Original Article

Cerebral Protection in Aortic Arch Surgery: Clinical Outcomes from Single Institute

Pramote Porapakkham MD[1], Pornwalee Porapakkham MD[2]

[1] Department of Cardiothoracic Surgery, Central Chest Institute of Thailand, Nonthaburi, Thailand
[2] Cardiology and Intervention Department, Central Chest Institute of Thailand, Nonthaburi, Thailand

Background: The current practices to prevent cerebral function from ischemic damage during aortic arch surgery include deep hypothermic circulatory arrest [DHCA], retrograde cerebral perfusion [RCP], and selective antegrade cerebral perfusion [SACP]. The optimal strategy for protecting the brain remains controversial. A ten-year clinical experience and follow-up of patients with aortic surgery involving arch was reported.

Objective: To evaluate clinical outcomes between different cerebral protection methods during aortic arch surgery.

Materials and Methods: Medical records of aortic aneurysm patients underwent circulatory arrest during the operations between January 2005 and December 2015 were reviewed.

Results: One hundred-thirteen patients underwent circulatory arrest during aortic surgery involving arch were studied. DHCA was employed in all patients. Of these, 79 patients received ACP as an adjunct (ACP group) and 34 patients used only DHCA or combined with RCP (non-ACP group). Duration of circulatory arrest time, bypass time, and cardiac ischemic time were significantly longer in ACP group (44.04±1.7 versus 29.4±1.9 minutes, $p<0.001$; 215.39±8.4 versus 174.7±12.6 minutes, $p = 0.009$, and 140.72±7.9 versus 76.78±9.7 minutes, $p<0.001$, respectively). There was no difference in clinical outcomes between the two groups, including 30-day mortality (14% versus 17.6%, $p = 0.61$), major stroke (6.3% versus 8.8%, $p = 0.63$) and minor stroke (10.1% versus 2.9%, $p = 0.19$).

Conclusion: The superiority of ACP over the other approach of cerebral protection was not proved in the present study. However, it is more likely to use ACP in case of complex arch operation with extended period of circulatory arrest time.

Keywords: Cerebral protection, Deep hypothermic circulatory arrest, Retrograde cerebral perfusion, Antegrade cerebral perfusion

J Med Assoc Thai 2018; 101 (5): 621-7
Website: http://www.jmatonline.com

Aortic aneurysm involving arch is a serious condition. Once a chest pain symptom occurs or the diameter itself is greater than 5.5 cm, it can possibly rupture and cause life threatening bleeding(1). Even though minimally invasive treatment such as endovascular stent is a good alternative treatment for high-risk patients, open repair still remains a gold standard treatment with excellent long-term outcomes.

The main concern for open aortic arch repair is brain protection since the cerebral blood flow must be manipulated and excluded during the procedure. Currently, three strategies including deep hypothermic circulatory arrest [DHCA], retrograde cerebral perfusion [RCP], and antegrade cerebral perfusion [ACP] have been used to minimize the brain injury. The benefits and drawbacks of each technique are described in many publications. According to the guidelines, ACP is recommended during open arch surgery(1). Nevertheless, DHCA and RCP or in combination still have role for brain protection in some centers(2,3).

The present study reported the clinical experience in different cerebral protection techniques for aortic arch surgery at the Central Chest Institute of Thailand [CCIT].

Materials and Methods

The present study was approved by the CCIT Ethics Committee. Data of the patients with aortic aneurysm involving aortic arch were retrieved from the medical records between January 2005 and December 2015. Only aortic aneurysm patients that underwent open surgery were studied. Patients' demographic data, location and size of aortic aneurysm, intraoperative details, and outcomes were obtained.

Preoperative diagnosis was confirmed by computed tomography [CT] scan, which could determine location,

Correspondence to:
Porapakkham P. Department of cardiothoracic surgery, Central Chest Institute of Thailand, Nonthaburi 11000, Thailand.
Phone: +66-2-5803423 ext. 7405
Email: prpkm@yahoo.co.th

How to cite this article: Porapakkham P, Porapakkham P. Cerebral protection in aortic arch surgery: clinical outcomes from single institute. J Med Assoc Thai 2018;101:621-7.

size, and surgical approach techniques. Transthoracic echocardiography was routinely done to detect other structural heart abnormalities and pumping function. Coronary angiography, if possible, was carried out in patients over 40 years of age or those with suspected ischemic heart disease.

Medial approach was determined in case of proximal arch, ascending or root involvement whereas left thoracotomy approach was considered if the pathology was only at the distal arch and descending aorta. In median sternotomy incision, choices of aortic cannulation for cardiopulmonary bypass either at femoral artery, axillary artery, or ascending aorta depended on the quality of the arterial wall and surgeons' decision. Single two-stage venous cannulation was used except for those with RCP strategy that needed two venous cannulations. Heart was decompressed via right superior pulmonary vein vent and antegrade or retrograde cardioplegia combined with topical heart cold irrigation were used for myocardial protection. In left thoracotomy incision, femoro-femoral bypass, main pulmonary artery cannulation, and venting at left superior pulmonary vein or left ventricular apex without cardioplegia were done routinely. All the patients were cooled down to 18 degrees Celsius. RCP or ACP was used as an adjunctive therapy for brain protection during circulatory arrest depending on surgeons' preference, exposure area, and arterial wall quality of the arch vessels. For example, RCP could not be used in left thoracotomy approach due to exposure limitation of right atrium and superior vena cava. Selective ACP was not chosen in cases with arterial plaque at the origin of innominate or left carotid artery to prevent dislodgement during direct cannulation. RCP was delivered by snaring and infusing blood up the SVC to perfuse the brain retrogradely and maintain the venous pressure of 20 to 25 mmHg during the circulatory arrest. ACP was initiated by clamping innominate artery if the axillary cannulation was performed. Left carotid artery was also perfused by mean of direct endoluminal cannulation through the opening arch. On the other hand, two endoluminal cannulations were inserted to innominate and left carotid artery if there was no axillary cannulation. Left subclavian artery was generally occluded with balloon-tip catheter to prevent vertebral steal phenomenon and make a bloodless operative field. The ACP flow rate was approximately 10 to 15 cc/kg/minute to maintain the pressure between 40 to 70 mmHg.

Follow-up information was derived from consecutive outpatient clinic visits, telephone interviews, or questionnaires mailed to patients or families.

Major stroke was defined as a disabling stroke where the patient is unable to carry out all usual activities and require intensive rehabilitation and constant care[4]. Minor stroke was defined as mild with no disabling symptoms in acute stage with good functional outcomes[5].

Neurologic complication postoperative aortic arch surgery using ACP and non-ACP for brain protection was used as a primary outcome and a sample size of 33 patients or more in each group was calculated by using a proportion of this adverse event reported as after matching in a recently published propensity-match analysis[6].

Statistical analysis

Results were expressed as mean ± SD. The Chi-square test and independent t-test were used for categorical variables and continuous variables, respectively. Analysis was performed using SPSS version 17. A *p*-value less than 0.05 was considered statistically significant.

Results

One hundred thirteen patients that underwent circulatory arrest during aortic surgery involving arch and were treated in the CCIT during the past ten years were included in our study. DHCA plus ACP (ACP group) was used in 79 patients, whereas DHCA with or without RCP (non-ACP group) was applied in 34 patients. A comparison between the two groups including age, gender, pathologic causes, and other underlying diseases showed no statistical difference (Table 1). Ascending aortic involvement was found significantly more often in ACP patients than in the other (78.5% versus 44.1%, $p = 0.001$).

The arterial cannulation sites in the ACP and non-ACP group were at the ascending aorta 17.7% and 2.9%, the axillary artery 10.1% and 0%, and the femoral artery 72.2% and 97.1%, respectively ($p = 0.01$). The circulatory arrest time, bypass time and cardiac ischemic time were significantly longer in ACP group (44.04±1.7 versus 29.4±1.9 minutes, $p<0.001$; 215.39±8.4 versus 174.7±12.6 minutes, $p = 0.009$ and 140.72±7.9 versus 76.78±9.7 minutes, $p<0.001$, respectively) (Table 2).

The thirty-day mortality was approximately 14% in ACP group and 17.6% in non-ACP group ($p = 0.61$). Morbidity between the two groups including major stroke (6.3% versus 8.8%; $p = 0.63$) and minor stroke (10.1% versus 2.9%; $p = 0.19$) were not significantly

Table 1. Demographic data of patients

	ACP (n = 79)	Non-ACP (n = 34)	*p*-value
Age (years)	58.82±1.51	59.03±2.2	0.94
Male	46 (58.2)	20 (58.8)	0.95
Pathology			0.66
Dissection	43 (45.6)	17 (50.0)	
Nondissection	36 (54.4)	17 (50.0)	
Location			<0.001
Ascending	62 (78.5)	15 (44.1)	
Descending	17 (21.5)	19 (55.9)	
Underlying disease			
HT	65 (82.3)	26 (76.5)	0.47
DM	13 (16.5)	5 (14.7)	0.81
Dyslipidemia	16 (20.3)	8 (23.5)	0.69
Stroke history	3 (3.8)	0 (0.0)	0.24
COPD	7 (8.9)	4 (11.8)	0.63
Marfan syndrome	3 (3.8)	2 (5.9)	0.62

ACP = antegrade cerebral perfusion; HT = hypertension; DM = diabetes mellitus; COPD = chronic obstructive pulmonary disease

Data presented as mean ± SD or number (%), *p*-value <0.05 is significant

Table 2. Intraoperative details of aortic arch surgery patients using ACP and non-ACP for brain protection

	ACP (n = 79)	Non-ACP (n = 34)	*p*-value
Incision			0.001
Median sternotomy	62 (78.5)	15 (44.1)	
Left Thoracotomy	17 (21.5)	19 (55.9)	
Arterial cannulation			0.010
Femoral artery	57 (72.2)	33 (97.1)	
Axillary artery	8 (10.1)	0 (0.0)	
Ascending aorta	14 (17.7)	1 (2.9)	
Stop circulation time (minutes)	44.04±1.7	29.4±1.9	<0.001
Bypass time (minutes)	215.39±8.4	174.7±12.67	0.009
Cross clamp time (minutes)	140.72±7.9	76.87±9.7	<0.001

ACP = antegrade cerebral perfusion

Data presented as mean ± SD or number (%)

different. There was also no significant difference in extubation time, ICU and hospital stay (27.3 versus 22.4 hours, $p = 0.37$; 3.7 versus 4.8 days, $p = 0.18$; 21.4 versus 25.4 days, $p = 0.28$). Mortality at one-year follow up was 15.2% and 17.6%, $p = 0.82$, respectively (Table 3).

Over all, there were eight major and nine minor strokes in the present series. Duration of circulatory time categorized into five groups (group 1: less than 30 minutes, group 2: 31 to 40 minutes, group 3: 41 to 50 minutes, group 4: 51 to 60 minutes, and group 5: more than 60 minutes) did not affect the major or minor strokes ($p = 0.58$ and 0.65, respectively) (Figure 1, 2).

Discussion

A main issue for aortic surgery involving aortic arch is postoperative neurologic complication, which is one of the major causes of morbidity and mortality. Incidence from 5% to 50% of neurologic complications and 2.4% to 20% of mortality were reported in literatures[6-8]. Overall, operative major stroke, minor stroke, and mortality were found in 7%, 8%, and 15%, respectively, in the present study.

Table 3. Clinical outcomes of patients using ACP and non-ACP for brain protection during arch surgery

	ACP (n = 79)	Non-ACP (n = 34)	*p*-value
Extubated time (hours)	27.3±3.7	22.4±3.38	0.37
ICU stay (days)	3.74±0.28	4.87±1.0	0.18
Hospital stay (days)	21.45±2.1	25.4±1.9	0.28
30-day mortality	11 (13.9)	6 (17.6)	0.61
1-year mortality	12 (15.2)	6 (17.6)	0.82
Minor stroke	8 (10.1)	1 (2.9)	0.19
Major stroke	5 (6.3)	3 (8.8)	0.63

ACP = antegrade cerebral perfusion; ICU = intensive care unit

Data presented as mean ± SD or number (%)

The aortic arch surgery is a complex procedure, since it needs to stop the circulation during anastomosis at the arch level. Three adjunctive options or in combinations were used to make a bloodless field and preserve the brain function at the same time. Deep hypothermia at 18 degrees Celsius was first successfully used to protect the brain during the circulatory arrest in 1975[10]. The main mechanism of DHCA to preserve

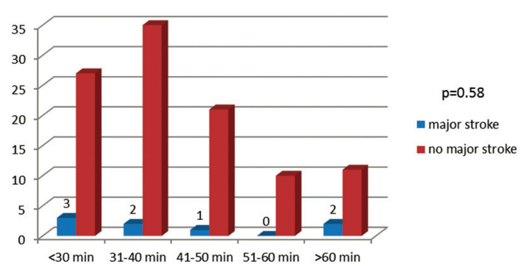

Figure 1. Incidence of postoperative major stroke and duration of circulatory arrested time.

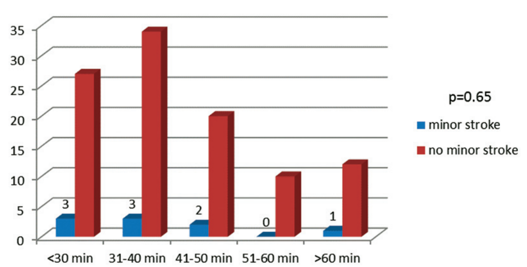

Figure 2. Incidence of postoperative minor stroke and duration of circulatory arrested time.

cerebral function is the suppression of metabolism that enables an extended period of brain ischemia. Nevertheless, the brain is still at risk of both ongoing ischemia and reperfusion injury, which can cause a consequent post-operative transient or permanent neurologic deficit. In general, DHCA less than 30 minutes is relatively safe to prevent the neurologic complications according to some publications[11]. In case of complex arch surgery where longer period of circulatory arrest is needed, most experts recommend using either RCP or ACP in addition to DHCA[12].

First described in 1980[13], RCP is initiated by perfusing oxygenated blood up to the snaring superior vena cava with a pressure of 20 to 25 mmHg. Adjunctive RCP can decrease both mortality and stroke rate compared to DHCA alone, in particular when the arrested time is longer than 60 minutes[14-17]. The major benefit of RCP besides continuously maintaining cerebral hypothermia with perfusion of cold blood is to flush embolic material such as clot, debris, and air out from the brain circulation[18]. However, some reports disagree with the need to provide cerebral oxygenation and nutrient with RCP to support cerebral metabolism[19-23]. Moreover, the other concern for RCP is cerebral edema, which can further increase brain injury. On the other hand, ACP is more physiologic than the two previous methods to support cerebral metabolism during arch anastomosis including lower intracranial pressure, lessen tissue acidosis, and cerebral swelling[24]. By inserting cannulas directly into innominate artery and left carotid artery or clamping the innominate artery in case of axillary cannulation, antegrade cerebral flow can initiate with a rate of 10 cc/kg/minute, which can provide sufficient time, up to 90 minutes, to perform complex procedures[25]. In the present study, there was no difference in neurologic complications, perioperative, and one-year mortality between the cerebral protection with ACP and DHCA combined with or without RCP. In our center, ACP was the preferred method for brain protection in complex arch surgery that required longer arrested time. Duration of circulatory arrest was significantly longer in the patients receiving antegrade cerebral flow with a mean time of 44 minutes (range from 16 to 95 minutes), whereas those using DHCA or in combination with RCP had a mean time of 29 minutes (range from 10 to 52 minutes). Furthermore, bypass time and cardiac ischemic time were also significantly longer in ACP group.

Concerning the cooling temperature, we used deep hypothermia with a temperature of 14.1 to 20 degrees Celsius according to the definition consensus from international panel of experts in high volume aortic centers[26]. At this range of temperature, cerebral metabolic rate for oxygen consumption is decreased by 50% to 70% and this allows a safe period of 20 to 30 minutes of arrested time[27,28]. With the addition of ACP, several papers demonstrated that there was no difference in mortality and morbidity when applying deep (14.1 to 20 degrees Celsius) or moderate (20.1 to 28 degrees Celsius) hypothermia during the procedure except the rate of postoperative bleeding was lower in the warmer group[29]. When using moderate hypothermia, ACP must be applied since it is only additive method reported with this temperature level. In our experience, some cases could not have the cannulas inserted for selective ACP during opening of the arch due to severe plaque around the ostia or proximal part of the arch vessels. As a result, the plan had to be changed to just applying cooling temperature or addition of RCP instead. For the safe side, we still applied deep hypothermia in every case for brain protection and we did not have much problem with the postoperative bleeding.

Neurologic problems post aortic arch surgery are not caused from only hypoperfusion during circulatory arrest, but also from the dislodgement of artheromatous plaque, mural thrombi during clamping, or manipulating at the arch vessels. Some reports stated that a major cause of neurologic complications was embolic event not related to the method of cerebral protection[30,31]. The present study showed no correlation of arrested time range and stroke complications. Unfortunately, quality of the aortic wall including calcium, artheromatous plaque, or mural thrombus was not revealed in the patient record forms. Embolization can also occur during arterial cannulation for cardiopulmonary bypass, especially at the pathologic ascending aorta or from retrograde flow from femoral artery cannulation in a significantly diseased aorta. Epiaortic ultrasound is beneficial for identifying free area of plaque or thrombus to decrease the incidence of stroke. Malperfusion of vital organs including brain during cardiopulmonary bypass may occur in cases where the cannulas were placed in the false lumen of the aortic dissection[32]. Right axillary artery generally free of calcified plaque and involvement of dissection is considered the first choice for arterial cannulation in the arch operation in some centers. The advantages include antegrade flow to exclude the chance of retrograde embolization from femoral cannulation, redirect flow into the true lumen due to less dissection in this vessel, and avoiding direct cannulation into innominate artery, which can cause dislodgement of plaque. In the present series, we just started using right axillary artery cannulation a few years ago and we found that it was a very good alternative to prevent retrograde embolization. The only drawback of this approach was to take longer time for cannulation with using small graft interposition instead of direct cannulation to prevent dissection of the artery.

Limitation

There were some limitations in the present study. Since this was a retrospective review that required medical record retrieval, some data were missed due to the incomplete recording of medical details. The causes of neurologic complications were not identified in the patients' records. For this reason, we could not conclude whether the stroke in each patient was caused from hypoperfusion during circulatory arrest or from dislodgement of artheromatous plaque.

Conclusion

Cerebral protection in aortic surgery involving aortic arch can be performed with deep hypothermia plus retrograde or antegrade cerebral perfusion with the same clinical outcomes including neurological complications, mortality, and other morbidities. Antegrade technique is a preferable choice in complex procedures that require longer arrested time.

What is already known on this topic?

The main concern for open aortic arch repair is brain protection since the cerebral blood flow must be manipulated and excluded during the procedure. Currently, three strategies including DHCA, RCP, and ACP have been used to minimize the brain injury. According to the guidelines, only ACP was recommended during circulatory arrest in open arch surgery (Class IIa level B).

What this study adds?

DHCA alone or in combination with RCP still had roles in preventing cerebral complications after arch surgery. Clinical outcomes were not significantly different between using ACP and DHCA alone or adjunct with RCP. However, ACP was the preferred method in complex arch operation when long circulatory arrest time was needed.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. Eur Heart J 2014;35:2873-926.
2. Okita Y, Takamoto S, Ando M, Morota T, Matsukawa R, Kawashima Y. Mortality and cerebral outcome in patients who underwent aortic arch operations using deep hypothermic circulatory arrest with retrograde cerebral perfusion: no relation of early death, stroke, and delirium to the duration of circulatory arrest. J Thorac Cardiovasc Surg 1998;115:129-38.
3. Estrera AL. Is retrograde cerebral perfusion dead? Eur J Cardiothorac Surg 2013;43:1071-2.
4. Staubach S, Soekeland K, Ledwoch J, Segerer M, Strohm H, Mudra H. Stroke rates after carotid artery stenting depend on study-specific definitions. EuroIntervention 2016;12:526-30.
5. Fischer U, Baumgartner A, Arnold M, Nedeltchev K, Gralla J, De Marchis GM, et al. What is a minor stroke? Stroke 2010;41:661-6.
6. Perreas K, Samanidis G, Thanopoulos A, Georgiopoulos G, Antoniou T, Khoury M, et al. Antegrade or retrograde cerebral perfusion in ascending aorta and hemiarch surgery? A propensity-matched analysis. Ann Thorac Surg 2016;101:146-53.
7. Ergin MA, Uysal S, Reich DL, Apaydin A, Lansman SL, McCullough JN, et al. Temporary neurological dysfunction after deep hypothermic circulatory arrest: a clinical marker of long-term functional deficit. Ann Thorac Surg 1999;67:1887-90.
8. Usui A, Miyata H, Ueda Y, Motomura N, Takamoto S. Risk-adjusted and case-matched comparative study between antegrade and retrograde cerebral perfusion during aortic arch surgery: based on the Japan Adult Cardiovascular Surgery Database: the Japan Cardiovascular Surgery Database Organization. Gen Thorac Cardiovasc Surg 2012;60:132-9.
9. Krüger T, Weigang E, Hoffmann I, Blettner M, Aebert H. Cerebral protection during surgery for acute aortic dissection type A: results of the German Registry for Acute Aortic Dissection Type A (GERAADA). Circulation 2011;124:434-43.
10. Griepp RB, Stinson EB, Hollingsworth JF, Buehler D. Prosthetic replacement of the aortic

arch. J Thorac Cardiovasc Surg 1975;70:1051-63.
11. Ehrlich MP, Ergin MA, McCullough JN, Lansman SL, Galla JD, Bodian CA, et al. Predictors of adverse outcome and transient neurological dysfunction after ascending aorta/hemiarch replacement. Ann Thorac Surg 2000;69:1755-63.
12. Griepp RB, Bonser R, Haverich A, Kazui T, Kouchoukos NT, Safi HJ, et al. Panel discussion: Session II–Aortic arch. Presented at Aortic Surgery Symposium X, New York, April 27-28, 2006. Ann Thorac Surg 2007;83:S824-31.
13. Mills NL, Ochsner JL. Massive air embolism during cardiopulmonary bypass. Causes, prevention, and management. J Thorac Cardiovasc Surg 1980;80:708-17.
14. Ueda Y, Miki S, Kusuhara K, Okita Y, Tahata T, Yamanaka K. Surgical treatment of aneurysm or dissection involving the ascending aorta and aortic arch, utilizing circulatory arrest and retrograde cerebral perfusion. J Cardiovasc Surg (Torino) 1990;31:553-8.
15. Coselli JS, LeMaire SA. Experience with retrograde cerebral perfusion during proximal aortic surgery in 290 patients. J Card Surg 1997;12:322-5.
16. Safi HJ, Letsou GV, Iliopoulos DC, Subramaniam MH, Miller CC, III, Hassoun H, et al. Impact of retrograde cerebral perfusion on ascending aortic and arch aneurysm repair. Ann Thorac Surg 1997;63:1601-7.
17. Bavaria JE, Pochettino A. Retrograde cerebral perfusion (RCP) in aortic arch surgery: efficacy and possible mechanisms of brain protection. Semin Thorac Cardiovasc Surg 1997;9:222-32.
18. Harrington DK, Fragomeni F, Bonser RS. Cerebral perfusion. Ann Thorac Surg 2007;83:S799-804.
19. Boeckxstaens CJ, Flameng WJ. Retrograde cerebral perfusion does not perfuse the brain in nonhuman primates. Ann Thorac Surg 1995;60:319-27.
20. Ye J, Yang L, Del Bigio MR, Summers R, Jackson D, Somorjai RL, et al. Retrograde cerebral perfusion provides limited distribution of blood to the brain: a study in pigs. J Thorac Cardiovasc Surg 1997;114:660-5.
21. Ehrlich MP, Hagl C, McCullough JN, Zhang N, Shiang H, Bodian C, et al. Retrograde cerebral perfusion provides negligible flow through brain capillaries in the pig. J Thorac Cardiovasc Surg 2001;122:331-8.
22. Oohara K, Usui A, Murase M, Tanaka M, Abe T. Regional cerebral tissue blood flow measured by the colored microsphere method during retrograde cerebral perfusion. J Thorac Cardiovasc Surg 1995;109:772-9.
23. Usui A, Oohara K, Liu TL, Murase M, Tanaka M, Takeuchi E, et al. Comparative experimental study between retrograde cerebral perfusion and circulatory arrest. J Thorac Cardiovasc Surg 1994;107:1228-36.
24. Hagl C, Khaladj N, Peterss S, Hoeffler K, Winterhalter M, Karck M, 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 2004;26:73-80.
25. Di Eusanio M, Schepens MA, Morshuis WJ, Di Bartolomeo R, Pierangeli A, Dossche KM. Antegrade selective cerebral perfusion during operations on the thoracic aorta: factors influencing survival and neurologic outcome in 413 patients. J Thorac Cardiovasc Surg 2002;124:1080-6.
26. Yan TD, Bannon PG, Bavaria J, Coselli JS, Elefteriades JA, Griepp RB, et al. Consensus on hypothermia in aortic arch surgery. Ann Cardiothorac Surg 2013;2:163-8.
27. Stecker MM, Cheung AT, Pochettino A, Kent GP, Patterson T, Weiss SJ, et al. Deep hypothermic circulatory arrest: I. Effects of cooling on electroencephalogram and evoked potentials. Ann Thorac Surg 2001;71:14-21.
28. James ML, Andersen ND, Swaminathan M, Phillips-Bute B, Hanna JM, Smigla GR, et al. Predictors of electrocerebral inactivity with deep hypothermia. J Thorac Cardiovasc Surg 2014;147:1002-7.
29. Kamiya H, Hagl C, Kropivnitskaya I, Bothig D, Kallenbach K, Khaladj N, 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.
30. Amarenco P, Duyckaerts C, Tzourio C, Henin D, Bousser MG, Hauw JJ. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. N Engl J Med 1992;326:221-5.
31. Blauth CI, Cosgrove DM, Webb BW, Ratliff NB, Boylan M, Piedmonte MR, et al. Atheroembolism from the ascending aorta. An emerging problem in cardiac surgery. J Thorac Cardiovasc Surg 1992;103:1104-11.
32. Wareing TH, Davila-Roman VG, Barzilai B, Murphy SF, Kouchoukos NT. Management of the

severely atherosclerotic ascending aorta during cardiac operations. A strategy for detection and treatment. J Thorac Cardiovasc Surg 1992;103: 453-62.