

Temperature Management for Aortic Arch Surgery

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Abstract

Surgical treatment of aortic arch disease is a technically challenging procedure that requires complex circulation management strategies involving the use of hypothermic circulatory arrest. The definition of hypothermia has evolved with comfort and surgical adjuncts. This review describes the various circulation and temperature management strategies used during hemiarch and total arch replacement.

Keywords

circulatory arrest, deep hypothermic circulatory arrest, therapeutic, hypothermia, aortic arch atheroma, neuroprotection

Introduction

Surgical therapy for aortic arch disease involves partial or complete replacement of the aortic arch with reimplantation of the great vessels while the cerebral blood flow is temporarily altered. Patients undergoing this mandatory period of circulatory arrest during arch replacement are at an increased risk for adverse neurologic outcomes, and strategies for cerebral protection must be implemented to achieve successful results. The optimal strategy for management of the circulation during aortic arch surgery remains controversial. Arch reconstruction has historically been associated with significant morbidity and mortality due to global ischemic end-organ damage occurring during the circulatory arrest period. As surgical techniques have evolved, survival has improved; however, neurologic dysfunction due to cerebral ischemia remains a significant concern.

Systemic hypothermia was the initial method of cerebral protection utilized during the period of circulatory arrest. The first successful series of arch reconstructions using deep hypothermic circulatory arrest (DHCA) with body temperatures of 18°C was reported in 1975.¹ Further efforts to improve cerebral protection during arch reconstruction have led to the development of antegrade cerebral perfusion (ACP) and retrograde cerebral perfusion (RCP) and the use of more moderate levels of hypothermia prior to the period of circulatory arrest. The optimal method of cerebral protection for aortic arch surgery remains a controversial topic and has yet to be determined.² In this review, we will describe the different strategies of cerebral protection that vary in temperature and the mode of cerebral perfusion.

Neurologic Injury and Hypothermia

As stated previously, arch replacement requires cessation of the native blood flow to the brain in order to reconstruct the arch and great vessels. This period of interruption of the native circulation has been termed “circulatory arrest” and provides a bloodless operative field to facilitate arch reconstruction. Patients undergoing arch replacement are at high risk for ischemic and embolic brain injury, and 2 different types of neurologic injury have been described: (1) permanent neurologic dysfunction (PND) and (2) temporary neurologic dysfunction (TND). PND, commonly referred to as stroke, manifests clinically as a focal deficit secondary to an embolism of particulate matter or air/gas bubbles that causes vascular occlusion resulting in an ischemic cerebral infarct. TND is a reversible, diffuse subtle injury that is attributed to inadequate cerebral protection.³ Patients with TND can experience confusion, agitation, delirium, prolonged obtundation, or parkinsonism without localizing signs in the immediate postoperative period. Brain imaging of this neurologic injury with computed tomography or magnetic resonance imaging is negative. TND is the clinical manifestation of a global cerebral ischemic injury.

In order to protect the end organs during the period of circulatory arrest, systemic hypothermia is utilized to reduce cellular metabolism. The brain, in particular, has an

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extraordinarily high metabolic rate that is 7.5 times the metabolism of nonnervous system tissues. Hypothermia has been shown to exponentially reduce cellular metabolism. When the brain temperature is reduced to 15°C, the cerebral metabolic rate is reduced to 84% of baseline values.⁴ Since the initial report of the use of DHCA for aortic arch replacement, cerebral protection and circulation management techniques have evolved to enable safe, reproducible arch replacement with excellent neurologic outcomes.¹

Deep Hypothermic Circulatory Arrest

“DHCA alone” or DHCA without adjunctive cerebral perfusion represents the simplest, most convenient form of cerebral protection. It does not require complex perfusion strategies or neuromonitoring and is the cerebral protection strategy of choice for surgeons who infrequently perform aortic arch reconstructions. After the initiation of cardiopulmonary bypass, systemic hypothermia is achieved by cooling the blood passing through the heat exchanger connected to the perfusion circuit. A temperature gradient (arterial inflow to venous return) that does not exceed 10°C is maintained during the cooling period to prevent the formation of gaseous emboli. The duration of the cooling period required to equilibrate blood and tissue temperatures is highly variable and is dependent on blood flow, temperature gradient (between perfusate and organs), and tissue-specific coefficients of temperature exchange. Patient-specific variables that affect cooling include occlusive vascular disease and body mass index.

There is no consensus regarding cooling strategies for HCA. Intraoperative monitoring of time, temperature, jugular venous bulb oxygen saturation, and electroencephalographic activity can assist in the evaluation of cerebral metabolic suppression during the cooling period. Temperature is monitored in many different sites including the inflow and outflow lines of the perfusion circuit and by probes inserted into the bladder, rectum, nasopharynx, and esophagus. In cases when DHCA without adjunctive cerebral perfusion is employed as the sole neuroprotection strategy, the esophageal or nasopharyngeal temperature should be used as the guide for initiation of HCA, as these sites have been shown to closely approximate brain temperature.⁵

Patients undergoing DHCA are cooled using cardiopulmonary bypass to a nasopharyngeal temperature of 14.1°C to 20°C. Once the goal temperature is achieved, cardiopulmonary bypass is halted to allow for a bloodless operative field and the arch reconstruction is performed. After completion of the arch reconstruction, cardiopulmonary bypass is reinstated with aggressive de-airing maneuvers. DHCA alone was used in Griep's initial successful series of arch replacements.¹

DHCA has been proven to provide excellent neuroprotection for arch replacements that require circulatory arrest times <40 minutes.^{6,7} In a contemporary series of 394 patients from the Yale group undergoing elective and emergent proximal and distal thoracic aortic repairs using DHCA alone, the mortality and stroke rates were 6.3% and 4.8%, respectively. The incidence of seizure and dialysis were 3.1% and 2.3%, respectively. The mean DHCA time was 31 minutes, and there was a trend toward an increased stroke risk in patients with a DHCA time exceeding 40 minutes.⁶ As surgeons began to perform more complex arch reconstructions with DHCA alone, it became clear that a sharp increase in adverse neurologic outcomes and mortality occurred when circulatory arrest times exceeded 30 minutes.⁶⁻⁸ This observation led to the introduction of adjunctive cerebral perfusion as an additional method of cerebral protection.

Retrograde Cerebral Perfusion

Retrograde cerebral perfusion was first described by Mills and Ochsner in the treatment of a massive air embolus during cardiopulmonary bypass.⁹ RCP is performed by cannulating and snaring the superior vena cava and infusing hypothermic arterial blood from the cardiopulmonary bypass circuit up the superior vena cava to perfuse the brain in a retrograde direction during the period of circulatory arrest. Generally accepted flow rates are 200 to 400 mL/min to maintain an SVC pressure of 15 to 25 mm Hg. If performed properly, RCP will produce dark blood (suggesting cerebral oxygen extraction) flowing retrograde into the open aortic arch during HCA. The theoretical cerebral protection benefits of RCP are (1) to flush embolic material (gaseous and particulate) from the cerebral circulation, (2) to maintain cerebral hypothermia by bathing the brain in cold blood, and (3) to support cerebral metabolism by providing sufficient cerebral flow during the period of HCA.

The addition of RCP to DHCA has markedly improved clinical outcomes following arch reconstruction. In a series of 479 patients undergoing elective and emergent arch repair, Coselli and Lemaire compared outcomes using DHCA (n = 189) versus DHCA + RCP (n = 290). The addition of RCP significantly reduced mortality (DHCA + RCP 3.4% vs DHCA 14.8%, $P < .001$) and stroke rates (DHCA + RCP 2.4% vs DHCA 6.5%, $P < .05$).¹⁰ In a series of 1107 arch repairs, Estrera et al compared outcomes using DHCA (n = 200) versus DHCA + RCP (n = 900). For the entire series, the mortality and stroke rates were 10.4% and 2.8%, respectively. In both univariate and multivariate analyses, the addition of RCP was protective against mortality ($P < .001$) and stroke ($P = .02$). However, the incidence of TND was 15.5% with relatively short mean RCP times of 26 minutes.¹¹ Although this is lower than the 25% incidence of TND associated with arch reconstruction using DHCA

alone,¹² it still represents a significant incidence of inadequate cerebral protection.

Selective Antegrade Cerebral Perfusion

De Bakey and colleagues were the first to successfully describe the use of selective antegrade cerebral perfusion (SACP) in the surgical repair of an arch aneurysm.¹³ In contrast to RCP, experimental data have confirmed the efficacy of SACP to provide adequate cerebral blood flow to support brain metabolism during the period of HCA. Numerous techniques have been described for the delivery of SACP. Bilateral SACP (bSACP) typically involves the introduction of perfusion cannulas into the ostia of the innominate and left carotid arteries via the open arch at the time of HCA. The disadvantages of this method include the risk of introducing air or atherosclerotic emboli and cluttering the operative field with additional cannulas. At Emory, the preferred method of cerebral perfusion is unilateral SACP (uSACP) via right axillary artery cannulation.^{14,15} An 8-mm graft is sewn end to side to the right axillary artery prior to sternotomy and used as the arterial inflow line to initiate cardiopulmonary bypass. At the time of HCA, blood flow is decreased to 10 mL/kg/min, and the base of the innominate and left common carotid arteries are occluded with vascular clamps. Left carotid occlusion is performed to pressurize the extracranial collateral system and minimize steal. This enables blood to flow via the right common carotid and right vertebral arteries to perfuse the brain and spinal cord. Critics of this technique argue that uSACP provides insufficient cerebral blood flow to the left cerebral hemisphere. However, both animal and clinical data have demonstrated that there is no significant difference in cerebral blood flow between unilateral and bilateral SACP, with and without an intact circle of Willis.^{16,17} Furthermore, data from a large, contemporary, propensity-matched analysis of 1097 patients undergoing arch replacement with HCA and SACP demonstrated no difference in morbidity and mortality between uSACP and bSACP. Interestingly, there was a trend toward a higher incidence of stroke in the bSACP group that was attributed to great vessel manipulation.¹⁸

Moderate Hypothermic Circulatory Arrest

The implementation of SACP as an adjunct to hypothermia for cerebral protection has prompted a departure from the use of deep hypothermia, to the use of moderate levels of hypothermia. The rationale behind this strategy is based on the concept that SACP has transformed total body circulatory arrest into lower body circulatory arrest. Since

cerebral perfusion is maintained with cold blood throughout the period of circulatory arrest, the primary purpose of systemic hypothermia is to provide protection to the visceral organs, skeletal muscle, and spinal cord via metabolic suppression. The metabolic rate of the visceral organs and skeletal muscle is significantly less than the brain; therefore, the visceral organs require a reduced degree of hypothermia for optimal protection and are more tolerant of ischemia. If ACP is used, the temperature that should be used to guide the initiation of hypothermic circulatory arrest should be the bladder or rectal temperatures. Since cold blood will be continuously perfusing the brain, it is visceral organ protection that becomes the primary goal of the utilization of systemic hypothermia.

Moderate hypothermic circulatory arrest (MHCA) and selective antegrade cerebral perfusion (MHCA/SACP) currently represents the preferred circulation management strategy for many high-volume aortic centers worldwide. At Emory, MHCA/uSACP is the standard cerebral protection method for elective and emergent, hemiarch and total arch replacements. Hemiarch replacement is routinely conducted at bladder temperatures of 28°C to 29°C with mortality rates in elective and emergent cases of 4.3% and 7.7%, respectively. There is a low incidence of PND (elective 1.9%, emergent 4.6%), TND (elective 3.8%, emergent 6.2%), and dialysis-dependent renal failure (elective 2.4%, emergent 9.2%) with this technique. Mean circulatory arrest times are 23 minutes in elective cases and 33 minutes in emergent cases.¹⁵ Total arch replacement is conducted at bladder temperatures of 25°C to 26°C for both emergent and elective cases. A recent review of 145 consecutive patients undergoing total arch replacement at Emory demonstrated an operative mortality of 9.7%. The incidence of PND, TND, and dialysis-dependent renal failure were 2.8%, 5.6%, and 2.8%, respectively. The mean duration of circulatory arrest for these patients was 55 minutes.¹⁹ Other high-volume aortic centers have reported similar outcomes confirming MHCA/SACP as a safe and effective strategy for circulation management in aortic arch surgery.²⁰⁻²²

Comparisons of Cerebral Protection Strategies

Currently, there is a lack of consensus regarding the optimal method of cerebral protection during arch reconstruction. Instead, the majority of high-volume aortic centers employ a variety of different techniques using varying degrees of hypothermia with or without adjunctive cerebral perfusion. Often the method of cerebral protection is based on institutional bias rather than outcome data. Contemporary cerebral protection strategies are composed of multiple clinical variables: arterial cannulation site,

temperature at the initiation of circulatory arrest, ACP versus RCP, and unilateral versus bilateral SACP. The majority of comparisons of cerebral protection strategies in the literature are essentially retrospective reviews of changes in circulation management strategies at any single institution over time. These comparisons are valuable, but limited by their retrospective nature, lack of randomization, and differences in several important variables including the extent of arch reconstruction, the temperature at HCA, ACP versus RCP, and the percentage of emergent cases.

Most high-volume aortic centers use either DHCA/RCP or MHCA/SACP for hemiarch replacements. A comprehensive review of the comparisons of the data between these 2 cerebral protection strategies is beyond the scope of this review. However, 2 recurring themes clearly emerge from analyses of the currently existing data in the literature: (1) an adjunct form of cerebral protection (SACP or RCP) is superior to DHCA alone and (2) the method of cerebral perfusion (SACP or RCP) has no impact on the incidence of stroke; however, SACP significantly reduces the incidence of TND. Furthermore, most experts agree that in patients undergoing extended/complex total arch reconstructions requiring prolonged periods of HCA, SACP is superior to RCP in preventing TND and is associated with improved overall neurologic outcomes.²³⁻²⁶

Selection of Cerebral Protection and Temperature Management Strategy

A comprehensive knowledge of the various cerebral protection strategies is required in order to tailor the approach to the patient's anatomy and comorbidities. In addition to the neuroprotection provided by the various methods described, one must strongly consider visceral organ protection during these arch reconstructive procedures requiring circulatory arrest. The aforementioned strategies all have advantages and disadvantages that must be considered prior to surgery. The main advantages of deep hypothermia include a bloodless operative field and maximum suppression of cellular activity. This unequivocally provides the greatest level of end-organ protection during the ischemic period. The disadvantage of deep hypothermia is that it requires a prolonged period of cardiopulmonary bypass to cool and rewarm the patients, which can have detrimental effects on the lungs, liver, and kidneys. Deep hypothermia has also been associated with vascular endothelial dysfunction, bleeding complications, and an increased systemic inflammatory response that can pose significant challenges in the peri- and postoperative settings.²⁷⁻³⁰ Accordingly, more moderate levels of hypothermia require shorter periods of cardiopulmonary bypass; however, this results in a reduced degree of metabolic suppression and requires the addition of ACP. MHCA may not result in clinically relevant organ dysfunction; however, lactate production

following visceral organ reperfusion appears to be higher with the use of MHCA.

In patients who are undergoing primary sternotomy and hemiarch replacement that will require a short (<30 minute) circulatory arrest time, any of the neuroprotection strategies can be employed with excellent outcomes. However, it is our opinion that patients with preoperative evidence of visceral organ dysfunction (eg, renal or liver due to chronic disease or malperfusion in the setting of aortic dissection) may benefit from colder temperatures (<28°C bladder) if using a strategy of MHCA/SACP. Anatomic issues that may preclude the strategy of right axillary artery cannulation and MHCA/SACP and the use of an alternative neuroprotective strategy include (1) an aberrant right subclavian artery, (2) the origination of the innominate artery from the false lumen in the setting of aortic dissection, or (3) the presence of thrombus in the false lumen of a dissected innominate or right common carotid at the time of acute type A aortic dissection repair. A detailed examination of the arch and great vessel anatomy on the preoperative imaging is critical to patient outcomes and may alter the circulation management plan.

Reoperative arch operations are extremely challenging, and careful preoperative planning regarding the arterial cannulation site, temperature management, and mode of cerebral perfusion is required to ensure optimal outcomes. Strong consideration should be given to right axillary artery and femoral venous cannulation in the setting of contained rupture or situations in which there is a high risk of aortic injury on sternal reentry. This cannulation strategy allows for the rapid initiation of cardiopulmonary bypass. It also enables the use of uSACP with either DHCA or MHCA. If there is aortic rupture or injury on sternal reentry, we favor the use of DHCA, as there will be a period of circulatory arrest without cerebral perfusion required to dissect out the heart and great vessels. However, RCP or SACP can be initiated once the appropriate structures are freely dissected. If the mediastinum is safely entered in the reoperative setting, DHCA or MHCA can be used, depending on the factors previously stated such as extent of arch reconstruction and patient comorbidities. Table 1 lists the advantages and disadvantages of the various methods of circulation management strategies.

Conclusions

Advancements in surgical techniques and cerebral protection strategies over the past 40 years have enabled surgeons to treat complex aortic arch pathology with excellent outcomes in the current era. Adverse neurologic outcomes remain the primary concern in surgical reconstruction of the aortic arch. A comprehensive understanding of the various temperature and circulation management strategies

Table 1. Advantages and Disadvantages of Commonly Used Cerebral Protection Strategies.

Strategy	Advantages	Disadvantages
DHCA (nasopharyngeal temperature 14.1° to 20.0°C)	<ul style="list-style-type: none"> • Simplicity • Bloodless operative field • Maximum cellular metabolic suppression 	<ul style="list-style-type: none"> • Safe duration: 30 minutes • Increased neurologic injury and mortality when DHCA > 30 minutes • Prolonged cardiopulmonary bypass • Increased systemic inflammatory response • Increased vascular endothelial dysfunction
DHCA + RCP (nasopharyngeal temperature 14.1°C to 20.0°C)	<ul style="list-style-type: none"> • Maximum cellular metabolic suppression • Highly effective in flushing embolic material (gaseous and particulate) from the cerebral circulation • Maintains cerebral hypothermia during circulatory arrest 	<ul style="list-style-type: none"> • Poor cerebral blood flow • Ineffective in supporting cerebral metabolism • Significant improvement in neurologic and overall outcomes compared to DHCA alone • Significant incidence of TND with prolonged circulatory arrest times
MHCA + SACP (nasopharyngeal temperature 20.1°C to 28°C; bladder temperature 28°C to 32°C)	<ul style="list-style-type: none"> • Reduced cardiopulmonary bypass times • Significant cerebral blood flow • Effective in supporting cerebral metabolism • Effective cerebral protection for extended circulatory arrest times • SACP superior to RCP in the prevention of TND 	<ul style="list-style-type: none"> • Reduced cellular metabolic suppression compared to DHCA • SACP requires manipulation of the innominate ± carotid arteries

Abbreviations: DHCA, deep hypothermic circulatory arrest; RCP, retrograde cerebral perfusion; SACP, selective antegrade cerebral perfusion; TND, temporary neurologic dysfunction.

allow for a nuanced approach to aortic arch replacement that can be tailored to each individual patient.

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References

1. Griep RB, Stinson EB, Hollingsworth JF, Buehler D. Prosthetic replacement of the aortic arch. *J Thorac Cardiovasc Surg.* 1975;70:1051-1063.
2. Leshnowar BG, Chen EP. Cerebral protection strategies for aortic arch surgery. In: Nazari S, ed. *Front Lines of Thoracic Surgery.* doi:10.5772/26099. <http://www.intechopen.com/books/front-lines-of-thoracic-surgery/surgical-therapy-for-diseases-of-the-aortic-arch>. Accessed September 23, 2016.
3. Ergin MA, Griep EB, Lansman SL, Galla JD, Levy M, Griep RB. Hypothermic circulatory arrest and other methods of cerebral protection during operations on the thoracic aorta. *J Card Surg.* 1994;9:525-537.
4. McCullough JN, Zhang N, Reich DL, et al. Cerebral metabolic suppression during hypothermic circulatory arrest in humans. *Ann Thorac Surg.* 1999;67:1895-1921.
5. Stone JG, Young WL, Smith CR, et al. Do standard monitoring sites reflect true brain temperature when profound hypothermia is rapidly induced and reversed? *Anesthesiology.* 1995;82:344-351.
6. Gega A, Rizzo JA, Johnson MH, Tranquilli M, Farkas EA, Elefteriades JA. Straight deep hypothermic arrest: experience in 394 patients supports its effectiveness as a sole means of brain preservation. *Ann Thorac Surg.* 2007;84:759-767.
7. 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.* 1993;106:19-31.

8. Ehrlich MP, Ergin MA, McCullough JN, et al. Predictors of adverse outcome and transient neurologic dysfunction after ascending aorta/hemiarch replacement. *Ann Thorac Surg.* 2000;69:1755-1763.
9. Mills NL, Ochsner JL. Massive air embolism during cardiopulmonary bypass: causes, preventions, and management. *J Thorac Cardiovasc Surg.* 1980;80:708-717.
10. Coselli JS, Lemaire SA. Experience with retrograde cerebral perfusion during proximal aortic surgery in 290 patients. *J Card Surg.* 1997;12:322-325.
11. Estrera AL, Miller CC 3rd, Lee TY, Shah P, Safi HJ. Ascending and transverse aortic arch repair: the impact of retrograde cerebral perfusion. *Circulation.* 2008;118:S160-S166.
12. Ergin MA, Uysal S, Reich DL, et al. Temporary neurological dysfunction after deep hypothermic circulatory arrest: a clinical marker of functional deficit. *Ann Thorac Surg.* 1999;67:1887-1890.
13. De Bakey ME, Crawford ES, Cooley DA, Morris GC Jr. Successful resection of fusiform aneurysm of the aortic arch with replacement homograft. *Surg Gynecol Obstet.* 1957;105:657-664.
14. Halkos ME, Kerendi F, Myung R, Kilgo P, Puskas JD, Chen EP. Selective antegrade cerebral perfusion via right axillary artery cannulation reduces morbidity and mortality after proximal aortic surgery. *J Thorac Cardiovasc Surg.* 2009;138:1081-1089.
15. Leshnower BG, Myung RJ, Thourani VH, et al. Hemiarch replacement at 28°C: an analysis of mild and moderate hypothermia in 500 patients. *Ann Thorac Surg.* 2012;93:1910-1915.
16. Ye J, Dai G, Ryner LN, et al. Unilateral antegrade cerebral perfusion through the right axillary artery provides uniform flow distribution to both hemispheres of the brain: a magnetic resonance and histopathological study in pigs. *Circulation.* 1999;(19 suppl):II309-315.
17. 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;33:402-408.
18. Zierer A, Risteski P, El-Sayed Ahmad A, Moritz A, Diegeler A, Urbanski PP. The impact of unilateral versus bilateral antegrade cerebral perfusion on surgical outcomes after aortic arch replacement: a propensity-matched analysis. *J Thorac Cardiovasc Surg.* 2014;147:1212-1217.
19. Leshnower BG, Kilgo PD, Chen EP. Total arch replacement using moderate hypothermic circulatory arrest and unilateral selective antegrade cerebral perfusion. *J Thorac Cardiovasc Surg.* 2014;147:1488-1492.
20. Zierer A, El-Sayed Ahmad A, Papadopoulos N, Moritz A, Diegeler A, Urbanski PP. 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;144:1042-1050.
21. Khaladj N, Shrestha M, Meck S, et al. Hypothermic circulatory arrest with selective antegrade cerebral perfusion in ascending aortic and aortic arch surgery: a risk factor analysis for adverse outcome in 501 patients. *J Thorac Cardiovasc Surg.* 2008;135:908-914.
22. Tsai JY, Pan W, Lemaire SA, et al. Moderate hypothermia during aortic arch surgery is associated with reduced risk of early mortality. *J Thorac Cardiovasc Surg.* 2013;146:662-667.
23. Griep RB, Bonser R, Haverich A, et al. Panel discussion: Session II—aortic arch, from the Aortic Surgery Symposium X. *Ann Thorac Surg.* 2007;83:S824-S831.
24. 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;93:1502-1508.
25. 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 Cardiovascular Surgery Database: the Japan Cardiovascular Surgery Database Organization. *Gen Thorac Cardiovasc Surg.* 2012;60:132-139.
26. Barnard J, Dunning J, Grossebner M, Bittar MN. In aortic arch surgery is there any benefit in using antegrade cerebral perfusion or retrograde cerebral perfusion as an adjunct to hypothermic circulatory arrest? *Interact Cardiovasc Thorac Surg.* 2004;3:621-630.
27. Mora Mangano CT, Neville MJ, Hsu PH, Mignea I, King J, Miller DC. Aprotinin, blood loss and renal dysfunction in deep hypothermic circulatory arrest. *Circulation.* 2001;104:276-281.
28. Cooper WA, Duarte IG, Thourani VH, et al. Hypothermic circulatory arrest causes multi-system vascular endothelial dysfunction and apoptosis. *Ann Thorac Surg.* 2000;69:696-702.
29. Livesay JJ, Cooley DA, Reul GJ, et al. Resection of aortic arch aneurysms: a comparison of hypothermic techniques in 60 patients. *Ann Thorac Surg.* 1983;36:19-28.
30. Qing M, Vazquez-Jimenez JF, Klosterhalfen B, et al. Influence of temperature during cardiopulmonary bypass on leukocyte activation, cytokine balance, and post-operative organ damage. *Shock.* 2001;15:372-377.