Original Article

Increased cerebrovascular resistance after retrograde cerebral perfusion: A Doppler study

Nobuhide Kin[1],*, Nagara Ono[2], Yoshiteru Mori[1], Jun Ninagawa[1], Yoshitsugu Yamada[1]

[1] *Department of Anesthesiology, The University of Tokyo, Bunkyo, Tokyo, Japan;*
[2] *Department of Anesthesiology, Mitsui Memorial Hospital, Chiyoda, Tokyo, Japan.*

Summary	Deep hypothermic circulatory arrest (DHCA) with retrograde cerebral perfusion (RCP) under high central venous pressure (CVP) is often used in aortic arch surgery under cardiopulmonary bypass (CPB). We hypothesized that DHCA with RCP under high CVP causes cerebral vascular compression because of increased perivascular pressure due to extravasation of fluid into intracranial tissue. In a retrospective study, we evaluated the pulsatility index (PI) and resistance index (RI) of the internal carotid arteries (ICA) and external carotid arteries (ECA) before and after CPB in 15 patients who underwent DHCA/RCP (group 1) and 17 patients who underwent regular CPB without DHCA/RCP (group 2). Both indices are known to reflect vascular resistance distal to the measurement point. The PI and RI of the ICA increased significantly after the procedure in group 1 but did not change in group 2. The PI and RI of the ECA did not change in either group. In group 1, the rate of increase in PI and RI correlated with the duration of RCP, which was significantly higher in patients who had postoperative delirium than in patients who did not experience postoperative delirium. As increases in PI/RI after DHCA/RCP occurred only in the ICA, we concluded that the changes were due to compression of vessels as a result of increased perivascular pressure. The greater increase in the PI/RI in patients who experienced postoperative delirium indicates that increased perivascular pressure plays a role in the occurrence of postoperative delirium after DHCA/RCP.

Keywords: Pulsatility index, resistance index, transesophageal echocardiography, delirium

1. Introduction

In complicated thoracic aortic surgeries using cardiopulmonary bypass (CPB), circulatory arrest is needed to obtain a bloodless surgical field (*1*). During circulatory arrest, either selective cerebral perfusion (SCP) or retrograde cerebral perfusion (RCP) with deep hypothermia is performed for cerebral protection (*2*). SCP is employed in many institutions but requires extra arterial cannulation and, in some cases, an extra arterial pump; thus, it is relatively complicated and time-consuming (*3*). In contrast, RCP can be instituted easily just by clamping the venous drainage tube of the inferior vena cava (IVC), snaring the superior vena

cava (SVC) cannula, and counter-rotating the CPB pump (*4*). However, this method is associated with two major concerns: insufficient cerebral oxygen supply (*5*) and cerebral edema with increased intracranial pressure due to high venous pressure (*6*). Cerebral edema caused by RCP has been found in animal models (*6,7*) but not specifically in humans. Because the intracranial space is limited by the cranium, cerebral edema can cause pressurization of the non-parenchymal area, vessels, and cerebral ventricles. When intracranial vessels are pressurized from the outside, their vascular resistance increases (*8,9*).

In the current study, Doppler echocardiography was used to evaluate the carotid arteries to determine whether cerebral vessel resistance increases after RCP. Intra-operative transesophageal echocardiography (TEE) was performed during the surgeries except where contraindicated. Carotid artery flow was detected with a TEE probe at the pharynx (*10,11*). In some patients, blood flow was followed distal to the carotid

*Address correspondence to:
 Dr. Nobuhide Kin, Department of Anesthesiology, The University of Tokyo, 7-3-1 Hongo, Bunkyo, Tokyo, 113-8655, Japan.
E-mail: nkin-tky@umin.net

bifurcation between the ICA and ECA. The peak systolic velocity (PSV), end-diastolic velocity (EDV), and mean velocity (MV) were measured using pulsed-wave Doppler ultrasound (*12,13*). The pulsatility index (PI) and resistance index (RI) are known to reflect vascular resistance distal to the position where the Doppler signal is received (*14,15*). PI is calculated as (PSV-EDV)/MV and RI as (PSV-EDV)/PSV. PI and RI were used to determine whether signs of increased cerebral vascular resistance were present after RCP.

2. Materials and Methods

2.1. *Patients*

This study was approved by the internal review board of the University of Tokyo Hospital. Informed consent was waived because of the retrospective nature of the study. Written informed consent for intra-operative TEE was obtained preoperatively. Data used were from carotid artery Doppler flow studies of 32 adult patients who underwent cardiovascular surgery at this institution between July 2008 and October 2010.

2.2. *Data collection*

Baseline Doppler data were collected when the TEE probe was inserted into the patient's esophagus. Post-CPB Doppler data were obtained just before the TEE probe was withdrawn from the patient's esophagus at the end of surgery. The carotid arteries were evaluated whenever they were easily visualized at the time of probe insertion and withdrawal to ensure that no pathology in these vessels was missed before surgery and that no new lesion was present after the surgery. The carotid artery was identified on one side or the other and traced peripherally towards the carotid bulb using color flow Doppler imaging. After the bifurcation at the carotid bulb, the vessel with flow parallel to the Doppler beam was the ICA, and the vessel with flow at an oblique angle to the Doppler beam was the ECA (*11*). Blood flow in the ICA and ECA was recorded Using pulsed-wave Doppler. At least three consecutive heartbeats were recorded and the average PI and RI calculated. Heart rate (HR), mean arterial blood pressure (MAP), hematocrit, and $PaCO_2$ were also recorded at the time of the Doppler measurements. Data from patients who were not in sinus or atrial pacing rhythm were excluded from analysis.

RCP was used in all cases in which deep hypothermic circulatory arrest (DHCA) was employed (group 1). When the tympanic temperature reached 18°C, CPB pump flow was stopped and the aortic aneurysm opened. RCP was performed by perfusing oxygenated blood through the SVC cannula as the IVC cannula was occluded and the SVC snared (*16*). The CPB flow rate was adjusted and periodically changed from 150 mL/min to 800 mL/min every 30 sec to vary the SVC pressure from 25 mmHg to 35 mmHg. This is designated 'RCP with intermittent pressure augmentation (IPA-RCP)' (*17,18*) and was used in all RCP cases. The target for the lowest rectal temperature during regular CPB without DHCA (group 2) was 32°C. In both groups, general anesthesia was induced with 5 mg/kg thiopental and 2 mcg/kg fentanyl, and end-tracheal intubation was facilitated with 0.1 mg/kg vecuronium. Anesthesia was maintained with 1% to 2% of sevoflurane and supplemental fentanyl. No additional medication for neuroprotection was given. The α-stat method of pH control was used in all cases. At the time of aorta cross-clamp release, low doses of catecholamine (dopamine 3-5 mcg/kg/min) and vasodilators (nitroglycerin 0.3-0.5 mcg/kg/min, nicardipine 0.5-1 mg/h) were started and continued until after the patients were transferred to the intensive care unit.

Bilateral cerebral oxygen saturation (ScO_2) was monitored continuously in all patients using near infrared spectroscopy (NIRO 200, Hamamatsu Photonics, Hamamatsu, Japan). ScO_2 values usually decrease during CPB and return to pre-operative values after termination of CPB. The change from the baseline, when initial PI and RI data were collected, was calculated for the minimal value during CPB and for the value at the end of surgery, when post-CPB PI and RI data were collected. The presence of postoperative delirium was determined by reviewing patient records from the intensive care unit after surgery.

2.3. *Statistical analysis*

Analysis of variance (ANOVA) with the Best-Hsu's MCB test was used to compare groups 1 and 2. Wilcoxon matched-pair sign-rank tests were used to compare the baseline and post-CPB values in each group.

3. Results

3.1. *Patient demographics*

The mean patient age was 65.3 ± 17.5 years. Of the 32 patients, 22 (69%) were male. Twenty-two patients underwent thoracic aortic surgery (*n* = 15 in group 1 and *n* = 7 in group 2). Ten patients underwent valve surgery with regular CPB (*n* = 15 in group 1 and *n* = 17 in group 2). Operating time, CPB time, and the total amount of fentanyl did not differ in groups 1 and 2 (Table 1). In both groups, HR was higher and the bispectral index (BIS) was lower after CPB compared to the baseline, but MAP, hematocrit, end-tidal sevoflurane, nasopharyngeal temperature, and $PaCO_2$ did not differ before and after CPB in either group or between the two groups (Table 2). The doses

Table 1. Operating, CPB, and RCP time

Items	Group 1 (n = 15)	Group 2 (n = 17)	p-value
Operating time (min)	435 ± 119	381 ± 108	0.2545
CPB time (min)	213 ± 55	188 ± 79	0.2847
Total amount of fentanyl (mcg/kg)	19 ± 18	23 ± 11	0.3626
DHCA time (min)	61 ± 23	N/A	N/A
RCP time (min)	53 ± 35	N/A	N/A

Data reported as means ± standard deviation. CPB, cardiopulmonary bypass; RCP, retrograde cerebral perfusion; DHCA, deep hypothermic circulatory arrest; N/A, not applicable.

Table 2. Vital signs and blood gas analysis

Items	Group 1 (n = 15)		Group 2 (n = 17)	
	Baseline	Post CPB	Baseline	Post CPB
HR (beat/min)	61 ± 10	81 ± 13*	62 ± 8	88 ± 15*
MAP (mmHg)	63 ± 15	79 ± 18	72 ± 16	76 ± 13
Hematocrit (%)	32.9 ± 3.8	32.2 ± 3.3	32.4 ± 3.7	32.0 ± 3.9
PaCO$_2$ (mmHg)	39.5 ± 5.8	37.6 ± 6.2	38.5 ± 3.6	39.9 ± 4.8
EtSEV (%)	1.0 ± 0.4	1.0 ± 0.9	1.2 ± 0.6	1.1 ± 0.8
BIS	53 ± 8.2	41 ± 9.5*	49 ± 10.1	39 ± 11.3*
TEMP naso (°C)	35.5 ± 0.6	36.0 ± 0.9	35.9 ± 0.7	36.1 ± 0.8

Data reported as mean ± standard deviation. HR, heart rate; MAP, mean arterial pressure; EtSEV, end-tidal sevoflurane; BIS, bispectral index; TEMP naso, nasopharyngeal temperature; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; RCP, retrograde cerebral perfusion. * $p < 0.05$ between the baseline and post-CPB in each group.

of catecholamine and vasodilators administered in the operating room did not differ for the groups.

3.2. PI and RI of ICA and ECA

The baseline PI and RI of the ICA did not differ between groups 1 and 2, but the post-CPB PI and RI of the ICA were higher in group 1 than in group 2. In the ECA, neither the baseline indices nor post-CPB PI and RI differed between the two groups. In group 1, the PI and RI of the ICA increased significantly after CPB compared to the baseline, but in group 2 the indices did not change after CPB. The PI and RI of the ECA did not change significantly after CPB in either group (Table 3, Figure 1). No patient suffered permanent neurological damage after the procedure. However, eight patients (four in each group) had temporary postoperative delirium while in the intensive care unit. Patients who experienced delirium were significantly older (75.0 *vs.* 61.4 years old, $p < 0.05$) than patients who did not experience delirium. The operating time, CPB time, hematocrit, MAP, ScO$_2$, and BIS did not differ between the patients who experienced delirium and patients who did not. In group 1, the patients who experienced delirium tended to be older (68.8 *vs.* 58.0 years, $p > 0.05$) and have a longer RCP time (37.8 *vs.* 87.5 min, $p < 0.05$) than the patients who did not experience delirium. Patients with delirium tended to have a higher post-CPB PI and RI of the ICA, and the increase in the PI and RI of the ICA after CPB was significantly higher

Table 3. Pulsatility and resistance indices of the internal carotid artery (a) and the external carotid artery (b)

(a)

ICA	PI		RI	
	Baseline	Post-CPB	Baseline	Post-CPB
Group 1 (n = 15)	1.53 ± 0.48	2.13 ± 0.67*	0.73 ± 0.11	0.84 ± 0.09*
Group 2 (n = 17)	1.78 ± 0.50	1.73 ± 0.48#	0.77 ± 0.08*	0.75 ± 0.07#

(b)

ECA	PI		RI	
	Baseline	Post-CPB	Baseline	Post-CPB
Group 1 (n = 15)	2.05 ± 0.53	1.97 ± 0.54	0.83 ± 0.06	0.82 ± 0.07
Group 2 (n = 17)	1.87 ± 0.51	1.95 ± 0.58	0.83 ± 0.09	0.85 ± 0.10

Data reported as mean ± standard deviation. ICA, internal carotid artery; PI, pulsatility index; RI, resistance index; CPB, cardiopulmonary bypass; ECA, external carotid artery. * $p < 0.05$ between the baseline and post-CPB. # $p < 0.05$ between group 1 and group 2.

than that in patients who did not experience delirium (Table 4). Moderate correlations were found between RCP time and increased ICA PI and RI (Figure 2). In group 2, the PI/RI of the patients who experienced delirium did not differ from the PI/RI of the patients who did not experience delirium.

3.3. ScO$_2$ changes

The average change in right and left ScO$_2$ from the baseline to the minimum value during CPB was significantly larger in group 1 than in group 2, but it did not differ between the two groups from the baseline to the end of surgery (Table 5). In group 1, the average change in right and left ScO2 from the baseline to the minimum value during CPB did not differ between patients who experienced delirium and patients who did not (39.2 *vs.* 34.4%, $p > 0.05$). No correlation was found between the extent of the increase in PI/RI and the average change in ScO$_2$ from the baseline to the minimum value during CPB in group 1.

4. Discussion

In the present retrospective study, the PI and RI of the ICA, but not of the ECA, increased after CPB when DHCA with RCP was used. As the PI and RI are known to reflect resistance distal to the measurement point (*14,15*), results indicated that DHCA with RCP, but not regular CPB without DHCA, increases the resistance of cerebral vessels distal to the ICA.

Cerebral blood flow and cerebrovascular resistance are affected by many factors, including cerebral electrophysiological activity, MAP, hematocrit, PaCO$_2$, temperature, anesthetics, catecholamines, and vasodilators (*20-23*). BIS decreased during CPB, possibly reflecting reduced cerebral electrophysiological activity. Such activity can reduce cerebral blood flow and increase cerebrovascular resistance. The increase in HR after CPB may have
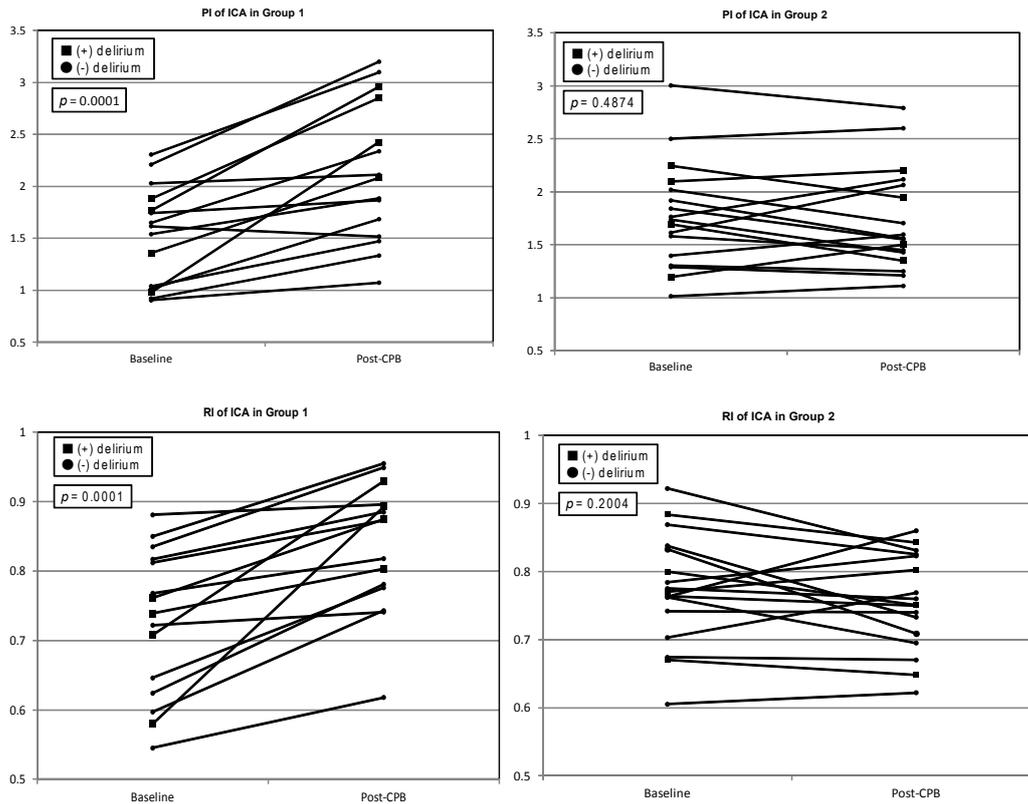
Figure 1. Pulsatility indices (PI) and resistance indices (RI) of the internal carotid artery (ICA) in group 1 (CPB with DHCA/RCP) and in group 2 (regular CPB without DHCA/RCP) patients.

Table 4. Pulsatility and resistance indices of the internal carotid artery of the patients in Group 1

| Items	PI			RI		
	Baseline	Post-CPB	PI ratio	Baseline	Post-CPB	RI ratio
Delirium (-) (*n* = 11)	1.54 ± 0.51	2.16 ± 0.29*	1.30 ± 0.22	0.74 ± 0.12	0.81 ± 0.03*	1.12 ± 0.08
Delirium (+) (*n* = 4)	1.50 ± 0.41	2.43 ± 0.46*	1.80 ± 0.46#	0.70 ± 0.08	0.87 ± 0.05*	1.27 ± 0.20#

Data reported as mean ± standard deviation. PI, pulsatility index; RI, resistance index; CPB, cardiopulmonary bypass. PI ratio = (post-CPB PI)/(baseline PI); RI ratio = (post-CPB RI)/(baseline RI). * $p < 0.05$ between the baseline and post-CPB. # $p < 0.05$ between Delirium (-) and Delirium (+).

affected the PI and RI, but the similar changes in BIS and HR in both groups do not explain why the PI and RI of the ICA increased only in group 1. Similar doses of fentanyl, catecholamine, and vasodilators were given to patients in both groups, so they should not have affected the groups differently. In addition, MAP, hematocrit, $PaCO_2$, end-tidal sevoflurane, and nasopharyngeal temperature did not differ between the baseline and the end of surgery. Thus, the increase in cerebrovascular resistance after DHCA with RCP was a result of some other factor(s).

One explanation is that DHCA with RCP may have increased the basic tone of the vessels. If vessels become hypercontractile, the PI and RI of the ECA would be similarly affected by the elevated capillary pressure. Since the indices did not change significantly after CPB in group 1, increased vascular tone is not likely to be a major mechanism. Another possible explanation is an increase in perivascular interstitial pressure around the vessel. During RCP, the SVC pressure was increased up to 35 mmHg. With this high pressure, fluid extravasation probably occurs from the venous lumen through the vessel wall into the extravascular space. Because the intracranial space is limited, extravasation of fluid into the cerebral parenchyma would cause an exaggerated increase in the perivascular pressure and compress the extra-parenchymal arteries and parenchymal arterioles, which are major resistance vessels (*24,25*). This scenario would lead to increased PI and RI in the ICA. DHCA with RCP could also have caused edema in the extracranial tissue, but unlike the intracranial space, the extracranial space is not limited by the cranium. Thus, tissue edema would not pressurize the arteries and arterioles and the PI and RI of the ECA would not increase.

Four of the five patients who had a RCP time of more than one hour experienced postoperative delirium.
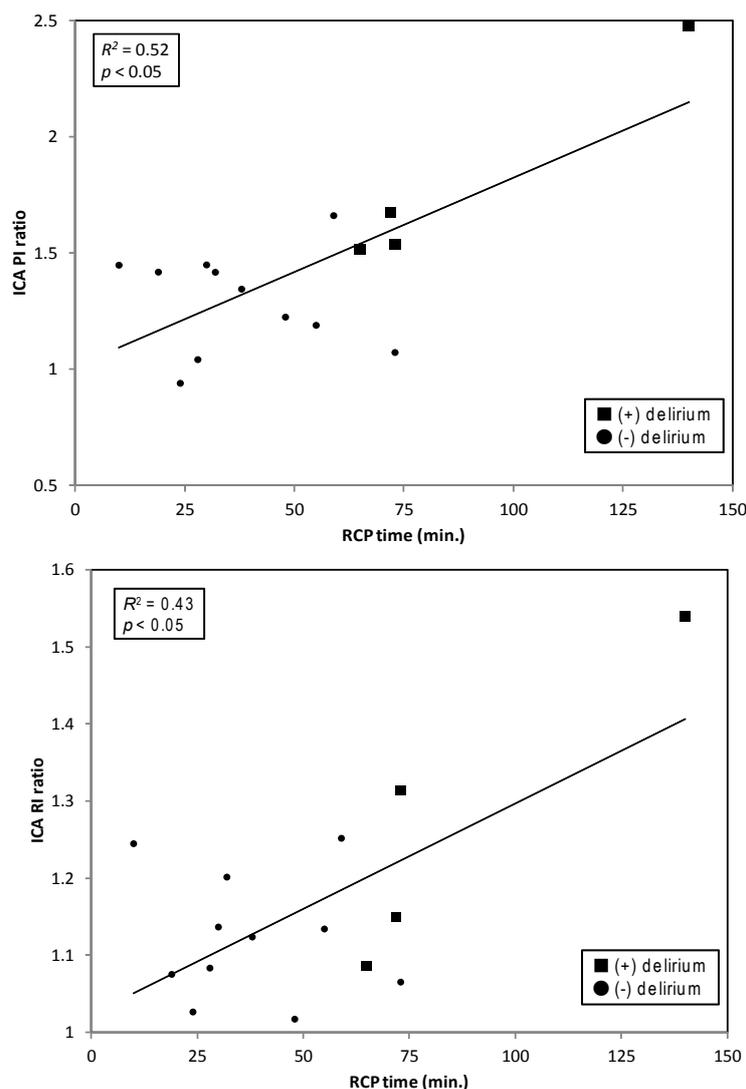
Figure 2. Relationship between the retrograde cerebral perfusion (RCP) time and the pulsatility index ratio (PI) and resistance index (RI) ratio of the post-CPB to the baseline.

Table 5. Change in ScO_2 from the baseline (%)

Items	Min. during CPB	End of surgery
Group 1 ($n = 15$)	-35.6 ± 14.3	-1.1 ± 9.4
Group 2 ($n = 17$)	$-20.0 \pm 8.4^{\#}$	-4.4 ± 8.4

Data reported as mean ± standard deviation. Min. = the minimum value. $^{\#}p < 0.05$ between group 1 and 2.

A moderate correlation was found between the change in the PI/RI of the ICA and the duration of RCP. Moreover, four of the five patients whose PI increased more than 50% after DHCA with RCP experienced postoperative delirium. This finding indicates that increased perivascular pressure may play some role in causing delirium after DHCA with RCP. RCP causes cerebral edema in animal models (*6,7*). Although this trend has not been verified in humans, a central venous pressure (CVP) as high as 35 mmHg is speculated to cause extravasation of fluid from intracranial blood vessels. In both groups, the patients who experienced delirium tended to be older. Patient age has been shown to be an important factor in the occurrence of delirium after cardiac surgery. Other factors associated with postoperative delirium include renal impairment, chronic lung disease, extracardiac arteriopathy, poor mobility, and electrolyte disturbances (*26*). In the present retrospective study, RCP duration tended to be longer for older patients. Most likely, patient age and other factors, and not the increased perivascular pressure itself, were the major causes of postoperative delirium.

ScO_2 was monitored with near infrared spectroscopy in all cases. A number of studies have shown that RCP may not provide enough oxygen to the brain during DHCA (*27-30*), which is consistent with the current findings although the two groups had a similar incidence of postoperative delirium. In group 1, the decrease in ScO_2 during CPB was not related to the occurrence of postoperative delirium. Thus, cerebral ischemia during DHCA with RCP may not be a major cause of postoperative delirium.

No patient underwent DHCA without RCP because performing DHCA without any measure aimed at providing oxygen to the brain is not standard practice. As selective antegrade cerebral perfusion was not performed at this institution during the period studied, data on this method are not available.

The PI and RI data for the ICA and ECA were collected from only some of the patients who underwent intra-operative TEE. Some patients had a high bifurcation of the ICA and ECA and each vessel could not be followed with the TEE probe. In addition, only one side of the carotid artery could be examined in some patients, which was probably due to the acoustic effect of the endotracheal tube. Therefore, the laterality of the change could not always be assessed.

Doppler flow data can be obtained for the ICA and ECA by transcutaneous carotid artery sonography rather than a TEE probe, but using a hand-held probe under all the surgical drapes and instruments is cumbersome and carries the risk of contaminating the sterile surgical field. In addition, checking the carotid artery flow intra-operatively, especially during aortic arch surgery, has other advantages, such as the detection of carotid malperfusion during CPB, finding a carotid dissection resulting from aortic cannulation, and confirming that debris is not flowing distally in the carotid artery at the time of aortic manipulation (*31*). Such intra-operative carotid monitoring can also be used during cannulation of the internal jugular vein (*32*). The current study suggests that monitoring carotid artery flow could also be used to detect potentially abnormal cerebrovascular dynamics.

In conclusion, the PI and RI of the ICA, but not of the ECA, increased after DHCA with RCP. These indices did not change after regular CPB without DHCA. Because the PI and RI are indicators of vascular resistance distal to the measurement site, these results indicate that cerebral vascular resistance increases after DHCA with RCP but does not change after regular CPB. This phenomenon can be explained by increased perivascular pressure, which potentially contributes to delirium after cardiac surgery with DHCA and RCP.

References

1. Graham JM, Stinnett DM. Operative management of acute aortic arch dissection using profound hypothermia and circulatory arrest. Ann Thorac Surg. 1987; 44:192-198.
2. Bachet J, Guilmet D. Brain protection during surgery of the aortic arch. J Card Surg. 2002; 17:115-124.
3. Ogino H, Sasaki H, Minatoya K, Matsuda H, Tanaka H, Watanuki H, Ando M, Kitamura S. Evolving arch surgery using integrated antegrade selective cerebral perfusion: Impact of axillary artery perfusion. J Thorac Cardiovasc Surg. 2008; 136:641-648.
4. Ergin MA, Griepp EB, Lansman SL, Galla JD, Levy M, Griepp RB. Hypothermic circulatory arrest and other methods of cerebral protection during operations on the thoracic aorta. J Card Surg. 1994; 9:525-537.
5. Griepp RB, Juvonen T, Griepp EB, McCollough JN, Ergin MA. Is retrograde cerebral perfusion an effective means of neural support during deep hypothermic circulatory arrest? Ann Thorac Surg. 1997; 64:913-916.
6. Usui A, Oohara K, Liu TL, Murase M, Tanaka M, Takeuchi E, Abe T. Determination of optimum retrograde cerebral perfusion conditions. J Thorac Cardiovasc Surg. 1994; 107:300-308.
7. Oshikiri N, Watanabe T, Saitou H, Iijima Y, Minowa T, Inui K, Shimazaki Y. Retrograde cerebral perfusion: experimental approach to brain oedema. Perfusion. 1999; 14:257-262.
8. Lupetin AR, Davis DA, Beckman I, Dash N. Transcranial Doppler sonography. Part 1. Principles, technique, and normal appearances. Radiographics. 1995; 15:179-191.
9. Bellner J, Romner B, Reinstrup P, Kristiansson KA, Ryding E, Brandt L. Transcranial Doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP). Surg Neurol. 2004; 62:45-51
10. Nanda NC, Miller AP, Nekkanti R, Aaluri S. Transpharyngeal echocardiographic imaging of the right and left carotid arteries. Echocardiography. 2001; 18:711-716.
11. Khanna D, Sinha A, Nanda NC, Gupta R, Sidhu M, Vengala S, Dod HS, Ilgenli TF. Transesophageal and transpharyngeal ultrasound demonstration of reversed diastolic flow in aortic arch branches and neck vessels in severe aortic regurgitation. Echocardiography. 2004; 21:349-353.
12. Juul R, Aakhus S, Bjornstad K, Gisvold SE, Brubakk AO, Edvinsson L. Calcitonin gene-related peptide (human α-CGRP) counteracts vasoconstriction in human subarachnoid haemorrhage. Neurosci Lett. 1994; 170:67-70.
13. Touati GD, Roux N, Carmi D, Carmi D, Szymanski C, Barry M, Trojette F, Caus T. Totally normothermic aortic arch replacement without circulatory arrest. Ann Thorac Surg. 2003; 76:2115-2117.
14. Albayrak R, Degirmenci B, Acar M, Haktanir A, Colbay M, Yaman M. Doppler sonography evaluation of flow velocity and volume of the extracranial internal carotid and vertebral arteries in healthy adults. J Clin Ultrasound. 2007; 35:27-33.
15. Bor-Seng-Shu E, Hirsch R, Teixeira MJ, De Andrade AF, Marino R. Cerebral hemodynamic changes gauged by transcranial Doppler ultrasonography in patients with posttraumatic brain swelling treated by surgical decompression. J Neurosurg. 2006; 104:93-100.
16. Reich DL, Uysal S, Ergin MA, Griepp RB. Retrograde cerebral perfusion as a method of neuroprotection during thoracic aortic surgery. Ann Thorac Surg. 2001; 72:1774-1782.
17. Kawata M, Sekino M, Takamoto S, Ueno S, Yamaguchi S, Kitahori K, Tsukihara H, Suematsu Y, Ono M, Motomura N, Morota T, Murakami A. Retrograde cerebral perfusion with intermittent pressure augmentation provides adequate neuroprotection: Diffusion- and perfusion-weighted magnetic resonance imaging study in an experimental canine model. J Thorac Cardiovasc Surg. 2006; 132:933-940.
18. Kitahori K, Takamoto S, Takayama H, Suematsu Y, Ono M, Motomura N, Morota T, Takeuchi, K. A novel protocol of retrograde cerebral perfusion with intermittent pressure augmentation for brain protection. J

    Thorac Cardiovasc Surg. 2005; 130:363-370.
19. Yasuura K, Takagi Y, Oohara Y, Takami Y. Total body retrograde perfusion during operations on the descending thoracic aorta. J Thorac Cardiovasc Surg. 1999; 118:559-561.
20. Bruder N, Cohen B, Pellissier D, Francois G. The effect of hemodilution on cerebral blood flow velocity in anesthetized patients. Anesth Analg. 1998; 86:320-324.
21. Doblar DD, Frenette L, Poplawski S, Gelman S, Boyd G, Ranjan D, Halsey JH. Middle cerebral artery transcranial Doppler velocity monitoring during orthotopic liver transplantation: Changes at reperfusion-a report of six cases. J Clin Anesth. 1993; 5:479-485.
22. Sulek CA, Blas ML, Lobato EB. Milrinone increases middle cerebral artery blood flow velocity after cardiopulmonary bypass. J Cardiothorac Vasc Anesth. 2002; 16:64-69.
23. Mahmood MA, Voorhees ME, Parnell M, Zweifler RM. Transcranial Doppler ultrasonographic evaluation of middle cerebral artery hemodynamics during mild hypothermia. J Neuroimaging. 2005; 15:336-340.
24. Faraci FM, Heistad DD. Regulation of large cerebral arteries and cerebral microvascular pressure. Circ Res. 1990; 66:8-17.
25. Ngai AC, Nguyen TS, Meno JR, Britz GW. Postischemic augmentation of conducted dilation in cerebral arterioles. Stroke. 2007; 38:124-130.
26. Koster S, Oosterveld FG, Hensens AG, Wijma A, van der Palen J. Delirium after cardiac surgery and predictive validity of a risk checklist. Ann Thorac Surg. 2008; 86:1883-1887.
27. Higami T, Kozawa S, Asada T, Obo H, Gan K, Iwahashi K, Nohara H. Retrograde cerebral perfusion *versus* selective cerebral perfusion as evaluated by cerebral oxygen saturation during aortic arch reconstruction. Ann Thorac Surg. 1999; 67:1091-1096.
28. Duebener L, Hagino I, Schmitt K, Sakamoto T, Stamm, C, Zurakowski D, Schafers, H, Jonas R. Direct visualization of minimal cerebral capillary flow during retrograde cerebral perfusion: An intravital fluorescence microscopy study in pigs. Ann Thorac Surg. 2003; 75:1288-1293.
29. Bonser RS, Wong CH, Harrington D, Pagano D, Wilkes M, Clutton-Brock T, Faroqui M. Failure of retrograde cerebral perfusion to attenuate metabolic changes associated with hypothermic circulatory arrest. J Thorac Cardiovasc Surg. 2002; 123:943-950.
30. Reich DL, Uysal S, Ergin MA, Bodian C, Hossain S, Griepp R. Retrograde cerebral perfusion during thoracic aortic surgery and late neuropsychological dysfunction. Eur J Cardiothorac Surg. 2001; 19:594-600.
31. Augoustides JG. Transpharyngeal imaging of the carotid artery and internal jugular vein: Possible roles in cerebral perfusion management during adult aortic arch repair. J Cardiothorac Vasc Anesth. 2007; 21:318-319.
32. Bevilacqua S, Romagnoli S, Ciappi F, Ridolfi N, Codecasa R, Rostagno C, Sorbara C. Transpharyngeal ultrasonography for cannulation of the internal jugular vein. Anesthesiology. 2005; 102:873-874.