Best strategy for cerebral protection in arch surgery - antegrade selective cerebral perfusion and adequate hypothermia

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Aortic arch surgery remains a complex surgical operation that necessitates specific neuroprotection strategies. Various approaches, such as hypothermic circulatory arrest (HCA), retrograde cerebral perfusion, and antegrade selective cerebral perfusion (aSCP), have each enjoyed periods of popularity. However, while the overall surgical approach tend to favour HCA with aSCP, technical factors, such as perfusion site, perfusate temperature and flow rate and pH management, have not been conclusively elucidated. The optimal extent of hypothermia during circulatory arrest is also unclear, particularly with recent partiality for warmer temperatures. The following perspective details the preferred surgical practice for cerebral protection in aortic arch surgery, based on existing evidence.

Keywords: Aortic arch surgery; hypothermic circulatory arrest; selective antegrade cerebral perfusion; cerebral protection

History of transverse arch surgery

Surgery for complex aortic pathologies, e.g., acute type A dissections and aneurysms involving the transverse arch, remains one of the technically most challenging endeavors in modern aortic surgery and requires the best neuroprotective strategy possible.

During the late 1950s Michael DeBakey, E. Stanley Crawford, and Denton A. Cooley in Houston developed the first surgical techniques to address aortic pathologies of the ascending, descending, and thoracoabdominal aorta, and the transverse arch (1,2). Neurologic complications were the reason that various innovative technical approaches to arch surgery developed in the decade thereafter were abandoned.

In 1964 Borst and colleagues in Munich closed an arterio-venous fistula—caused by a bullet from WWII that had found it's way to the mediastinum injuring both the aorta and the pulmonary artery—and for the first time under deep hypothermic circulatory arrest (DHCA) (3). A decade later, in 1975, the first series of routine aortic arch operations using profound hypothermic circulatory arrest—at an average lowest rectal temperature of 18 ℃ with an average circulatory arrest time of 43 minutes—was published by Randall Griepp and colleagues (4). This introduction of profound hypothermia—allowing for safe periods of circulatory arrest—by Borst and Griepp in the mid-seventies eventually paved the way for modern aortic arch surgery.

The limitations of hypothermia and HCA

Despite the protective effects of hypothermia the safety it provides is limited to a certain duration of circulatory arrest of likely no more than approximately 9 minutes at 30 ℃, 14 minutes at 25 ℃, 21 minutes at 20 ℃, 31 minutes at 15 ℃, and 45 minutes at 10 ℃ (5). Particularly in the elderly, durations of HCA exceeding 25 minutes have been suggested to be associated with transient neurologic dysfunctions (TND) and fine motor deficits (6,7). Fischer and colleagues suggested that after 30 minutes of HCA at 15 ℃ the regional oxygen saturation falls below 60% and

HCA durations exceeding 30 mins increase the risk for adverse outcome (8). Prolonged CPB during cooling and rewarming almost certainly causes increased endothelial permeability and edema formation that may contribute to organ malperfusion (9).

About 15% of the total cardiac output at rest is estimated to constitute normal physiological cerebral blood flow (CBF; approximately 0.55 cc/min/gram of cerebral tissue), with its autoregulation maintained over a broad spectrum of arterial pressures (mean 50-150 mmHg) to ensure optimal perfusion (10,11).

Cerebral autoregulation during cooling may only be maintained by an increase in vascular resistance down to temperatures of approximately 22-25 ℃ (12). Extracorporeal circulation may result in a 'luxury' perfusion of the brain once deeper temperatures are reached—with a risk of increased intracerebral pressures that ultimately may result in endothelial damage and cerebral edema (12).

The introduction of antegrade selective cerebral perfusion

The next milestone in the evolution of modern aortic arch surgery was successfully introduced into the clinical arena by Jean Bachet and Daniel Guilmet in Europe and by Teruhisa Kazui and colleagues in Japan in 1986: antegrade selective cerebral perfusion (SCP), in combination with hypothermia, significantly reduced the incidence of neurologic complications (13,14). This new neuroprotective strategy, 'cold *cerebroplegia*' by Bachet and Guilmet comprising of profound (6-12 ℃) selective cerebral perfusion (SCP) via the carotid arteries during circulatory arrest in deep hypothermia (26 ℃), allowed for longer operation times in more complex procedures with lower neurologic complications while avoiding profound hypothermic body core temperatures (<20 ℃) and its complications (13,15). In the same year, the Stanford group published their experience with antegrade SCP (unilaterally via a 14F cannula directly into the innominate artery with occlusion of the left carotid and left subclavian arteries in six patients, unilaterally via the left carotid in one patient, and bilaterally in three patients via the innominate and carotid arteries) during low flow CPB (30 mL/kg/min) at 26-28 ℃ (16). During the procedure simultaneous distal aortic perfusion was achieved via a 20F cannula in the femoral artery that was connected via a Y-connector to the SCP line (16)—a safety measure also used by Kazui and Bachet, which has (unfortunately) been widely abandoned in arch

aneurysm surgery for a while (15,17).

Current clinical results with antegrade SCP

Antegrade cerebral perfusion, aiming for near-physiologic conditions to ensure optimal cerebral protection, requires target cerebral blood flow (CBF), arterial blood pressure and hemodilution, and intracranial pressure to be carefully monitored—and adjusted for—during and after surgery.

Bilateral or unilateral antegrade SCP?

Cannulation techniques

Direct cannulation of atherosclerotic arteries—particularly the supraaortic branches—is associated with an increased risk of embolism (e.g., from manipulation, such as plaque mobilisation during cannulation or by jet flow, particularly by small bore cannulas inadvertently directed toward atherosclerotic plaques) (18,19). Commonly, antegrade SCP (aSCP) is establish via either direct cannulation or a prosthetic graft anastomosed to (I) the right subclavian artery, the (II) innominate artery, (III) the right common carotid artery, which may be combined with left common carotid artery perfusion to achieve bilateral aSCP.

Antegrade SCP may also be established—regardless of the initially chosen cannulation site—via balloon occludable perfusion catheters (18,20-22). Routine cannulation of the axillary artery for CPB allows for unilateral SCP during distal arrest without the need of manipulating supraaortic vessels, and is easily 'upgradable' to bilateral SCP during HCA by the insertion of an additional balloon occludable perfusion catheter to the left carotid artery, which is usually combined with a occlusive ballon on the left subclavian to avoid steal (23). In 2003, Spielvogel *et al*. introduced a technique utilizing a prefabricated trifurcated graft allowing for atraumatic and direct SCP during aortic arch reconstruction (24).

Unilateral SCP appears to provide sufficient safety for the majority of patients without significant pathologies of the supraaortic and cerebral arteries. Most published series comparing unilateral *vs*. bilateral antegrade SCP, however, utilized unilateral perfusion only if backflow from the contralateral carotid artery proved sufficient collateralization, or if near-infrared spectroscopy (NIRS) monitoring excluded contralateral malperfusion. The initial unilateral approach therefore can only be considered 'intention to treat' and numbers as to how many patients were eventually perfused bilaterally are obscure (25). A

prospective randomized trial initiated by the Vascular Domain of the European Association of Cardiothoracic Surgery is currently underway.

Bilateral cerebral perfusion might be advantageous for patients with carotid artery stenosis, previous stroke or cerebrovascular anomalies (e.g., an incomplete Circle of Willis). Although variations in the configuration of the Circle of Willis are well known, perfusion deficiencies based on anomalous anatomy seldom occurs clinically, particularly if the circulatory arrest time is short (30-50 minutes) (26).

While preoperative CT angiography might allow for identification of high-risk patients, most HCA aortic reference centers rely on intraoperative monitoring modalities instead (e.g., transcranial Doppler or near infrared-spectroscopy, NIRS) (25,27). Extracranial collateral pathways may interestingly play an important role during unilateral SCP in patients with incomplete circle of Willis (27,28). Insufficient unilateral perfusion usually appears to be detectable by NIRS monitoring, which is therefore routinely utilized at our institution to ensure sufficient cerebral perfusion during bilateral antegrade SCP. Leshnower and colleagues reported on a clinical series of over 400 aortic procedures involving the aortic arch (344 hemiarch and 68 total arch replacements), utilizing unilateral SCP with a perfusate temperature of 16 ℃ and an average distal arrest of 30±15 minutes at 26 ℃, and showed an overall mortality of 7%, and transient (TND) and permanent (PND) neurological deficits of 5.1% and 3.6%, respectively (29).

More recently, Urbanski and colleagues presented their outstanding results with unilateral SCP at a perfusate temperature of 28 ℃ and moderate-to-mild lower body circulatory arrest (LBCA) of up to 31.5 ℃ (range, 26.0-35.0 ℃) for an average duration of 18 minutes in hemiarch repairs (n=270) and 29 minutes for total arch replacements (n=77), achieving a remarkably low 30-day mortality of 0.9% (overall mortality of 1.2%), TND of 2.3%, PND of 0.9% and no occurrence of paraplegia (30). Postoperatively five out of 347 patients required dialysis and only one patient suffered from bowel ischemia (30).

While Urbanski and colleagues conclude from their report that '*systemic mild-to-moderate hypothermia that is adapted to the duration of circulatory arrest is a simple, safe, and effective method of organ protection and can be recommended in routine aortic arch surgery with circulatory arrest and cerebral perfusion*'—we do believe that a word of caution is of outmost importance and the surgeon's adequate judgement is crucial: when in doubt always opt for a lower temperature

to allow for a broader safety margin.

Despite the promising results with the use of unilateral antegrade SCP (29,31), many surgeons aim for bilateral SCP to ensure bihemispherical perfusion (18,25,32). Malvindi and colleagues in their literature review—encompassing more than 3,500 patients undergoing aortic surgery with either unilateral (n=599) or bilateral (n=2,949) cerebral perfusion—concluded that '*while both [unilateral and bilateral antegrade SCP] are acceptable, once the ASCP time is expected to rise over 40-50 min, bilateral cerebral perfusion is the technique that is best documented to be safe*' (26).

At our institution bilateral cerebral perfusion is routinely utilized. Under direct vision it usually requires only an additional 30 seconds to position a balloon-occludable perfusion catheter, connected via a Y-connector to the SCP line, to the left carotid artery (and a second occlusive balloon to the left subclavian). We believe in the additional safety that 'physiologic' bilateral perfusion may provide whenever prolonged durations (>40-50 mins) of circulatory arrest cannot be prevented with certainty, even (or particularly) in atherosclerotic patients.

Controversially, a contemporary meta-analysis by Angeloni of over 5,400 patients suggested equal overall mortality and PND rates for unilateral and bilateral SCP. The observed TND rates, however, appeared slightly higher in the bilateral SCP group, possibly resulting from additional manipulation of atherosclerotic vessels in bilateral cannulation (33), underscoring that bilateral cannulation is to be executed with caution in patients with atherosclerotic disease.

Management of aSCP: pressure, flow and pH during antegrade SCP

Depending on the method of cannulation, our patients are fitted with two radial lines for bilateral pressure monitoring and an additional femoral artery catheter to monitor distal perfusion pressure. Like most aortic reference centers using antegrade SCP, we perfuse the brain at a rate of 8-12 cc/min/kg of body weight (0.6 cc/min/g of cerebral tissue) and a perfusion pressure of 40-60 mmHg at temperatures between 23 and 28 ℃ (10). Haldenwang comparing various flow rates during SCP demonstrated that high-flow SCP significantly increases CBF and intracranial pressure (ICP), resulting in cerebral edema with no cerebral metabolic benefit (34). Avoidance of hemodilution during SCP may also prevent higher CBF and associated cerebral injury (35). The strategy of pH-management for SCP remains controversial: alpha-

stat pH-management, in contrast to pH-stat management, has been shown to prevent 'luxury' perfusion by sustaining cerebral autoregulation, potentially decreasing the risk of deleterious embolization (36).

The danger of prolonged distal circulatory arrest at moderate to mild hypothermia

The Kobe group recently presented their excellent results with 321 consecutive patients undergoing total arch replacement utilizing antegrade SCP at a tympanic temperatures of 20-23 ℃ (tolerating moderate rectal temperatures below 30 ℃). In this landmark analysis Okada and colleagues reported an overall mortality of 4.4% (1.9% in elective cases) and a permanent neurologic deficit of 4.4% (2.8% in elective cases) (37). Encouraged by the success of antegrade SCP and profound HCA in routine cases many surgeons have begun to progressively aim for higher CPB and SCP perfusate temperatures (25,38,39). Despite the absence of confirmative data for the safety of higher body core temperatures, more and more aortic centers have started using moderate-to-mild (28-35 ℃) hypothermic or even normothermic body core temperatures during routine arch repair, and increasingly even for complex surgery, including acute type A aortic dissections (30). The safe limits of prolonged distal ischemia during antegrade SCP close to normothermia for the viscera and the spinal cord are not well recognized in clinical practice.

Driven not only by pure medical considerations (and possibly to some degree even for economic reasons), this trend has continued during the past decade. Inappropriate temperature management (core temperatures too high for the required duration of distal arrest) is probably highly underrecognized while the risk of hypothermia-associated bleeding complications may be widely overestimated. High temperatures may become a dangerous trade-off, jeopardizing effective protection with yet unpredictable consequences for long-term outcome, particularly for the spinal cord. Patients who require complex reconstructions or present with a previous neurologic deficit may especially be at increased risk with this strategy. In 2007, Kamiya et al. was the first to report on the possible hazard of neurologic complications during prolonged LBCA and moderate hypothermia at 28 ℃ (40). In a subgroup analysis Kamiya and colleagues observed a 6-fold increase in mortality and ischemic spinal cord injury: their propensity score matched analysis clearly demonstrated a significantly increased mortality of 27% and a rate of paraplegia of 18% in 92

patients with SCP and a prolonged LBCA of more than 60 minutes at a body core temperature of 25 to 28 ℃ (40). In comparison, the paraplegia rate in patients operated on during SCP and LBCA (>60 mins) at deep hypothermia (20-24 ℃) was 0% (40).

Sufficient neuro- and visceral protection has to be *a conditio-sine-qua-non* for elective arch surgery

There does not seem to be a clinically significant difference in neuroprotection between profound and deep HCA; in 2007 the Bologna group published their results of 305 aortic arch operations utilizing profound (<22 ℃) *vs.* deep hypothermia (up to 26 ℃) during an average antegrade SCP time of up to 60 minutes (39) with no differences between both groups with regard to 30-day mortality (12.7% *vs.* 13.8%), PND (3.1% *vs.* 1.7%; P=0.72), and TND (7.9% *vs.* 8.6%) (39).

More recently, the Emory group compared the outcome after elective and emergent hemiarch replacements with SCP for 25 minutes at deep and moderate temperatures (24.3 *vs.* 28.6 ℃) (41), with propensity matched analysis revealing a significantly reduced rate of PND (2.5% *vs.* 7.2%) in the moderate group. While there were no significant differences in bleeding, TND, or renal failure, propensity matching did not consider complexity of arch repair and previous neurologic status—risk factors well known to influence outcome after arch surgery (41).

Antegrade *vs.* retrograde cerebral perfusion (RCP)

In 1990, Ueda *et al.* were the first to introduce retrograde cerebral perfusion (RCP) in combination with deep HCA to provide retrograde perfusion and additional cooling of the central nervous system (CNS) via the valveless cerebral venous system, potentially offering the additional benefit of back-flushing of air emboli and debris from the cerebral circulation (42). Although RCP was routinely used by many centers shortly after its clinical introduction, the neuroprotective effect of this method proved limited and most likely related to sufficient continuous cooling rather than true nutritive flow (18,43). RCP has even been suspected to counteract antegrade cerebral perfusion from recruitment of arterial collaterals in patients with vascular anomalies (e.g., with incomplete Circle of Willis), and patients with significant carotid stenosis (28). The efficacy of RCP might also be impaired by venous valves in the human internal jugular veins necessitating higher

perfusion pressures—demonstrated by Hagl and colleagues to inevitably result in significantly reduced neurological outcome, likely due to increased ICP (44).

Therefore, in comparison with antegrade perfusion techniques the neuroprotective potential of RCP is certainly very limited, despite the effective de-airing of the cerebral perfusion at the end of the procedure, and this approach has been abandoned by most aortic centers (32).

Adjunctive distal aortic perfusion

The concept of distal perfusion via the femoral artery to avoid lower body ischemia during aortic arch surgery was already used by DeBakey as early as 1957 (45), and has proven since to be superior to the 'clamp-and-sew' technique for extended thoracoabdominal aneurysm repair (46-48). Recently, distal perfusion via the femoral artery has also been successfully used in selective cases during total aortic arch replacement to sustain spinal cord and visceral integrity at moderate hypothermia. In 2006, Della Corte *et al.* used thoracoabdominal perfusion (TAP) during aortic arch surgery in 80 patients, via descending endoluminal cannulation (n=62) or femoral artery cannulation (n=18), and compared the postoperative outcome to 122 patients with aortic arch operations without additional distal perfusion (49). Despite the fact that overall mortality and PND rates did not significantly differ between both groups, a significantly lower incidence of respiratory (18.2% *vs.* 30.5%) and renal (6.5% *vs.* 18.6%) failure with shorter durations of mechanical ventilation (18 *vs.* 58 h), and ICU and hospital stay (P=0.02) was seen in the TAP group (49). In 2007, Nappi *et al.* published their small series utilizing an innovative technique for antegrade descending (distal) aortic perfusion (via a cuffed endotracheal tube for descending aortic perfusion) with no permanent neurologic complications in 12 patients at a body core temperature of 26 ℃ (50). Another technical solution routinely utilized at our institution when prolonged arch reconstructions are required and deep core temperatures can not be established is the use of grafts with a prefabricated sidearm allowing for distal perfusion once the distal aortic anastomosis has been finalized (31,51).

Aoki *et al.* successfully used additional perfusion of the lower body via a balloon occlusion catheter during aortic arch repair in an elderly patient at a moderate body core temperature of 28 ℃ for 60 minutes (52). Touati and colleagues even performed aortic arch repair at normothermic conditions with unilateral SCP, intermittent myocardial perfusion, and distal femoral perfusion in a small number of patients (53). However, with regard to the above-mentioned clinical and experimental findings it must be clear to the surgeon utilizing this strategy at normothermia that there is no room for error (40,45,54,55).

Additional distal perfusion during aortic arch surgery has been shown to reduce the incidence of end-organ complications, particularly in more extensive and time-consuming procedures (49,50).

Distal perfusion may therefore be a bail-out tool for aortic arch operations started at moderate to mild body core temperatures that become more complex than expected. The risk of retrograde distal perfusion via the femoral artery (embolism by air or debris) seems to be low, as long as retrograde perfusion is used only during distal cross clamping or balloon catheter occlusion (52,53,56). Caution, however, is mandated in the majority of acute type A aortic dissections (usually DeBakey type I) that extend into the thoracoabdominal aorta, as retrograde perfusion might increase late mortality.

Conclusions and future perspective of aSCP

Using SCP and deep HCA, experienced centers have achieved excellent results that represent the benchmark against which future concepts of organ protection will have to surmount (21,57). However, the limitations of moderate hypothermia during aortic arch surgery have been clearly reported (40), and this paradigm shift towards the routine use of moderate-to-mild (28-35 ℃) core temperatures, driven by the excellent results of expert aortic surgeons, is a double-edged sword. Guidelines for the safe use of antegrade SCP and lower body circulatory arrest with regard to temperature management are not available due to the lack of expert consensus. Antegrade SCP utilizing a 'complexity adopted temperature management' during circulatory arrest, possibly combined with distal aortic perfusion as an effective adjunct in patients with degenerative disease (58), should currently be considered the state-of-the-art for transverse arch surgery.

Acknowledgements

References

1. Cooley DA, De Bakey ME. Surgical considerations of intrathoracic aneurysms of the aorta and great vessels. Ann

Surg 1952;135:660-80.

2. De Bakey ME, Cooley DA. Successful resection of aneurysm of thoracic aorta and replacement by graft. J Am Med Assoc 1953;152:673-6.

3. Borst HG, Schaudig A, Rudolph W. Arteriovenous fistula of the aortic arch: Repair during deep hypothermia and circulatory arrest. J Thorac Cardiovasc Surg 1964;48:443-7.

4. Griepp RB, Stinson EB, Hollingsworth JF, et al. Prosthetic replacement of the aortic arch. J Thorac Cardiovasc Surg 1975;70:1051-63.

5. McCullough JN, Zhang N, Reich DL, et al. Cerebral metabolic suppression during hypothermic circulatory arrest in humans. Ann Thorac Surg 1999;67:1895-9; discussion 1919-21.

6. Ergin MA, Griepp EB, Lansman SL, et al. Hypothermic circulatory arrest and other methods of cerebral protection during operations on the thoracic aorta. J Card Surg 1994;9:525-37.

7. Reich DL, Uysal S, Sliwinski M, et al. Neuropsychologic outcome after deep hypothermic circulatory arrest in adults. J Thorac Cardiovasc Surg 1999;117:156-63.

8. Fischer GW, Benni PB, Lin HM, et al. Mathematical model for describing cerebral oxygen desaturation in patients undergoing deep hypothermic circulatory arrest. Br J Anaesth 2010;104:59-66.

9. Haverich A, Hagl C. Organ protection during hypothermic circulatory arrest. J Thorac Cardiovasc Surg 2003;125:460-2.

10. Bachet J. Re: Selective cerebral perfusion using moderate flow in complex cardiac surgery provides sufficient neuroprotection. Are children young adults? Eur J Cardiothorac Surg 2012;42:710-1.

11. Lassen NA. Cerebral blood flow and oxygen consumption in man. Physiol Rev 1959;39:183-238.

12. Ehrlich MP, McCullough JN, Zhang N, et al. Effect of hypothermia on cerebral blood flow and metabolism in the pig. Ann Thorac Surg 2002;73:191-7.

13. Guilmet D, Roux PM, Bachet J, et al. A new technic of cerebral protection. Surgery of the aortic arch. Presse Med 1986;15:1096-8.

14. Kazui T. Update in surgical management of aneurysms of the thoracic aorta. Rinsho Kyobu Geka 1986;6:7-15.

15. Bachet J, Guilmet D, Goudot B, et al. Antegrade cerebral perfusion with cold blood: a 13-year experience. Ann Thorac Surg 1999;67:1874-8; discussion 1891-4.

16. Frist WH, Baldwin JC, Starnes VA, et al. A reconsideration of cerebral perfusion in aortic arch replacement. Ann Thorac Surg 1986;42:273-81.

17. Kazui T, Yamada O, Komatsu S. Emergency graft replacement of the aortic arch for acute type A aortic dissection. J Cardiovasc Surg (Torino) 1992;33:211-5.

18. Hagl C, Khaladj N, Karck M, et al. Hypothermic circulatory arrest during ascending and aortic arch surgery: the theoretical impact of different cerebral perfusion techniques and other methods of cerebral protection. Eur J Cardiothorac Surg 2003;24:371-8.

19. Griepp RB. Cerebral protection during aortic arch surgery. J Thorac Cardiovasc Surg 2001;121:425-7.

20. Hagl C, Ergin MA, Galla JD, et al. Neurologic outcome after ascending aorta-aortic arch operations: effect of brain protection technique in high-risk patients. J Thorac Cardiovasc Surg 2001;121:1107-21.

21. Kazui T, Yamashita K, Washiyama N, et al. Aortic arch replacement using selective cerebral perfusion. Ann Thorac Surg 2007;83:S796-8; discussion S824-31.

22. Misfeld M, Leontyev S, Borger MA, et al. What is the best strategy for brain protection in patients undergoing aortic arch surgery? A single center experience of 636 patients. Ann Thorac Surg 2012;93:1502-8.

23. Etz CD, Plestis KA, Kari FA, et al. Axillary cannulation significantly improves survival and neurologic outcome after atherosclerotic aneurysm repair of the aortic root and ascending aorta. Ann Thorac Surg 2008;86:441-6; discussion 446-7.

24. Spielvogel D, Mathur MN, Lansman SL, et al. Aortic arch reconstruction using a trifurcated graft. Ann Thorac Surg 2003;75:1034-6.

25. Harrer M, Waldenberger FR, Weiss G, et al. Aortic arch surgery using bilateral antegrade selective cerebral perfusion in combination with near-infrared spectroscopy. Eur J Cardiothorac Surg 2010;38:561-7.

26. Malvindi PG, Scrascia G, Vitale N. Is unilateral antegrade cerebral perfusion equivalent to bilateral cerebral perfusion for patients undergoing aortic arch surgery? Interact Cardiovasc Thorac Surg 2008;7:891-7.

27. Urbanski PP, Lenos A, Blume JC, et al. Does anatomical completeness of the circle of Willis correlate with sufficient cross-perfusion during unilateral cerebral perfusion? Eur J Cardiothorac Surg 2008;33:402-8.

28. Liebeskind DS. Collateral circulation. Stroke 2003;34:2279-84.

29. Leshnower BG, Myung RJ, Kilgo PD, et al. Moderate hypothermia and unilateral selective antegrade cerebral perfusion: a contemporary cerebral protection strategy for aortic arch surgery. Ann Thorac Surg 2010;90:547-54.

30. Zierer A, El-Sayed Ahmad A, Papadopoulos N, et

al. Selective antegrade cerebral perfusion and mild (28°C-30°C) systemic hypothermic circulatory arrest for aortic arch replacement: results from 1002 patients. J Thorac Cardiovasc Surg 2012;144:1042-49.

31. Urbanski PP, Lenos A, Bougioukakis P, et al. Mild-to-moderate hypothermia in aortic arch surgery using circulatory arrest: a change of paradigm? Eur J Cardiothorac Surg 2012;41:185-91.

32. Harrington DK, Fragomeni F, Bonser RS. Cerebral perfusion. Ann Thorac Surg 2007;83:S799-804; discussion S824-31.

33. Angeloni E, Benedetto U, Takkenberg JJ, et al. Unilateral versus bilateral antegrade cerebral protection during circulatory arrest in aortic surgery: A meta-analysis of 5100 patients. J Thorac Cardiovasc Surg 2012. [Epub ahead of print].

34. Haldenwang PL, Strauch JT, Amann I, et al. Impact of pump flow rate during selective cerebral perfusion on cerebral hemodynamics and metabolism. Ann Thorac Surg 2010;90:1975-84.

35. Halstead JC, Wurm M, Meier DM, et al. Avoidance of hemodilution during selective cerebral perfusion enhances neurobehavioral outcome in a survival porcine model. Eur J Cardiothorac Surg 2007;32:514-20.

36. Halstead JC, Spielvogel D, Meier DM, et al. Optimal pH strategy for selective cerebral perfusion. Eur J Cardiothorac Surg 2005;28:266-73; discussion 273.

37. Okada K, Omura A, Kano H, et al. Recent advancements of total aortic arch replacement. J Thorac Cardiovasc Surg 2012;144:139-45.

38. Jacobs MJ, de Mol BA, Veldman DJ. Aortic arch and proximal supraaortic arterial repair under continuous antegrade cerebral perfusion and moderate hypothermia. Cardiovasc Surg 2001;9:396-402.

39. Pacini D, Leone A, Di Marco L, et al. Antegrade selective cerebral perfusion in thoracic aorta surgery: safety of moderate hypothermia. Eur J Cardiothorac Surg 2007;31:618-22.

40. Kamiya H, Hagl C, Kropivnitskaya I, et al. The safety of moderate hypothermic lower body circulatory arrest with selective cerebral perfusion: a propensity score analysis. J Thorac Cardiovasc Surg 2007;133:501-9.

41. Leshnower BG, Guyton RA, Myung RJ, et al. Expanding the indications for the David V aortic root replacement: early results. J Thorac Cardiovasc Surg 2012;143:879-84.

42. Ueda T, Hayashi I, Iseki H, et al. A case report of combined composite valve graft replacement of the aortic root and graft replacement of the abdominal aorta. Kyobu Geka 1990;43:61-3.

43. Reich DL, Uysal S, Ergin MA, et al. Retrograde cerebral perfusion during thoracic aortic surgery and late neuropsychological dysfunction. Eur J Cardiothorac Surg 2001;19:594-600.

44. Hagl C, Khaladj N, Weisz DJ, et al. Impact of high intracranial pressure on neurophysiological recovery and behavior in a chronic porcine model of hypothermic circulatory arrest. Eur J Cardiothorac Surg 2002;22:510-6.

45. De Bakey ME, Crawford ES, Cooley DA, et al. Successful resection of fusiform aneurysm of aortic arch with replacement by homograft. Surg Gynecol Obstet 1957;105:657-64.

46. Jacobs MJ. Brain and spinal cord protection during aortic surgery. Tex Heart Inst J 2010;37:667-8.

47. Bisdas T, Redwan A, Wilhelmi M, et al. Less-invasive perfusion techniques may improve outcome in thoracoabdominal aortic surgery. J Thorac Cardiovasc Surg 2010;140:1319-24.

48. Estrera AL, Miller CC 3rd, Chen EP, et al. Descending thoracic aortic aneurysm repair: 12-year experience using distal aortic perfusion and cerebrospinal fluid drainage. Ann Thorac Surg 2005;80:1290-6; discussion 1296.

49. Della Corte A, Scardone M, Romano G, et al. Aortic arch surgery: thoracoabdominal perfusion during antegrade cerebral perfusion may reduce postoperative morbidity. Ann Thorac Surg 2006;81:1358-64.

50. Nappi G, Maresca L, Torella M, et al. Body perfusion in surgery of the aortic arch. Tex Heart Inst J 2007;34:23-9.

51. Kazui T, Washiyama N, Muhammad BA, et al. Improved results of atherosclerotic arch aneurysm operations with a refined technique. J Thorac Cardiovasc Surg 2001;121:491-9.

52. Aoki A, Sangawa K. Protection of visceral organs with an aortic occlusion balloon catheter and by femoral perfusion in aortic arch replacement. Kyobu Geka 2008;61:191-4.

53. Touati GD, Marticho P, Farag M, et al. Totally normothermic aortic arch replacement without circulatory arrest. Eur J Cardiothorac Surg 2007;32:263-8; discussion 268.

54. Kazui T. Editorial comment: Normothermic selective cerebral perfusion - how safe is it? Eur J Cardiothorac Surg 2007;32:268-9.

55. Etz CD, Luehr M, Kari FA, et al. Selective cerebral perfusion at 28 degrees C--is the spinal cord safe? Eur J Cardiothorac Surg 2009;36:946-55.

56. Fernandes P, Mayer R, Adams C, et al. Simultaneous individually controlled upper and lower body perfusion for valve-sparing root and total aortic arch replacement: a case

study. J Extra Corpor Technol 2011;43:245-51.

57. Spielvogel D, Etz CD, Silovitz D, et al. Aortic arch replacement with a trifurcated graft. Ann Thorac Surg 2007;83:S791-5; discussion S824-31.

58. Jacobs MJ, de Mol BA, Legemate DA, et al. Retrograde aortic and selective organ perfusion during thoracoabdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 1997;14:360-6.