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Original Research

The neurologic protection of unilateral versus bilateral antegrade cerebral perfusion in aortic arch surgery with deep hypothermic circulatory arrest: A study of 77 cases

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ABSTRACT

Backgroud: Unilateral and bilateral antegrade cerebral perfusions (ACP) are recognized methods of cerebral protection in aortic arch surgery. However, the adequacy of cerebral protection in aortic arch surgery with deep hypothermic circulatory arrest is controversial. In this study, we compared unilateral and bilateral ACP of cerebral protection in aortic arch surgery by assessing the patient's intraoperative and postoperative brain function.

Methods: A total of 77 patients undergoing aortic arch surgery were included in this study. Unilateral ACP was performed using a cannula in the innominate artery ($n = 40$), whereas bilateral ACP was conducted using an additional cannula in the left carotid artery ($n = 37$). Levels of S-100β and neuron specific enolase (NSE) were assayed at the beginning of cardiopulmonary bypass (T1), the beginning of circulatory arrest (T2), and post ACP at T = 25 min (T3), the end of ACP (T4), the end of cardiopulmonary bypass (T5), and at T = 1 h (T6), T = 6 h (T7), and T = 24 h (T8). Transcranial Doppler ultrasonography was used both preoperatively and intraoperatively to detect the blood flow of bilateral middle cerebral artery (MCA), and neurologic deficit incidence and mortality rates were obtained.

Results: At time points T1, T2, and T3, plasma levels of S-100β and NSE were not statistically different between groups. However, S-100β and NSE levels for each time point ranging from T = T4 to T = T8 did show statistically significant differences between groups. Patients who with one side of the middle cerebral artery stenosis, used bilateral antegrade cerebral perfusions method, intraoperative Transcranial Doppler ultrasonography examination showed narrow side blood flow weaker than the normal side during the deep hypothermic circulatory arrest (DHCA), however no significant differences could be observed between the two sides ($P > 0.05$). The incidence of neurological dysfunction was higher in the unilateral ACP group compared to the bilateral ACP group (25% vs. 8.11%, respectively, $P = 0.028$). Moreover, no marked differences were observed in mortality (2.5% vs. 5.41%, respectively, $P = 1.000$).

Conclusions: When the duration of DHCA was 25 min or less, no significant differences were observed between unilateral and bilateral ACP. However, when DHCA exceeded 25 min, bilateral ACP was more effective compared to unilateral ACP. Due to the high variations in circle of Willis as well as increased safety, simplicity, and efficiency, the bilateral ACP approach is preferred over the unilateral technique.

1. Introduction

Aortic arch surgery requires circulatory arrest, therefore it is extremely important to protect the brain. Deep hypothermic circulatory arrest (DHCA) without brain perfusion does not meet the minimum cerebral blood flow demand and retrograde cerebral perfusion is not consistent with the physiological situation. However, antegrade cerebral perfusion (ACP) is physiological and the most widely used approach of brain perfusion. During aortic arch surgery, significant improvements have been made in cerebral protection, however incidences of transient neurological

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dysfunction (TND) and permanent neurological dysfunction (PND) still occur. Several different ACP methods, such as unilateral and bilateral ACP, have more or less complications of neurological dysfunction in addition to DHCA [1–3]. Due to high variation in the circle of Willis (CoW), the adequacy of unilateral ACP remains controversial.

When neurons and glial cells are damaged during cardiac surgery, biomarkers of neurological dysfunction are produced and trigger apoptosis and reactive astrogliosis. This causes active or passive intracellular components to be released into the extracellular space, leading to the presence of potential biomarkers in th cerebrospinal fluid [4]. These biomarkers can be detected into the blood.

S-100 proteins are a class of small molecular mass of EF-hand calcium-binding proteins, in which the S-100β protein is highly neuron-specific and is highly abundant in the brain. S-100β has a half-life of 2 h and is either secreted by astrocytes or it can leak from injured cells and enter the extracellular space or bloodstream. During the acute phase of brain damage in patients, serum levels of S-100β are elevated [5]. Moreover, during brain injury, S-100β proteins are transported from the cerebrospinal fluid through the blood-brain barrier and enter the bloodstream. Damage of the central nervous system upregulates S-100β levels in both the cerebrospinal fluid and the blood and suggest that S-100β may be an important indicator of brain injury [6].

Neuron specific enolase (NSE) is one of the three enolase isoenzymes found in mammals, and in humans, is encoded by the ENO2 gene. This isoenzyme, a homodimer, is found in mature neurons and others cells of neuronal origin. In brain-related injuries, such as cerebral infarction, brain trauma, and cerebral anoxia, the levels of NSE in the blood and cerebrospinal fluid are significantly increased, and are closely related to the severity of the injury [7].

This study compares unilateral and bilateral ACP during total aortic arch replacement in relation to postoperative neurological dysfunction. Neurological injury was assessed and plasma levels of S-100β and NSE from right jugular vein blood samples obtained during and after ACP were evaluated.

2. Materials and methods

2.1. Patients and surgical methods

From May 2013 to May 2015, 77 patients who underwent total aortic arch replacement at our institute were included in this study. Patients' data is summarized in Table 1. For patients who underwent unilateral ACP, the mean age was 50.14 ± 6.48 years. Twenty-eight patients (70%) had acute aortic dissection, 9 patients (22.5%) had chronic aortic dissection, and in 3 patients (7.5%) a thoracic aortic aneurysm was observed. Thirty-three patients (82.5%) suffered from a hypertensive disease, 8 patients (20%) had diabetes mellitus, 1 patient (2.5%) had COPD, and in 1 patient (2.5%) renal insufficiency was observed. For patients who underwent bilateral ACP, the mean age was 49.71 ± 7.28 years. Twenty-seven patients (73%) had acute aortic dissection, 8 patients (21.6%) had chronic aortic dissection, and 2 in patients (5.4%) a thoracic aortic aneurysm was found. Thirty-five patients (94.6%) suffered from hypertensive disease, 10 patients (27.0%) had diabetes mellitus, 1 patient (2.7%) had COPD, and 1 patient (2.7%) had renal insufficiency. All 77 patients underwent a total aortic arch replacement. In 56 of these patients (72.7%) an emergency operation was performed. Moreover, in 75 patients (97.4%) a descending or thoracoabdominal aortic repair was performed. An ascending aortic repair was performed in 29 patients (37.7%), whereas an aortic root replacement was performed in 17 patients (22.1%).

Table 1
Clinical characteristics of patients.

	Unilateral group	Bilateral group
Age (years)	50.14 ± 6.48	49.71 ± 7.28
Male/female (*n*)	27/13	28/9
Weigh t (kg)	58.62 ± 11.08	60.39 ± 9.15
Body surface area (m^2)	1.88 ± 0.19	1.89 ± 0.17
LVEF (%)	58.5 ± 3.3	58.4 ± 4.1
Type of aortic disease (*n*)		
Acute AD	28	27
Chronic AD	9	8
Thoracic AA	3	2
Comorbidities (*n*)		
Hypertensive disease	33	35
Diabetes mellitus	8	10
COPD	1	1
Renal insufficiency	1	1
Unilateral MCA stenosis	0	9
Operation time (h)	6.77 ± 1.25	6.78 ± 1.13
CPB time (min)	187.64 ± 73.02	198.71 ± 59.83
Circulatory arrest time (min)	45.02 ± 16.02	44.87 ± 17.33
ACP time (min)	43.50 ± 17.25	42.21 ± 19.72
Aortic cross-clamp time (min)	104.36 ± 34.07	107.14 ± 36.78
Ventilator use time (h)	16.6 ± 5.12	11.5 ± 3.11[a]
ICU residence Time (day)	6.1 ± 2.3	3.4 ± 1.2[a]
Complications (%)		
Heart failure	0	0
Respiratory failure	5	2.7
Renal failure	2.5	0
TND	20	8.11[b]
PND	5	0
Mortality	5.41	2.5

[a] The ventilator using time and ICU residence time of bilateral ACP group was significantly shorter than the unilateral group *$p<0.05$*.
[b] The incidence of transient neurological dysfunction in the bilateral ACP group was significantly lower compared to the unilateral group $p < 0.05$.

2.2. Cerebral protection methods

In 40 patients, cerebral protection was performed by DHA with unilateral ACP, whereas 37 patients underwent DHA with bilateral ACP. In brief, a 15-cm catheter was placed retrograde at the jugular venous bulb in the right internal jugular vein to collect blood samples at different time points. In all patients, a midline sternotomy incision was made. Cardiopulmonary bypass (CPB) was established by placing a 22–24F arterial cannula in the right subclavian artery or aortic arch, and a two-stage venous cannula in the right atrium. The aortic root was addressed during cooling to moderately deep hypothermia (nasopharyngeal temperature of 18 °C–22 °C). The left side of the heart was vented through a right superior pulmonary vein catheter and cold blood cardioplegia was used for myocardial protection.

Upon reaching the target temperature, circulatory arrest was initiated. Patients were placed in a Trendelenburg position, the head was packed in ice throughout the DHCA, and the aortic arch was opened. A self-made balloon-tip cannula was inserted directly into the innominate artery from inside the aortic arch in the unilateral ACP group. An additional self-made balloon-tip cannula was inserted in the left common carotid artery in the bilateral ACP group. The balloons were filled with sodium chloride. In the unilateral ACP group, both the left subclavian artery, and the left common carotid artery were clamped with vascular clamps. In the bilateral ACP group, only the left subclavian artery was clamped. The perfusion flow, which restored the right radial artery pressure to 30–40 mmH, was 5 ~ 6 ml kg^{-1} min^{-1} for unilateral ACP, whereas for bilateral ACP the perfusion flow was 6 ~ 8 ml kg^{-1} min^{-1}. Intraoperatively, a pH-stat strategy was used for blood gas management [8]. A Medtronic BIO-TREND hematocrit (HCT) determinator was used to monitor HCT content and maintain it at