et al.* (93) reported a protective effect of RCP compared with NCP across 42 centers: although gross comparisons were not significant, multivariable analysis showed an 86.5% relative risk reduction (OR 0.135; 95% CI: 0.023–0.783; P=0.03) of stroke compared to NCP. Consistently, Ghoreishi *et al.* (67) demonstrated that RCP was associated with a reduced risk of stroke compared with NCP (OR 0.75; P=0.008) or ACP (OR 0.75; P=0.007). These data indicate that the presence of cerebral perfusion, rather than its modality, is a key determinant of neuroprotection.

This concept is supported by Misfeld *et al.* (97), who, in a cohort of 636 patients (2003–2009) found no significant differences in PND among ACP, RCP, and NCP when analyzed separately (P=0.1). However, when ACP (uni- or bilateral) was compared with non-ACP strategies (RCP or NCP), PND was significantly lower in the ACP group (9% *vs.* 15%; P=0.035), suggesting a possible advantage of antegrade flow.

Importantly, most of these studies involve CA times ≤30 minutes (93,95), within which RCP appears to be a reasonable alternative to ACP in both elective (93,94,98) and emergency settings (67).

Temporary neurological deficit (TND)

Data on TND is more heterogeneous. Nakahara *et al.* (99) reported no significant difference between RCP (16/70) and ACP (50/162), with no association with CA duration. In contrast, Usui *et al.* (94) found higher TND with RCP (5.8% *vs.* 3%; P=0.022), while Okita *et al.* (100) reported similar findings after total arch replacement (33.3% *vs.* 13.3%; P=0.05). Perreas *et al.* (101) further demonstrated that ACP was associated with a 76.5% decreased risk (risk ratio, 0.235; 95% CI: 0.079 to 0.699) of all types of neurologic complications and a trend toward decreased 30-day and midterm mortality in comparison with RCP. Overall, these results suggest a potential advantage of ACP in reducing temporary neurological complications, although evidence remains inconsistent.

Regarding operative times, several studies suggest that RCP may shorten CA duration. Nakahara *et al.* (99), Samanidis *et al.* (102), and Sugiura *et al.* (103) all reported significantly shorter CA times with RCP (all P<0.05), likely due to avoidance of supra-aortic vessel cannulation. However, this advantage is not universal: O'Hara *et al.* (104), analyzing 4,395 patients from the STS database, found no difference between techniques. Thus, any time-saving benefit appears institution-dependent rather than generalizable.

Mortality

When comparing outcomes in terms of mortality, the available literature remains highly heterogeneous, with substantial variability in protocols, surgical techniques, and patient populations. This heterogeneity makes it difficult to establish reliable and direct comparisons. Although both RCP and SACP have consistently demonstrated superiority over DHCA, operative mortality does not appear to differ significantly between RCP and ACP across studies (94-96,99,101-106).

An important meta-analysis of more than 7,000 patients indicated that DHCA + ACP has an advantage over DHCA + RCP in terms of temporary neurological dysfunction (95% CI: 0.58–0.90, whereas the two methods show similar results in terms of PND [pooled relative risk (RR) 0.99, 95% CI: 0.75–1.33], early mortality (RR 1.18, 95% CI: 0.96–1.46) and stroke (pooled RR 1.39, 95% CI: 0.75–2.57) (107).

In 2021, an analysis from the International Registry of Acute Aortic Dissection (108) showed that MHCA combined with ACP is at least as safe as DHCA in acute type A aortic dissection repair. These findings, suggesting potential advantages of ACP, have likely contributed to its increased adoption over time and the decline in the use of DHCA alone.

In this context, the trend in the most recent guidelines for the treatment of aortic disease is to recommend selective ACP methods in complex arch procedures (62).

The global increase in the use of SACP is largely driven by its more physiological replication of cerebral perfusion compared with DHCA alone or RCP. In addition, technical advancements, improved neuromonitoring, and growing institutional experience with this technique have contributed to increasingly favorable outcomes (58,77,109).

Current evidence suggests that most centers worldwide are moving toward cerebral protection strategies that more closely replicate physiological conditions, favoring antegrade perfusion combined with moderate hypothermia. However, significant variability persists within this approach, reflecting the heterogeneity of patient populations and surgical practices. In particular, differences exist in cannulation techniques, types of cannulae used, target flow rates during cerebral perfusion, and whether perfusion is delivered unilaterally or bilaterally.

In fact, SACP can be established in different ways depending on the arterial cannulation site.

Unilateral antegrade cerebral perfusion (uACP) can be obtained by cannulating the axillary artery, the innominate artery, or one of the common carotid arteries. An upgrade to bilateral antegrade cerebral perfusion (bACP) can be established with the insertion of an additional balloon occludable perfusion catheter into the contralateral carotid artery.

Both methods have shown satisfactory results; however, it remains a matter of debate which provides the most effective cerebral perfusion. Bilateral cerebral perfusion is generally considered more physiological (110), providing adequate cerebral protection during CA (109), and may be advantageous in patients with an incomplete circle of Willis (111), although the anatomical integrity of the circle of Willis does not appear to correlate with functional cerebral cross-perfusion (112). Furthermore, recent studies suggest that, beyond the configuration of the circle of Willis, other cerebrovascular anatomical variants, such as vertebral artery dominance and a posterior inferior cerebellar artery (PICA)-ending vertebral artery, may also significantly influence collateral cerebral perfusion during SACP.

On the other hand, unilateral cerebral perfusion is more manageable, reducing the manipulation of supra-aortic vessels and, in case of right axillary artery cannulation, guaranteeing a smooth switch from standard CPB to cerebral perfusion, avoiding the interruption of blood flow to the brain (57,113,114).

Finally, unilateral cerebral perfusion via right axillary artery cannulation is associated with reduced embolic risk (50), shorter CA/CPB times (76), and equal effectiveness compared with bilateral cerebral perfusion (115,116).

Consistently, an important meta-analysis of retrospective studies including 5,100 patients found similar rates of mortality (8.6% *vs.* 9.2% for uACP and bACP, respectively; P=0.78), PND (6.1% *vs.* 6.5%; P=0.80) and TND (7.1% *vs.* 8.8%; P=0.46) between bACP and uACP (117). Although many studies have shown no significant difference between these techniques (118,119), bilateral antegrade selective cerebral perfusion remains the method of choice in complex cases, especially when time-consuming aortic repair is preoperatively anticipated (116,120).

Conclusions

Cerebral protection in aortic arch surgery represents a multimodal and continuously evolving discipline. Over the past two decades, a consistent paradigm shift has occurred, moving away from DHCA as the sole neuroprotective strategy toward integrated approaches that combine SACP with moderate or mild hypothermia.

Intraoperative neuromonitoring, through the combined use of NIRS, EEG, TCD, and SSEPs, provides essential real-time information to guide perfusion decisions and detect early ischemic changes. Multimodal monitoring is increasingly adopted in high-volume centers, although standardized protocols and robust evidence from prospective randomized trials remain to be established.

Contemporary cerebral protection in aortic arch surgery is moving toward strategies that more faithfully replicate physiological conditions, favoring antegrade perfusion combined with moderate hypothermia and supported by real-time multimodal neuromonitoring. However, significant practice variability persists, and the field still lacks the high-quality prospective evidence needed to formulate universally applicable recommendations. Future efforts should focus on the design of standardized, multicenter randomized trials and on the development of individualized, patient-centered protocols that integrate perfusion strategy, temperature management, cannulation technique, and neuromonitoring into a cohesive and reproducible approach.

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