Protecting the Brain During Aortic Surgery: An Enduring Debate With Unanswered Questions

Louis H. Stein, MD, MHS, and John A. Elefteriades, MD

REPAIR OF THE aortic arch is one of the most technically demanding procedures faced by cardiovascular surgeons. A salient feature contributing to the complexity of these procedures is the interruption of the natural cerebral perfusion. Advanced and popularized by Greipp et al,[1] deep hypothermic circulatory arrest (DHCA) became a classic strategy for cerebral protection during repair of the aortic arch. This method provides the required bloodless field, allowing for meticulous inspection of the aorta while avoiding cross-clamping a potentially fragile aortic wall.

Although DHCA proved effective, concerns grew because some studies showed neurologic sequelae resulting from prolonged periods of DHCA.[2] Thus, perfusion methods to extend the duration of safe access to the aortic arch were explored. This was addressed by supplying direct perfusion of the brain via selective antegrade cerebral perfusion (SACP) or retrograde cerebral perfusion (RCP).

SACP during DHCA was proposed as a mechanism by which the duration of bypass could be safely extended.[3] Studies have confirmed the safety of this technique; however, it has been criticized as cumbersome and adding to the complexity of the procedure.[4] Advocates for RCP conjecture it provides longer operative times by providing intermittent perfusion in addition to protection from embolic events by virtue of "washing out" debris from the great vessels.

The goal of this review is to examine the 3 main strategies of intraoperative cerebral protection. A summary of the published data on each of these techniques reviewed is presented in Table 1. The fundamental principles supporting these 3 strategies as well as some of the salient studies of these approaches in clinical practice are examined. Finally, some of the trials in which these techniques were directly compared are explored.

From the Section of Cardiothoracic Surgery, Yale University School of Medicine, New Haven, CT.

Address reprint requests to Louis H. Stein, MD, MHS, Section of Cardiothoracic Surgery, Yale University School of Medicine, 330 Cedar Street, Boardman 204, New Haven, CT 06510. E-mail: louis.stein@yale.edu

1053-0770/10/2402-0020$36.00/0

doi:10.1053/j.jvca.2009.05.016

Key words: aorta, thoracic/surgery, aortic aneurysm, surgery, cerebrovascular circulation/physiology, hypothermia, induced, brain ischemia, prevention and control, cerebrovascular circulation

DEEP HYPOTHERMIC CIRCULATORY ARREST

The normal human brain sustains extraordinary energetic requirements. DHCA capitalizes on the exponential decrease in the cellular metabolic demands of the brain that occurs with hypothermia.[5,6] DHCA is generally recognized as safe for short periods, but many raise concerns for the safety of prolonged periods of circulatory arrest.

Both severe neurologic deficits (stroke with permanent neurologic injury) and minor neurologic deficits (transient ischemic attack and memory impairment) have been associated with the duration of DHCA. Svensson et al[2] showed an increase in stroke rate after 45 minutes of DHCA and death with procedures >65 minutes. Among cases using DHCA, Gega et al[7] of the authors' group found an overall mortality rate of 6.3% using DHCA alone and a stroke rate of 4.3%. In that article, the prevalence of stroke increased to 13.1% among cases with >45 minutes of circulatory arrest. Major morbidity and mortality also have been found to be more likely in emergent cases with DHCA protection.[7]

Other studies have attempted to evaluate the risk of DHCA on transient neurologic dysfunction. Reich et al[8] found fine-motor and memory deficits in patients who underwent >25 minutes of DHCA. A subsequent study performed at the authors' institution of 29 highly educated professionals who underwent aortic arch surgery with and without DHCA found no difference in pre- or postoperative responses to neuropsychometric questionnaires. The results of the patients also correlated well with the responses of familial informants (Fig 1).[9]

SELECTIVE ANTEGRADE CEREBRAL PERFUSION

Selective antegrade cerebral perfusion seeks to extend total operative time with the intermittent infusion of cooled blood directly into the cerebral vessels.[10] The innominate or carotid arteries are cannulated and perfused with blood cooled to 6° to 12°C.[3,11] In the current era, this is usually performed by the axillary cannula that is used for systemic perfusion. During DHCA, this perfuses the innominate artery and its 2 branches. Controversies include the following: (1) Should the left carotid artery be cannulated directly in the field and perfused as well? (2) Does the left subclavian artery need to be occluded to prevent shunting of blood out the left vertebral? and (3) What is the appropriate rate of cerebral perfusion (to avoid cerebral edema because the normal homeostatic regulation of cerebral blood flow is incapacitated during DHCA)? Certainly, the

Table 1. Overview of Large Studies Reviewing Individual Methods of Cerebral Protection

Technique	Year	n	Mortality (%)	Stroke (%)
DHCA[2,7]	1993, 2007	394, 656	6.3-12.0	4.8-7.0
SACP[15,16,18,19]	1999-2007	77-472	11-19.4	3.2-20
RCP[21,31-33]	1994-2002	33-163	6-8	2.8-9.1

potential to do more harm than good is present if cerebral perfusion is used but uneven or excessive brain perfusion is produced. Also, the potential for injury from direct cannulation (especially of dissected or fragile vessels) or from the embolization of debris (especially in heavily arteriosclerotic arteries) is very real.

The comparison of straight (unaugmented) DHCA with SACP in animal studies showed that SACP was associated with faster electrophysiologic recovery and less cerebral edema, which were indicated by lower intracranial pressures during reperfusion and shorter cerebral acidosis.[12] Additionally, some groups have published promising results using SACP with "moderate" hypothermia (26°-28°C).[13,14] Avoiding deep hypothermia, with its prolongation of perfusion time for warming and cooling, is one of the major advantages of SACP; total cerebral perfusion time varies widely between 52 and 86 minutes.[10,15,16]

In smaller, early studies, permanent neurologic injury was reported to affect 9% of patients with antegrade cerebral perfusion. Other studies have found that permanent neurologic injury has been shown in 0 to 9.3% of patients.[15,17,18] In 2002, Kazui et al[10] found that the duration of cerebral perfusion was not associated with neurologic injury; however, a later study from this group found pump time and previous cerebrovascular accident to be risk factors for permanent neurologic injury.[16] It certainly is fair to say that SACP permits longer DHCA times than would be feasible with straight DHCA, where time does matter, because the brain is not receiving blood flow.

Postoperative mortality for antegrade cerebral perfusion (ACP) ranges between 11% and 16%.[10,13,18] Presumably, institutional experience with operative technique improves outcomes. This is shown in a study of 462 patients in whom Kazui et al[16] found a decreased mortality rate of 4.3% in their most recent subset of 266 patients. This mortality rate was lower than their previously reported mortality rate of 11.2%.[10] Five-year survival for patients protected with ACP ranges between 59.0% and 65.3%.[13,19] Regression analysis has found renal failure, postoperative dialysis, and increased cerebral perfusion time to be predictive of perioperative mortality.[13] Others have found that age >60 years was a significant mortality factor.[20]

RETROGRADE CEREBRAL PERFUSION

Retrograde cerebral perfusion is an alternative adjunct technique aimed at extending the overall safe operative time.[21] It is conjectured that this technique increases the safety of DHCA by 2 means: (1) providing "backward" perfusion of the brain tissue, and (2) flushing away toxic products of metabolism and embolic debris.[22] In this method, a bridge connecting the arterial and venous catheters of the bypass circuit is created, which provides retrograde perfusion via the superior vena cava at a pressure of 20 to 30 mmHg. Again, the induction of cerebral edema must be avoided.

Many argue that RCP can provide cooling of the brain's surface but does not provide adequate support for the brain's metabolic requirements. During RCP, cerebral oxygen extraction, CO_2 production, and blood pH decrease in a linear fashion throughout the procedure.[23] This inadequate perfusion has been explained by the tendency of blood to flow to capacitance vessels and dependent compartments and not supply the small arteries and capillaries of the brain. Animal studies have attested to this, showing only a small portion of the retroperfused blood actually supplies the small vessels of the brain.[24,25] Human cadaveric studies have found that the presence of valves in the internal jugular veins increases the requirement for perfu-

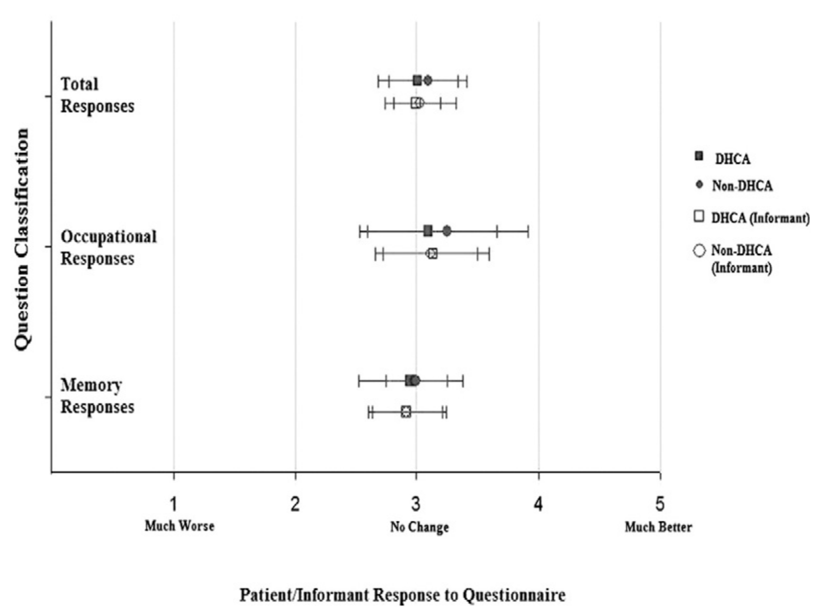

Fig 1. Results of pre- and postoperative neuropsychometric assessment of patients undergoing aortic surgery with and without DHCA. No difference in questionnaire responses was noted among any group. (Reprinted with permission.[9])

sion pressure.[26,27] This is complicated by the finding that excessive perfusion pressures may contribute to cellular edema with RCP.[28]

RCP is also thought to provide neurologic protection by clearing microemboli. Animal studies have shown decreased embolization after RCP; however, RCP yielded no histopathologic or neurologic improvements.[29] Most studies show the rate of stroke in patients protected with RCP to be between 2.8% and 9.1%.[21,30-33] No correlation has been shown between the duration of RCP and neurologic complication.[34] Others have shown that patient age, rather than time of circulatory arrest, predicts postoperative neurologic complications.[35]

The overall mortality among patients undergoing procedures of the aortic arch under RCP ranges from 6% to 8%.[30,31] Follow-up has shown a 91% survival rate at 6 months.[30] Bavaria et al[31] found a 55% risk of death in RCP-supported patients with preoperative strokes.

STUDIES DIRECTLY COMPARING TECHNIQUES

DHCA Compared With SACP

The authors' review of the literature found 2 studies directly comparing DHCA with SACP in adult patients (Table 2). No statistically significant differences in sex, age, or urgency of operation were found in a 1995 study comparing 19 patients protected with DHCA with 16 patients protected with selective SACP.[36] This study found no statistically significant difference in the average length of cerebral perfusion arrest, early death, or stroke rates.[36] In a subsequent, larger study, Immer et al[37] reviewed 363 patients who underwent arch repair with DHCA with and without SACP. Their method stratified patients according to the length of the procedure (<20 minutes, 20-29 minutes, and >30 minutes). Among all strata, no statistical difference in stroke rate was shown between DHCA patients supported with or without SACP. An overall stroke rate of 6.5% in those patients with DHCA was found, compared with a 1.0% stroke rate among those patents in whom ACP was used.[37] This study was limited by the large proportion of patients undergoing DHCA compared with SACP (322 *v* 41) and no group of straight ACP.[37]

DHCA Compared With RCP

In a prospective trial, Harrington et al[38] randomized 38 patients undergoing surgery of the aortic arch into protection with either DHCA or RCP. At 6 and 12 weeks postoperatively, no neuropsychometric differences could be detected.[38] A retrospective study comparing 15 patients protected with DHCA with 50 patients protected with RCP found no difference in cerebral ischemic time.[39] This study found a significantly increased number of postoperative deaths and stroke in patients protected with DHCA; however, this study was significantly compromised by a large size discrepancy between treatment groups.[39] Moon and Sundt[40] retrospectively compared 36 patients in whom DHCA and 36 patients in whom RCP was used and found no difference in mortality between groups. In their cohort of 161 patients, 120 of whom received RCP, Safi et al[33] found that RCP was protective against stroke among patients older than 70 years. Wong and Bonser[41] used multiple logistic regression analysis of 130 patients undergoing arch repair; in this study, RCP was used for 96 patients. Advanced age and straight DHCA duration were associated with higher mortality and stroke rate. Of note, the use of RCP was associated with an

Table 2. Outcomes From Studies Directly Comparing Various Forms of Cerebral Protection

Group Comparison	Author (Year)	n	Mortality (%)	Stroke (%)	Comments
DHCA *v* SACP	Alamani (1995)	DHCA: 19 SACP: 16	DHCA: 26.3 SACP: 18.7	DHCA: 15.7 SACP: 12.5	Retrospective Comparative study Compared DHCA with SACP
	Immer (2002)	DHCA: 322 SACP: 41	Overall: 8.6	DHCA: 6.5 SACP: 1.0	Retrospective study
DHCA *v* RCP	Safi (1997)	DHCA: 41 RCP: 120	Overall: 6	DHCA: 9 RCP: 3	Retrospective study with large size discrepancy between groups; RCP was protective against stroke in patients >70 years old.
	Wong (1999)	DHCA: 34 RCP: 96	Overall: 16.9	Overall: 6.9	Nonrandomized. RCP was not protective for mortality or stroke.
	Moon (2002)	DHCA: 36 RCP: 36	DHCA: 8.0 RCP: 11.0	DHCA: 25 RCP: 2.0	Retrospective case-control No statistically significant difference in mortality or stroke between groups
	Harrington (2003)	DHCA: 18 RCP: 20	DHCA: 5.5 RCP: 5.0	Overall: 2.6	Prospective randomized trial to evaluate effect of procedure neuropsychometric outcomes; no difference found between groups; although underpowered
	Dong (2003)	DHCA: 50 RCP: 15	DHCA: 20 RCP: 2.0	DHCA: 25 RCP: 2.0	Retrospective Large size discrepancy between patient groups
SACP *v* RCP	Okita (2001)	SACP: 30 RCP: 30	SACP: 6.6 RCP: 6.6	SACP: 6.6 RCP: 3.3	Only difference found was higher incidence of transient brain dysfunction in RCP patients.
DCHA *v* SACP *v* RCP	Matalanis (2003)	DHCA: 14 SACP: 25 RCP: 23	Overall: 8.0	Overall: 6.4	Retrospective No significant differences in mortality or stroke rate among groups

Table 3. Theoretic and Known Benefits and Dangers of Each Cerebral Protection Strategy

Technique	Advantages	Dangers	Comments
DHCA	Safe for short periods of circulatory arrest Avoids cross-clamping an already diseased aorta	Questions of safety for long periods of circulatory arrest; increased incidence of permanent neurologic injury with >45 min of circulatory arrest; conflicting data on transient effects with shorter (approximately 25 min) ischemia	Generally used in more straightforward cases Many of the survey's respondents commented on use of DHCA with SACP.
SACP	Permits longer periods of circulatory arrest than with straight DHCA	Requires the handling of sclerotic vessels; may result in the release of emboli	Technique most often used Controversies regarding ideal site of cannulation for optimal perfusion
RCP	Flushes cerebral vasculature of toxic metabolic products and microemboli	Perfusion may be limited to the brain's surface.	

increased duration of cerebral perfusion.[41] These results are summarized in Table 2.

Antegrade Compared With Retrograde Perfusion

Okita et al[42] performed a prospective study of aortic arch replacement in 60 consecutive patients alternately assigned RCP and ACP protection strategies. No difference in mortality was noted between groups nor was there a difference between groups in stroke rate; however, there was a significantly higher incidence of transient brain dysfunction in the RCP group.[42] This work is contrasted against studies comparing other techniques in Table 2.

Comparison of All 3 Techniques: DHCA, SACP, and RCP

Matalanis et al[43] reviewed 14 patients with DHCA, 25 with SACP, and 23 with RCP protection. Their study found no significant differences in survival or incidence of neurologic complications. Only cerebral perfusion time for patients protected with ACP was significantly longer than that for patients protected with HCP or RCP.

CONCLUSION

The controversy over the ideal method of cerebral protection stems from the divergent theories and supporting evidence (Table 3). Because of this, these methods have achieved varying degrees of popularity over the past 2 decades. To gain some insight into current practices, the authors of this review surveyed aortic arch surgeons at several academic medical centers in the United States known for their aortic focus, asking which method of cerebral protection they preferred. Of those who responded (n = 16), 50% stated they prefer selective ACP. Thirty-eight percent used some combination, whereas RCP and DHCA each had 1 respondent (6%) using those techniques exclusively.

This discrepancy is not particularly surprising. DHCA has been shown to be a safe procedure. Its proponents argue that it prevents overcomplicating an already challenging procedure; however, its detractors cite data showing compromised outcomes in longer procedures. While adding steps to the procedure, data do support the safe use of SACP. RCP has experienced profound criticism recently, although this technique does present several conceptual advantages.

Given the relative benefits and disadvantages of each strategy, it becomes clear that different techniques, DHCA, SACP, or RCP, may be appropriate for distinctive subsets of patients. For example, known risk factors such as a previous cerebrovascular accident may contraindicate the use of RCP. Adjunct strategies to DHCA should be considered when especially complex procedures are indicated, necessitating a long duration of circulatory arrest.

At the authors' center, straight DHCA is used almost exclusively based on favorable experience (as reported in the previously cited studies) and the recognition that the competing techniques, SCAP and RCP, while offering conceptual advantages and liabilities, have not led to lower mortality or stroke rates than those the authors have achieved with straight DHCA.

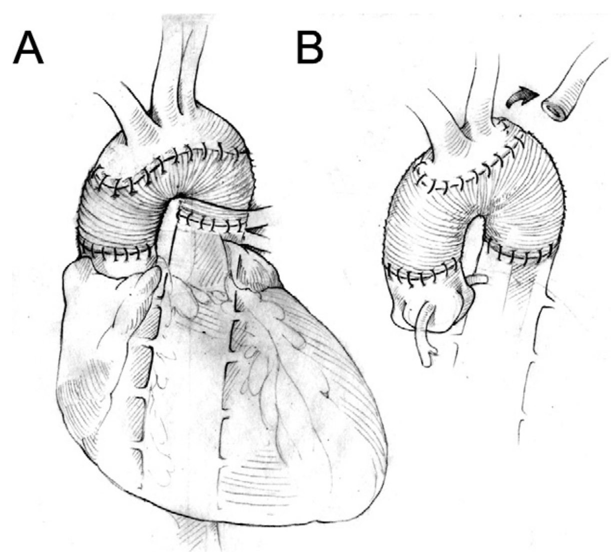

Fig 2. A comparison of the traditional technique of arch replacement with the modified technique used at the Yale-New Haven Hospital. (A) The traditional technique calls for the innominate, left carotid, and left subclavian arteries to be included in a Carrel patch. (B) In the modified technique, only the innominate and left carotid vessels are anastomosed to the graft in a single Carrel patch. Later, after cardiopulmonary bypass is terminated, the left subclavian artery is anastomosed with an interposition Dacron graft. This provides for a more efficient procedure by bringing the Carrel patch closer to the surgeon, making it smaller, and providing for excellent access if subsequent hemostasis is required.

Especially for short-to-moderate DHCA (30-45 minutes), the authors are confident that straight DHCA provides excellent cerebral protection and surgical results. The authors believe that, especially for urgent operations for acute type-A dissection in which the arrest time can be anticipated to be short for an open distal anastomosis, there is no need to complicate or prolong the procedure for adjunct perfusion techniques. Additionally, there is an interplay between the preferred method of cerebral protection and the surgical technique. For example, the authors use a specific technique for total arch replacement (Fig 2) in which only the innominate and left carotid vessels are included in a single Carrel patch. The left subclavian artery is anastomosed later, after the termination of cardiopulmonary bypass, with an interposition Dacron graft (DuPont, Wilmington, DE) (Fig 2B). This technique brings the Carrel patch close to the surgeon, makes it smaller, and provides for excellent access if subsequent hemostasis is required. An elephant trunk–type distal anastomosis is performed first followed by the 2-vessel Carrel patch; this combination easily can be accomplished within 30 to 40 minutes, obviating the need for perfusion adjuncts to straight DHCA.

Future carefully designed and appropriately powered studies are required to evaluate these competing (or complementary) strategies. At the present time, it can be said that no one technique of cerebral perfusion has been shown to prevail unequivocally; aortic arch surgery remains an art.

REFERENCES

1. Griepp RB, Stinson EB, Hollingsworth JF, et al: Prosthetic replacement of the aortic arch. J Thorac Cardiovasc Surg 70:1051-1063, 1975

2. Svensson LG, Crawford ES, Hess KR, et al: Deep hypothermia with circulatory arrest. Determinants of stroke and early mortality in 656 patients. J Thorac Cardiovasc Surg 106:19-28, 1993

3. Bachet J, Guilmet D, Goudot B, et al: Cold cerebroplegia. A new technique of cerebral protection during operations on the transverse aortic arch. J Thorac Cardiovasc Surg 102:85-93, 1991

4. Kazui T, Inoue N, Yamada O, et al: Selective cerebral perfusion during operation for aneurysms of the aortic arch: A reassessment. Ann Thorac Surg 53:109-114, 1992

5. Greeley WJ, Kern FH, Ungerleider RM, et al: The effect of hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral metabolism in neonates, infants, and children. J Thorac Cardiovasc Surg 101:783-794, 1991

6. Harrington DK, Fragomeni F, Bonser RS: Cerebral perfusion. Ann Thorac Surg 83:S799-S804, 2007

7. Gega A, Rizzo JA, Johnson MH, et al: Straight deep hypothermic arrest: Experience in 394 patients supports its effectiveness as a sole means of brain preservation. Ann Thorac Surg 84:759-766, 2007

8. Reich DL, Uysal S, Sliwinski M, et al: Neuropsychologic outcome after deep hypothermic circulatory arrest in adults. J Thorac Cardiovasc Surg 117:156-163, 1999

9. Percy A, Widman S, Rizzo JA, et al: Deep hypothermic circulatory arrest in patients with high cognitive needs: Full preservation of cognitive abilities. Ann Thorac Surg 87:117-123, 2009

10. Kazui T, Yamashita K, Washiyama N, et al: Usefulness of antegrade selective cerebral perfusion during aortic arch operations. Ann Thorac Surg 74:S1806-S1809, 2002

11. Frist WH, Baldwin JC, Starnes VA, et al: A reconsideration of cerebral perfusion in aortic arch replacement. Ann Thorac Surg 42: 273-281, 1986

12. Hagl C, Khaladj N, Peterss S, et al: Hypothermic circulatory arrest with and without cold selective antegrade cerebral perfusion: Impact on neurological recovery and tissue metabolism in an acute porcine model. Eur J Cardiothorac Surg 26:73-80, 2004

13. 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 31:618-622, 2007

14. Minatoya K, Ogino H, Matsuda H, et al: Evolving selective cerebral perfusion for aortic arch replacement: High flow rate with moderate hypothermic circulatory arrest. Ann Thorac Surg 86:1827-1831, 2008

15. Di Bartolomeo R, Di Eusanio M, Pacini D, et al: Antegrade selective cerebral perfusion during surgery of the thoracic aorta: Risk analysis. Eur J Cardiothorac Surg 19:765-770, 2001

16. Kazui T, Yamashita K, Washiyama N, et al: Aortic arch replacement using selective cerebral perfusion. Ann Thorac Surg 83:S796-S798, 2007

17. Matsuda H, Nakano S, Shirakura R, et al: Surgery for aortic arch aneurysm with selective cerebral perfusion and hypothermic cardiopulmonary bypass. Circulation 80:I243-I248, 1989

18. Bachet J, Guilmet D: Brain protection during surgery of the aortic arch. J Card Surg 17:115-124, 2002

19. Tabayashi K, Ohmi M, Togo T, et al: Aortic arch aneurysm repair using selective cerebral perfusion. Ann Thorac Surg 57:1305-1310, 1994

20. Bachet J, Guilmet D, Goudot B, et al: Antegrade cerebral perfusion with cold blood: A 13-year experience. Ann Thorac Surg 67:1874-1878, 1999

21. Ueda Y, Miki S, Okita Y, et al: Protective effect of continuous retrograde cerebral perfusion on the brain during deep hypothermic systemic circulatory arrest. J Card Surg 9:584-594, 1994

22. Wong CH, Bonser RS: Retrograde cerebral perfusion: Clinical and experimental aspects. Perfusion 14:247-256, 1999

23. Cheung AT, Bavaria JE, Pochettino A, et al: Oxygen delivery during retrograde cerebral perfusion in humans. Anesth Analg 88:8-15, 1999

24. Boeckxstaens CJ, Flameng WJ: Retrograde cerebral perfusion does not perfuse the brain in nonhuman primates. Ann Thorac Surg 60:319-327, 1995

25. Ehrlich MP, Hagl C, McCullough JN, et al: Retrograde cerebral perfusion provides negligible flow through brain capillaries in the pig. J Thorac Cardiovasc Surg 122:331-338, 2001

26. Kunzli A, Zingg PO, Zund G, et al: Does retrograde cerebral perfusion via superior vena cava cannulation protect the brain? Eur J Cardiothorac Surg 30:906-909, 2006

27. de Brux JL, Subayi JB, et al: Retrograde cerebral perfusion: Anatomic study of the distribution of blood to the brain. Ann Thorac Surg 60:1294-1298, 1995

28. Usui A, Oohara K, Liu TL, et al: Determination of optimum retrograde cerebral perfusion conditions. J Thorac Cardiovasc Surg 107:300-308, 1994

29. Juvonen T, Weisz DJ, Wolfe D, et al: Can retrograde perfusion mitigate cerebral injury after particulate embolization? A study in a chronic porcine model. J Thorac Cardiovasc Surg 115:1142-1159, 1998

30. Deeb GM, Jenkins E, Bolling SF, et al: Retrograde cerebral perfusion during hypothermic circulatory arrest reduces neurologic morbidity. J Thorac Cardiovasc Surg 109:259-268, 1995

31. Bavaria JE, Brinster DR, Gorman RC, et al: Advances in the treatment of acute type A dissection: An integrated approach. Ann Thorac Surg 74:S1848-S1852, 2002

32. Lytle BW, McCarthy PM, Meaney KM, et al: Systemic hypothermia and circulatory arrest combined with arterial perfusion of the

superior vena cava. Effective intraoperative cerebral protection. J Thorac Cardiovasc Surg 109:738-743, 1995

33. Safi HJ, Letsou GV, Iliopoulos DC, et al: Impact of retrograde cerebral perfusion on ascending aortic and arch aneurysm repair. Ann Thorac Surg 63:1601-1607, 1997

34. Okita Y, Takamoto S, Ando M, et al: 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 115:129-138, 1998

35. Ergin MA, Galla JD, Lansman L, et al: Hypothermic circulatory arrest in operations on the thoracic aorta. Determinants of operative mortality and neurologic outcome. J Thorac Cardiovasc Surg 107:788-797, 1994

36. Alamanni F, Agrifoglio M, Pompilio G, et al: Aortic arch surgery: Pros and cons of selective cerebral perfusion. A multivariable analysis for cerebral injury during hypothermic circulatory arrest. J Cardiovasc Surg (Torino) 36:31-37, 1995

37. Immer FF, Lippeck C, Barmettler H, et al: Improvement of quality of life after surgery on the thoracic aorta: Effect of antegrade cerebral perfusion and short duration of deep hypothermic circulatory arrest. Circulation 110:II250-II255, 2004

38. Harrington DK, Bonser M, Moss A, et al: Neuropsychometric outcome following aortic arch surgery: A prospective randomized trial of retrograde cerebral perfusion. J Thorac Cardiovasc Surg 126:638-644, 2003

39. Dong PQ, Guan YL, He ML, et al: [Clinical application of retrograde cerebral perfusion for brain protection during the surgery of ascending aortic aneurysm: 50 cases report]. Zhonghua Wai Ke Za Zhi 41:109-111, 2003

40. Moon MR, Sundt TM 3rd: Influence of retrograde cerebral perfusion during aortic arch procedures. Ann Thorac Surg 74:426-431, 2002

41. Wong CH, Bonser RS: Does retrograde cerebral perfusion affect risk factors for stroke and mortality after hypothermic circulatory arrest? Ann Thorac Surg 67:1900-1903, 1999

42. Okita Y, Minatoya K, Tagusari O, et al: Prospective comparative study of brain protection in total aortic arch replacement: Deep hypothermic circulatory arrest with retrograde cerebral perfusion or selective antegrade cerebral perfusion. Ann Thorac Surg 72:72-79, 2001

43. Matalanis G, Hata M, Buxton BF: A retrospective comparative study of deep hypothermic circulatory arrest, retrograde, and antegrade cerebral perfusion in aortic arch surgery. Ann Thorac Cardiovasc Surg 9:174-179, 2003