The Occurrence and Association of Impaired Cerebral Autoregulation With Outcomes in Aortic Arch Surgery: A Single-Center, Retrospective Study

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Research Article

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Abstract

Background Impairment of cerebral autoregulation (CA) has been observed in patients undergoing cardiopulmonary bypass (CPB), but little is known about its occurrence and associations with outcomes. The objective of this study was to analyze the occurrence of impaired CA, based on cerebral oximetry index (COx), in patients undergoing total aortic arch replacement with CPB and moderate hypothermic circulatory arrest (MHCA). We also evaluated the association between impaired CA and patient outcomes.

Methods Sixty-four patients who underwent total aortic arch replacement with stented elephant trunk implantation under CPB and MHCA at our hospital were retrospectively analyzed. Patients were defined as having new-onset impaired CA if post-CPB COx > 0.3, calculated based on a moving linear correlation coefficient between regional cerebral oxygen saturation ($rScO_2$) and mean blood pressure (MAP). Postoperative complication and in-hospital mortality were compared between patients with normal and impaired CA.

Results Of the 64 patients, 19(29.7%) developed new-onset impaired CA after CPB with MHCA. Compared with normal CA patients, those with impaired CA showed a significantly longer duration of $rScO_2$ <55%, and significantly higher rates of in-hospital mortality and postoperative complications (acute kidney injury, delirium, mechanical ventilation > 24h, and respiratory infection).

Conclusions In our cohort, 29.7% of patients who underwent total aortic arch replacement developed new-onset impaired CA after CPB with MHCA. Impaired CA might be associated with significantly increased rates of postoperative complications and in-hospital mortality.

Clinical trial registration: ChiCTR1800014545 with registered date 20/01/2018.

Background

Cerebral autoregulation (CA) ensures a constant supply of oxygenated blood flow to the brain over a wide range of blood pressures [1]. However, when CA is damaged, cerebral blood volume (CBV) may become correlated with blood pressure, leading to cerebral hypo- or hyperperfusion in patients whose blood pressure is uncontrolled. It also predisposes patients with low blood pressure to cerebral ischemia and patients with high blood pressure to hyperemia [1]. CA may become damaged in up to 20–24% of patients undergoing moderate hypothermic cardiopulmonary bypass (CPB) [1,2].

Impaired CA has been linked to neurological dysfunction in patients undergoing hypothermic CPB [1,3]. Brain ischemic injury with low arterial pressure and increased cerebral embolic load with high arterial pressure are proposed mechanisms of neurological dysfunction in patients with impaired CA [1]. Whether CPB and hypothermic circulatory arrest (HCA) increase the risk of impaired CA in aortic dissection patients is unclear. On the one hand, Neri et al's work revealed that HCA combined with retrograde cerebral perfusion might damage CA [4]. And on the other hand, Ono et al's study indicated that deep HCA

could preserve CA better than moderate hypothermic CPB without circulatory arrest [5]. Therefore, the effect of HCA on CA remains unclear and requires further investigation.

Regional cerebral oxygen saturation ($rScO_2$) monitoring using near-infrared spectroscopy (NIRS) has been widely applied in cardiac surgeries, carotid endarterectomy, and shoulder surgeries in beach-chair position [6–9]. $rScO_2$ takes into account cerebral arterial, capillary, and venous blood, essentially reflecting the balance between cerebral oxygen supply and demand [10]. Particularly for patients who underwent total aortic arch replacement under CPB and HCA, $rScO_2$ monitoring could help to manage the flow rate of cerebral perfusion [11–13]. In previous research, it has been demonstrated that the change of $rScO_2$ was coherent with CBV in patients undergoing CPB or in those with an intracranial injury [14,15]. And the function of CA can be assessed by measuring a moving linear correlation coefficient between $rScO_2$ and mean blood pressure (MAP), which is called the cerebral oximetry index (COx) [14]. If the COx approached 1, it implied that CBV depended on blood pressure and CA was damaged. If the COx value approached 0, it indicated that blood pressure did not correlate with CBV and CA was functional. An average COx > 0.3 was regarded as the threshold of impaired CA [5]. Furthermore, COx analysis has shown high sensitivity (92%) and moderate specificity (63%) for detecting CA impairment [16], and it agrees well with the mean velocity index (Mx) determined by transcranial Doppler (TCD) [14,17]. The feasibility of using COx to monitor CA during cardiac surgery has been demonstrated for adult and pediatric patients [18,19].

In this retrospective study, we aimed to identify the occurrence of new-onset impaired CA by COx calculation in patients undergoing total aortic arch replacement involving CPB and moderate hypothermic circulatory arrest (MHCA). We also analyzed the relations between impaired CA and short-term outcomes.

Methods

Study design and population

We retrospectively reviewed the electronic medical records of 73 adult patients who underwent total aortic arch replacement with stented elephant trunk implantation for acute type A aortic dissection from February 2017 to February 2018. Four patients for whom $rScO_2$ data were unavailable because of technical problems with the measuring device were excluded, as well as one patient who had preoperative renal dysfunction. Finally, 68 cases were enrolled in this study (Fig. 1). This study was approved by the Ethics Committee of West China Hospital, Sichuan University (protocol number: 2017342). Written informed consent was waived because of retrospective and observational study. All procedures performed in studies involving human participants were in accordance with the Helsinki declaration. Furthermore, the study was registered in the chictr.org.cn with registration number: ChiCTR1800014545 on 20/01/2018.

Perioperative care and anesthesia

Five-lead electrocardiography (ECG), pulse oxygen saturation (SpO_2), nasopharyngeal and rectal temperature, and invasive blood pressures via the bilateral radial arteries and left dorsal pedis artery were routinely monitored. General anesthesia was induced using midazolam (0.04–0.1 mg/kg), sufentanil (1–2μg/kg), and rocuronium (0.5–1.2 mg/kg), then maintained using sevoflurane inhalation (1–2%) and intermittent administration of sufentanil and cisatracurium besilate. After tracheal intubation, pressure-controlled mechanical ventilation was achieved and adjusted to keep end-tidal carbon dioxide ($EtCO_2$) in the normal range. Transesophageal echocardiographic examination (iE33; Phillips Medical System, Andover, MA, USA) was routinely performed before surgery. Vasoactive agents were administrated necessarily to stabilize hemodynamics as much as possible.

Surgical procedures

All patients underwent total aortic arch replacement with stented elephant trunk implantation through median sternotomy in supine position. Aortic cannulation, right axillary artery, or femoral artery cannulation was performed for systemic perfusion, and systemic venous return was achieved by vena cava cannulation or trans-femoral venous cannulation. Moderate hypothermia (nasopharyngeal temperature 26–28°C and rectal temperature 28–30°C) was reached after the establishment of circulatory arrest. During the cooling phase before MHCA, the pump flow rate decreased gradually from 2.6 to 2.2 L/min/m^2. If MAP lower than 50 mmHg, vasoconstrictor, including metaraminol (0.2–0.5 mg) or norepinephrine (5–10 μg), was administrated intermittently; when MAP higher than 80 mmHg, vasodilator, including urapidil (3–5 mg) or perdipine (0.3–0.5 mg) was used. After the establishment of MHCA, antegrade cerebral perfusion was performed initially via innominate artery cannulation. If left $rScO_2$ was 10% lower than right $rScO_2$ during right antegrade cerebral perfusion, unilateral antegrade cerebral perfusion was immediately switched to bilateral antegrade cerebral perfusion through both innominate artery and left common carotid artery cannulations. The flow rate of antegrade cerebral perfusion was adjusted between 6 and 12 mL/min/kg under the guidance of right radial artery blood pressure or perfusion pressure. The right radial artery pressue was maintained between 40 and 70 mmHg as possible, while the cerebral perfusion pressure was kept between 40 and 50 mmHg. Alpha–stat management was used during cooling and rewarming phases and pH-stat was applied during MHCA. All patients were transferred to the intensive care unit (ICU) after surgery for respiratory and circulatory support.

$rScO_2$ monitoring and COx calculation

Two self-adhesive transcutaneous oximetry sensors (EGOS-600A, Suzhou Engine Bio-medical Electronics, Suzhou, China) were placed on the right and left sides of the forehead for bilateral $rScO_2$ monitoring. MAPs and $rScO_2$ were sampled every 2 seconds and saved in SAM 1.0 software (Senton Netease, Chengdu, China) and the EGOS-600A system respectively. For COx calculation, the saved MAP and $rScO_2$ data were extracted and redisplayed by Visual Studio 2013 software (Microsoft Corporation, WA, USA) on a personal computer (Lenovo XiaoXin Air 13 Pro). Of note, the MAP, measured in the left radial artery, was preferred for COx calculation. A continuous, moving Pearson correlation coefficient between MAP and

$rScO_2$ was calculated to generate COx [14]. Consecutive, paired, non-overlapping 10-second averaged MAP and $rScO_2$ values were calculated over 300-sec interval, yielding 30 data points, which were used to determine the average COx for that interval. Then, the COx of all 300-sec intervals for the pre- and post-CPB periods were averaged respectively to identify impaired CA. A COx near 1 indicates that CBV depends on blood pressure and so CA is damaged; a COx near 0 indicates that CBV does not correlate with blood pressure and therefore CA is functional [14]. New-onset impaired CA was defined as both right and left average COx > 0.3 after CPB and ≤ 0.3 before CPB [5]. Figure 2 shows one patient's COx data in MAP bins of 5mmHg. The threshold of low $rScO_2$ was defined as lower than 55% according to that $rScO_2$ below 55% was related to the occurrence of neurological events [20,21].

Outcomes

The primary outcome was the occurrence of new-onset impaired CA, while secondary outcomes were major postoperative complications including delirium, acute kidney injury (AKI), cardiac dysfunction, mechanical ventilation > 24 h, respiratory infection, and reoperation. Lengths of stay in the ICU and hospital generally were also recorded. Postoperative delirium was measured with the Confusion Assessment Method (CAM) or CAM-ICU for intubated patients. AKI was diagnosed according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria as a 50% increase from baseline serum creatinine level or a 26.4 mmol/L increase from baseline within 48 h [22]. Cardiac dysfunction was defined as postoperative minimal ejection fraction (EF) < 50%. Postoperative respiratory infection was identified as follows: if a patient received antibiotics for suspected respiratory infection and met at least one of the following criteria: new or changed sputum, new or changed lung opacities, fever, leukocyte count > 12,000 $\times 10^9$ L^{-1} [23].

Statistical analysis

A preliminary analysis of ten patients showed that three patients suffered from impaired CA after MHCA. Thus a sample size of 60 from a population of 73 could produce a two-side 95% confidence interval with a precision (half-width) of 0.05 when the actual impaired CA occurrence was near 0.3. Continuous variables were expressed as mean ± standard deviation (SD), and categorical data as frequency in percentage or absolute number. Normality of the continuous data was tested using the Kolmogorov-Smirnov method. Inter-group differences in continuous variables were assessed for significance using Student's *t*-test, and differences in categorical variables were assessed using χ^2 test. Statistical analyses were performed using SPSS version 17.0 (IBM, Chicago, IL, USA), GraphPad Prism 7.0 (GraphPad Software, USA), and PASS 15.0 software. Differences with $P < 0.05$ were considered statistically significant.

Results

Four patients were excluded from the final statistical analysis because they already had impaired CA prior to CPB by COx calculation. Patients' demographics, preoperative and intraoperative characteristics were

listed in Table 1. A total of 19 (29.7%) patients presented new-onset impaired CA after CPB with MHCA. Patients with new-onset impaired CA were more likely to have a history of diabetes and previous cerebral infarction, which was not secondary to the acute aortic dissection. Patients with previous cerebral infarction were fully recovered without any residual neurological symptoms or signs, and their baseline of right and left $rScO_2$ showed no significant difference (61.5 ± 3.2% vs 62.2 ± 2.0%, p = 0.69). There were no differences in temperature, pH, carbon dioxide partial pressure ($PaCO_2$), arterial oxygen partial pressure (PaO_2), lactate, or hemoglobin between patients with impaired and normal CA during MHCA (Table 2). Impaired CA patients showed a significantly longer period of intraoperative $rScO_2$ < 55% than normal CA patients (Fig. 3). Compared to patients with normal CA, those who developed impaired CA had higher frequencies of in-hospital mortality, postoperative delirium, AKI, mechanical ventilation > 24 h, and respiratory infection, and they stayed significantly longer in the ICU (Table 3).

Discussion

In our study, based on COx, 29.7% of our cohort developed new-onset impaired CA after CPB with MHCA. The occurrence of impaired CA in adult patients undergoing CPB with MHCA was consistent with children in previous reports [24,25].

Factors known to influence CA during CPB include temperature, PaO_2, $PaCO_2$, perfusion pressure, flow rate, and hematocrit [24–27]. Temperature reduction exponentially decreases cerebral metabolism and preserves cellular stores of high-energy adenosine triphosphate [25]. Carbon dioxide is a potent cerebrovasodilator, and elevated $PaCO_2$ can obviously increase CBF volume in both awake and anesthetized states [26]. In our cohort, the patients with impaired or normal CA did not differ significantly in the above factors (Table 2). The reason for the elevated $PaCO_2$ during MHCA was that we used pH-stat for blood gas management to ensure sufficient cerebral perfusion. High $PaCO_2$ might be detrimental to preserve the function of CA. However, the $PaCO_2$ showed no significant difference between patients with impaired and normal CA in our study.

We found that impaired CA seems to associate with intraoperative low $rScO_2$. The period of $rScO_2$ < 55% in impaired CA patients was longer than in normal CA patients (Fig. 3). This result was consistent with previous studies that the period of $rScO_2$ less than 55% during aortic surgery was closely related to the occurrence of postoperative neurological events [20,21]. These results indicated that by regulating cerebral perfusion blood flow rate and pressure alone might not avoid the events of $rScO_2$ lower than 55%. Other methods also should be considered, including raising hematocrit to improve oxygen delivery, maintaining deep hypothermia during the circulatory arrest to suppress cerebral metabolism, and minimizing the duration of HCA. Whereas using α-stat management during moderate hypothermia produces better neurologic outcomes than observed with pH-stat management, it is unclear which strategy is superior in adults when MHCA is used [28].

Our results suggested that patients with impaired CA had a higher rate of postoperative delirium, consistent with several studies in coronary artery bypass grafting or valve surgery [29,30]. Patients with impaired CA were also at increased risks of in-hospital mortality, AKI, mechanical ventilation > 24 h, respiratory infection, and length of ICU stay. Like the present study, other work reported that impaired CA was associated with longer mechanical ventilation and hospital stay [29]. The onsets of AKI, respiratory infection, and postoperative death were affected by many factors, including the cardiac function, bleeding, and the duration of mechnical ventilation. Although the events of low cardiac output and reoperation due to bleeding showed no significant difference between patients with impaired CA and those with normal CA, the causal relationship between impaired CA and postoperative death, AKI and respiratory infection was uncertain from our study which merits prospective studies. Our findings might indicate that impaired CA was one of the manifestations of systemic organ injury in patients who underwent CPB with MHCA. These observations suggested the need to comprehensively monitor patients who undergo CPB and MHCA to ensure sufficient oxygen delivery to key organs. In particular, patients with impaired CA may require early interventions before postoperative complications onset, such as increasing systemic oxygen delivery, providing renal replacement therapy, and/or giving mild hypothermia therapy. Randomized controlled trials were needed to examine whether these early interventions can improve patient outcomes.

We found that patients with a history of diabetes or previous cerebral infarction were more likely to develop impaired CA after CPB with MHCA (Table 1). This was consistent with previous work suggesting that diabetes may associate with the occurrence of impaired CA by inducing cerebral microvascular endothelial dysfunction and cardiovascular autonomic neuropathy [31–33]. The previous cerebral infarction may weaken or damage the response of CBV to changes in blood pressure [34,35]. In our cohort, the patients with previous cerebral infarction showed normal preoperative $rScO_2$ and CA function, but they might still suffer CA impairment after CPB with MHCA. These findings suggested that it was necessary to assess CA through COx calculation in patients with a history of diabetes or previous cerebral infarction even though their preoperative $rScO_2$ were normal.

Our study presents several limitations. First, we were able to enroll only 64 cases because of the relatively small number of total aortic arch replacement surgeries for acute type A aortic dissection at our institution. Second, COx < 0.3 was tested in the animal study as a threshold of impaired CA. Thus, perspective studies were ongoing to validate COx < 0.3 as a measurement tool for impaired CA in adult patients. Third, because $rScO_2$ monitoring was not routinely performed in our ICU, we could not continuously assess postoperative CA. Fourth, not all patients received a rigorous assessment by a neurologist or psychiatrist to identify the postoperative neurological complications. This may lead to an underestimation of the occurrence of postoperative neurological complications. In addition, only the temporary rather than permanent neurological complications were evaluated. Fifth, we did not analyze the potential impact of vasoconstrictors or inotropics on CA because the accuracy of the dosage and usage time could not be ensured. Finally, there is no control group without MHCA in our study. But the occurrence of new-onset impaired CA in patients who underwent CPB and HCA was higher than those

who underwent CPB alone in literature. This might reveal that HCA increased the risk of new-onset impaired CA. Large, prospective trials are needed to understand more about changes in CA and its impact on patient outcomes.

Conclusions

Our single-site retrospective study showed that a substantial proportion of patients who undergo total aortic arch replacement under CPB and MHCA suffered new-onset CA impairment. Impaired CA might be associated with the increased rates of postoperative complications and in-hospital mortality.

Abbreviations

CA
cerebral autoregulation, CBV:cerebral blood volume, CPB:cardiopulmonary bypass, COx:cerebral oximetry index, HCA:hypothermic circulatory arrest, MHCA:moderate hypothermic circulatory arrest, $rScO_2$:regional cerebral oxygen saturation, MAP:mean blood pressure, Mx:mean velocity index, TCD:transcranial Doppler, ECG:electrocardiography, SpO_2:pulse oxygen saturation, $EtCO_2$:end-tidal carbon dioxide, ICU:intensive care unit, AKI:acute kidney injury, KDIGO:Kidney Disease Improving Global Outcomes, EF:ejection fraction, SD:standard deviation, $PaCO_2$:carbon dioxide partial pressure, PaO_2:arterial oxygen partial pressure, BMI:body mass index, ACEI:angiotensin-converting enzyme inhibitor, CCB:calcium-channel blocker, BNP:b-type natriuretic peptide, CVP:central venous pressure, RBC:red blood cell, T:temperature, BE:base excess, d:days

Declarations

Ethics approval and consent to participate: This study was approved by Ethics Committee of West China Hospital, Sichuan University (protocol number 2017342). Written informed consent was waived because of retrospective and observational study. All procedures performed in studies involving human participants were in accordance with the Helsinki declaration.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and analysed during this study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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participated to draft the manuscript, and LP revised it critically. All authors read and approved the manuscript.

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Tables

Table 1
Demographics, preoperative and intraoperative characteristics of the patients with impaired or normal cerebral autoregulation.

Parameter	Impaired autoregulation (n = 19)	Normal autoregulation (n = 45)	*P* value
Age (years)	48.7 ± 12.1	46.4 ± 11.2	0.481
BMI (kg/m^2)	25.3 ± 3.3	24.2 ± 3.7	0.245
Female, n (%)	1(5.3)	8(17.8)	0.194
Preoperative medication, n (%)	5 (26.3)	9 (20.0)	0.577
β-blockers	8 (42.1)	16 (35.6)	0.621
ACEI	10 (52.6)	18 (40.0)	0.352
CCB	3 (15.8)	2 (4.4)	0.122
Insulin	98.2 ± 32.2	92.6 ± 69.1	0.667
Creatinine (μmol/L)			
Hemoglobin (g/L)	126.6 ± 19.2	134.5 ± 20.7	0.156
BNP (pg/mL)	854.5 ± 1635.2	1037.2 ± 2853.3	0.764
Diabetes, n (%)	6 (31.6)	5(11.1)	0.047*

Parameter	Impaired autoregulation (n = 19)	Normal autoregulation (n = 45)	*P* value
Hypertension, n (%)	10 (52.6)	21 (46.7)	0.672
Cerebral infarction, n (%)	4 (21.1)	1 (2.2)	0.010*
Ejection fraction < 50%, n (%)	3(15.8)	6(13.3)	0.796
Emergency surgery, n (%)	9 (47.4)	16 (35.6)	0.376
ACP	16(84.2)	40(88.9)	0.685
uACP, n(%)	3(15.8)	5(10.1)	0.685
biACP, n(%)	14(73.6)	31(68.9)	0.773
Systemic perfusion	3(15.7)	8(17.8)	0.847
Trans-femoral artery, n(%)	2(10.7)	6(13.3)	0.756
Trans-aorta, n(%)	62.3 ± 6.3	62.0 ± 7.6	0.893
Trans-axillary artery, n(%)	48.0 ± 5.7	51.1 ± 6.7	0.086
MAP (mmHg)	52.0 ± 3.9	53.9 ± 4.6	0.090
Pre-CPB	5.7 ± 3.2	7.2 ± 3.8	0.211
During CPB	8.1 ± 3.3	10.2 ± 3.5	0.071
Post-CPB	521.3 ± 98.7	477.4 ± 107.1	0.122
CVP(cmH_2O)	282.9 ± 54.8	201.6 ± 77.3	0.702
Pre-CPB	144.1 ± 47.9	127.1 ± 48.0	0.136
Post-CPB	201.6 ± 43.7	180.2 ± 49.7	0.112
Operation time (min)	35.1 ± 8.0	34.1 ± 10.3	0.690
CPB time (min)	6 (31.6)	11 (24.4)	0.555
Post-CPB time (min)			
Cross-clamp time (min)			
Arrest time (min)			
RBC infusion, n (%)			

Parameter	Impaired autoregulation (n = 19)	Normal autoregulation (n = 45)	*P* value
Values are n (%) or mean ± SD, unless otherwise noted. *Abbreviations:* BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitor; CCB, calcium-channel blocker; BNP, b-type natriuretic peptide; ACP, antegrade cerebral perfusion; uACP, unilateral antegrade cerebral perfusion; biACP, bilateral antegrade cerebral perfusion; MAP, mean arterial blood pressure; CVP, central venous pressure; CPB, cardiopulmonary bypass; RBC, red blood cell *P* < 0.05			

Table 2
Temperatures and blood gas analysis of patients averaged over hypothermic circulatory arrest, stratified by impaired or normal cerebral autoregulation.

Parameter	Impaired autoregulation (n = 19)	Normal autoregulation (n = 45)	*P* value
Nasopharyngeal T_{mean}(℃)	26.5 ± 1.7	26.8 ± 2.2	0.522
Nasopharyngeal T_{min}(℃)	26.3 ± 1.7	26.5 ± 2.3	0.732
Rectal T_{mean}(℃)	28.1 ± 2.1	28.5 ± 2.0	0.442
Rectal T_{min}(℃)	27.9 ± 2.0	28.4 ± 1.9	0.407
pH	7.2 ± 0.1	7.2 ± 0.1	0.755
$PaCO_2$ (mmHg)	62.2 ± 13.7	59.6 ± 13.0	0.519
PaO_2 (mmHg)	191.3 ± 85.3	221.2 ± 93.6	0.251
Lactate (mmol/L)	4.8 ± 2.0	5.4 ± 2.7	0.447
BE	-3.6 ± 2.3	-5.0 ± 2.6	0.056
Hemoglobin (g/L)	78.0 ± 10.2	82.2 ± 11.0	0.180
Glucose (mmol/L)	9.8 ± 2.7	11.0 ± 4.1	0.200
Values are mean ± SD, unless otherwise noted.			
Abbreviations: T, temperature; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; BE, base excess			

Table 3
Outcomes of patients after cardiopulmonary bypass with hypothermic circulatory arrest, stratified by impaired or normal cerebral autoregulation.

Outcome	Impaired autoregulation (n = 19)	Normal autoregulation (n = 45)	*P* value
Length of ICU stay (d)	9.7 ± 10.3	5.7 ± 4.6	0.045*
Hospitalization (d)	24.8 ± 13.2	22.9 ± 7.3	0.570
Re-operation, n (%)	1 (5.26)	5 (11.1)	0.463
Ejection fraction < 50%, n (%)	5(26.3)	11(24.4)	0.874
Acute kidney injury, n (%)	9 (47.4)	8 (17.8)	0.014*
Delirium, n (%)	13 (68.4)	16 (35.6)	0.016*
Mechanical ventilation > 24 h, n (%)	16 (84.2)	26 (57.8)	0.042*
Lung infection, n (%)	10 (52.6)	11 (24.4)	0.028*
In-hospital death, n (%)	7 (36.8)	4 (8.9)	0.007*

Values are n (%) or mean ± SD, unless otherwise noted.
Abbreviations: d, days; ICU, intensive care unit

* $P < 0.05$

Figures

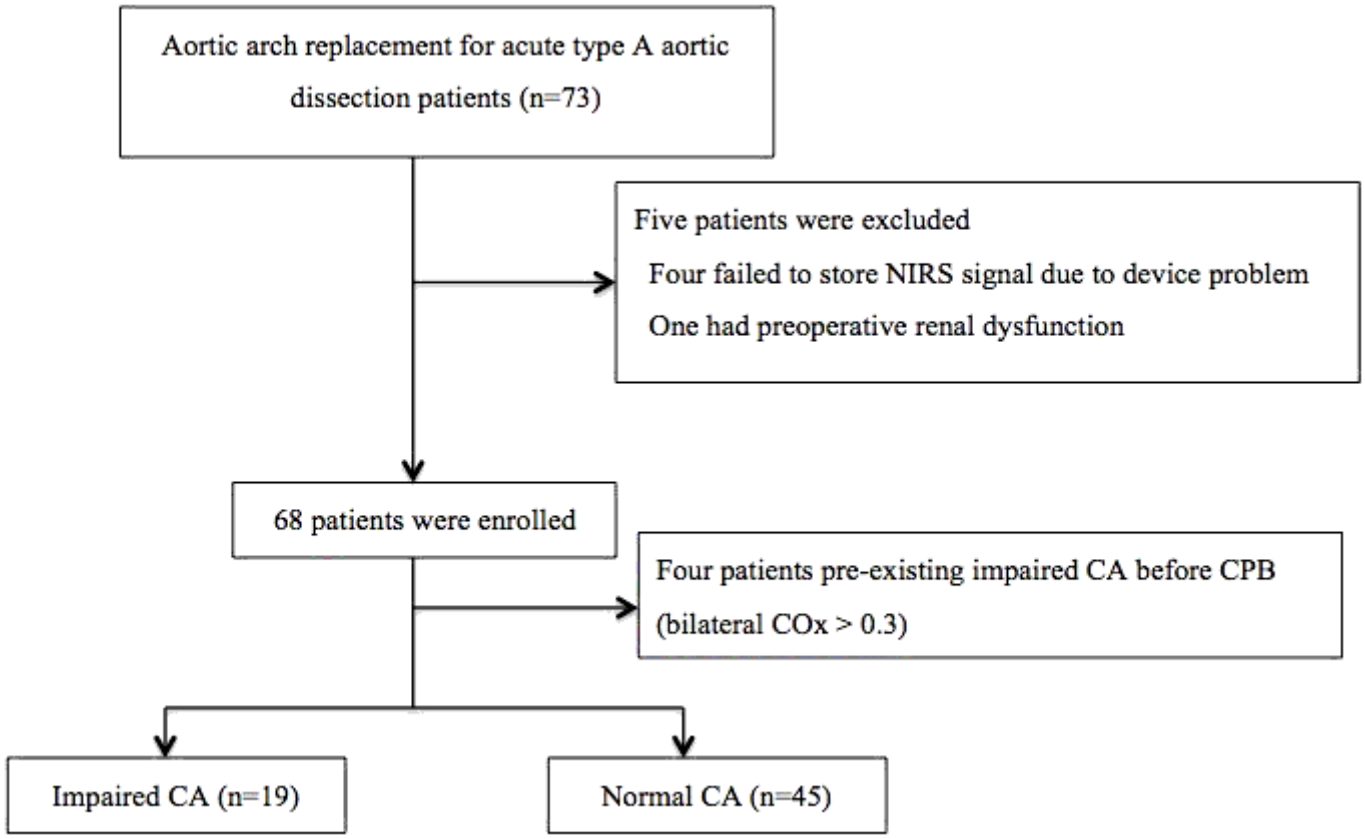

Figure 1

Flow chart of patient selection. CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; CA, cerebral autoregulation; NIRS, near-infrared spectroscopy

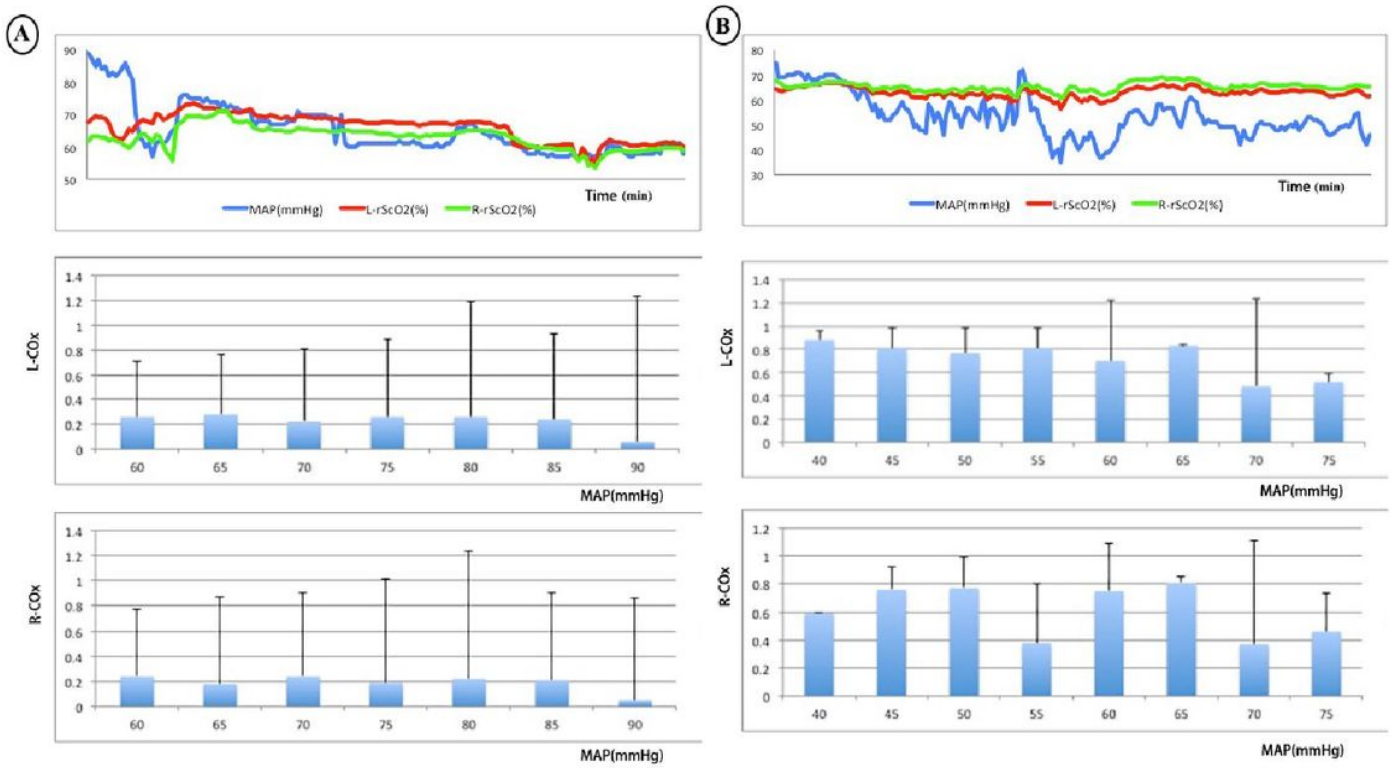

Figure 2

Examples of regional cerebral oxygen saturation (rScO2), mean arterial blood pressure (MAP) and cerebral oximetry index (COx) recording in a patient with normal cerebral autoregulation (CA) before cardiopulmonary bypass (CPB) with hypothermic circulatory arrest (A) but became impaired after the procedures (B). Graphs in the top row shows MAP, rScO2 of left brain (L- rScO2) and right brain (R-rScO2) from pre-induction of anesthesia until the end of surgery. Graphs in the middle graph show COx values for left side of brain, and graphs in the bottom row show COx for the right side of brain.

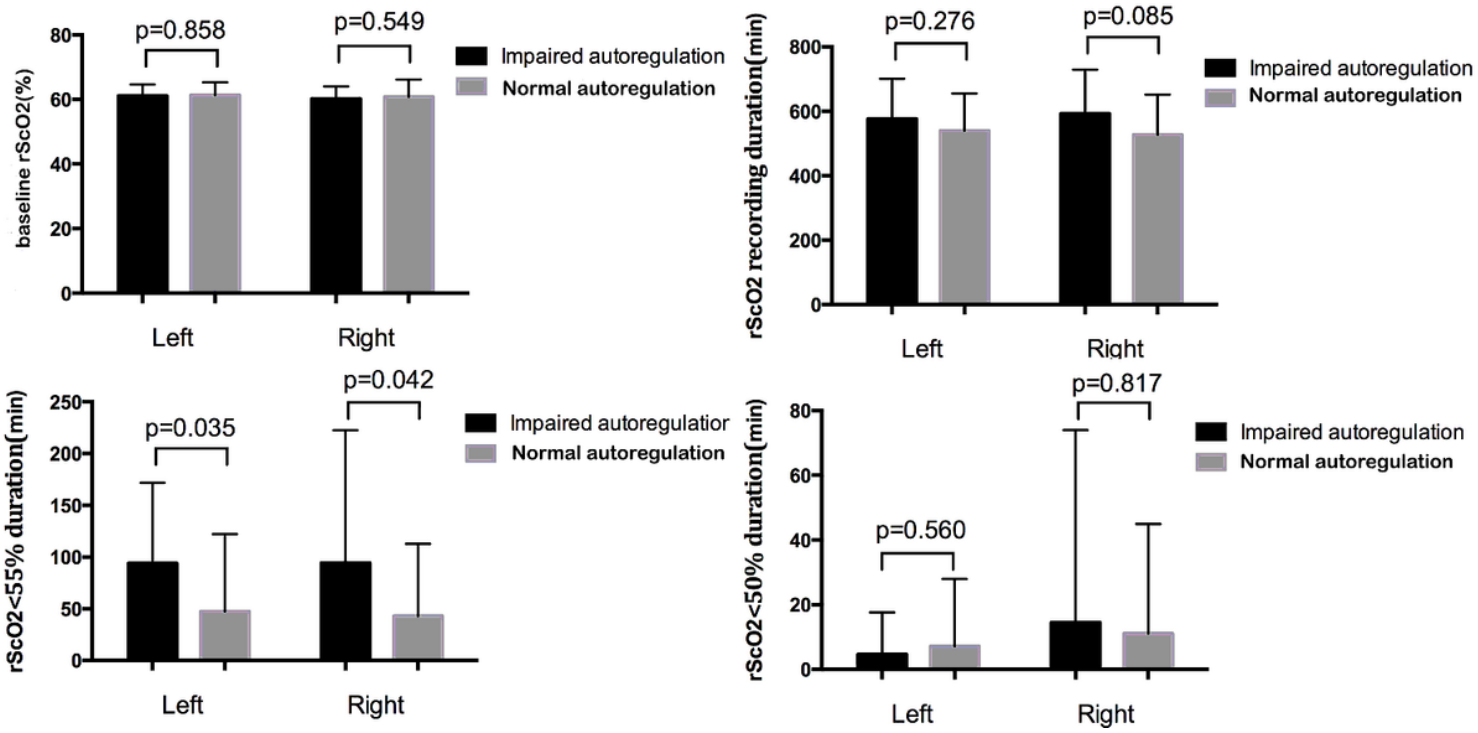

Figure 3

Comparison of the baseline of regional cerebral oxygen saturation (rScO2) value, as well as durations of rScO2 recording, rScO2<50% and rScO2<55% between patients with impaired and normal cerebral autoregulation.