

## Original Articles

# Deep Hypothermic Circulatory Arrest vs. Antegrade Cerebral Perfusion in Cerebral Protection during the Surgical Treatment of Chronic Dissection of the Ascending and Arch Aorta

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**Abstract:** Circulatory arrest during aortic surgery presents a risk of neurological complications. The present study aimed to investigate the effectiveness of deep hypothermic circulatory arrest (DHCA) vs. antegrade cerebral perfusion (ACP) in cerebral protection during the surgical treatment of chronic dissection of the ascending and arch aorta and to assess the quality-of-life (QoL) in the long-term postoperative period with respect to the used cerebral protection method. In a prospective, randomized study, 58 patients with chronic type I aortic dissection who underwent ascending aorta and aortic arch replacement surgery were included. Patients were allocated in two groups: 29 patients who underwent surgery under moderate hypothermia (24°C) combined with ACP and 29 patients who underwent surgery under DHCA (18°C) with craniocerebral hypothermia. The regional hemoglobin oxygen saturation (rSO<sub>2</sub>, %) were compared during surgery, neurological complications were analyzed during the early postoperative period, QoL was compared in the long-term postoperative period (1-year follow-up). During

the early postoperative period, 37.9% of patients in the DHCA group exhibited neurological complications, compared with 13.8% of those in the ACP group ( $p < .05$ ). The risk of neurological complications in the early postoperative period was dependent on the extent of rSO<sub>2</sub> decrease during circulatory arrest. In the ACP group, rSO<sub>2</sub> decreased by  $\leq 17\%$  from baseline during circulatory arrest. In the DHCA group, a more profound decrease in rSO<sub>2</sub> ( $>30\%$ ) was recorded ( $p < .05$ ). QoL in the long-term period after surgery improved, but it was not dependent on the cerebral protection method used during surgery. ACP during aortic replacement demonstrated the most advanced properties of cerebral protection that can be evidenced by a lesser degree of neurological complications, compared with patients who underwent surgery under conditions of DHCA. QoL after surgery was not dependent on the cerebral protection method used during surgery. **Keywords:** aortic prosthesis, cerebral oxygenation, cerebral protection, neurologic injury. *J Extra Corpor Technol. 2017;49:16–25*

Aortic dissection is a major concern in cardiothoracic surgery associated with high inhospital mortality and risk of neurological complications (1,2). Protection of cerebrum,

which is the most vulnerable target at the stage of ascending aorta replacement, is crucial because deterioration of neurological status has direct impact on quality-of-life (QoL) of these patients (3).

Currently, there is no consensus about what method of cerebral protection is the best. By the study of Chau et al., it has been given quite positive attitude to use of deep hypothermic circulatory arrest (DHCA) in terms of preservation of patient's neurocognitive function (4). In this study, DHCA approved itself as an equal to antegrade and retrograde cerebral perfusion.

Received for publication May 23, 2016; accepted October 18, 2016.  
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The senior author has stated that the authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

Other authors reported benefits of antegrade and retrograde cerebral perfusion as methods permitting longer safe period of circulatory arrest and allowing use of moderate hypothermia. But these methods have their own limitations. Antegrade cerebral perfusion (ACP) is difficult to apply and cannot be used every time because patients with aortic dissection can have comorbid occlusive and stenotic lesions of brachiocephalic arteries. The method of retrograde cerebral perfusion does not allow precise estimation of perfusion volume and that can lead to inadequate neuroprotection (5,6).

Besides considerations of technical success and general outcome, the assessment of QoL after major surgical interventions is of increasing interest. Previous studies have shown that patients with acute type A aortic dissection had a postoperative QoL inferior to patients who underwent surgery for aortic aneurysm (7). Other authors have shown that the application of DHCA in surgery of thoracic aortic aneurysms frequently results in an impairment of QoL as it has been observed especially in patients older than 70 years (8).

The goal of this study was testing the hypothesis that ACP combined with moderate hypothermia during aortic replacement surgery is more effective method of cerebral protection than DHCA combined with craniocerebral hypothermia. And that use of ACP in the setting of moderate hypothermia during aortic replacement surgery leads to higher level of QoL in the long-term postoperative period than DHCA combined with craniocerebral hypothermia.

## MATERIALS AND METHODS

This was a prospective, randomized, blinded study. Allocation of patients to treatment groups was provided by simple blind randomization method using sealed envelopes. This study was approved by the local hospital ethics committee, with written informed consent obtained from all patients before their inclusion in the study. Study identifier is NCT01456975. We analyzed data from 58 patients, who were diagnosed with type I chronic aortic dissection according to DeBakey classification (>2 weeks after initial intimal injury), underwent ascending aorta and aortic arch surgery between January 2011 and December 2012. According to the etiology of the process, systemic atherosclerosis prevailed (48 patients, 83% of cases). Marfan syndrome was observed for six cases (10%), bicuspid aortic valve was observed for four patients (7%). The standard protocol of instrumental preoperative evaluation included multislice computed tomography of aorta, ultrasound duplex scanning of brachiocephalic arteries, coronary angiography, echocardiography, magnetic resonance imaging (MRI) of the brain, and electroencephalography (EEG).

## Inclusion Criteria

1. The presence of type I chronic aortic dissection (according to DeBakey classification) with indication to surgical replacement of the ascending aorta and aortic arch.
2. The presence of closed circle of Willis according to computed angiography scan.

## Exclusion Criteria

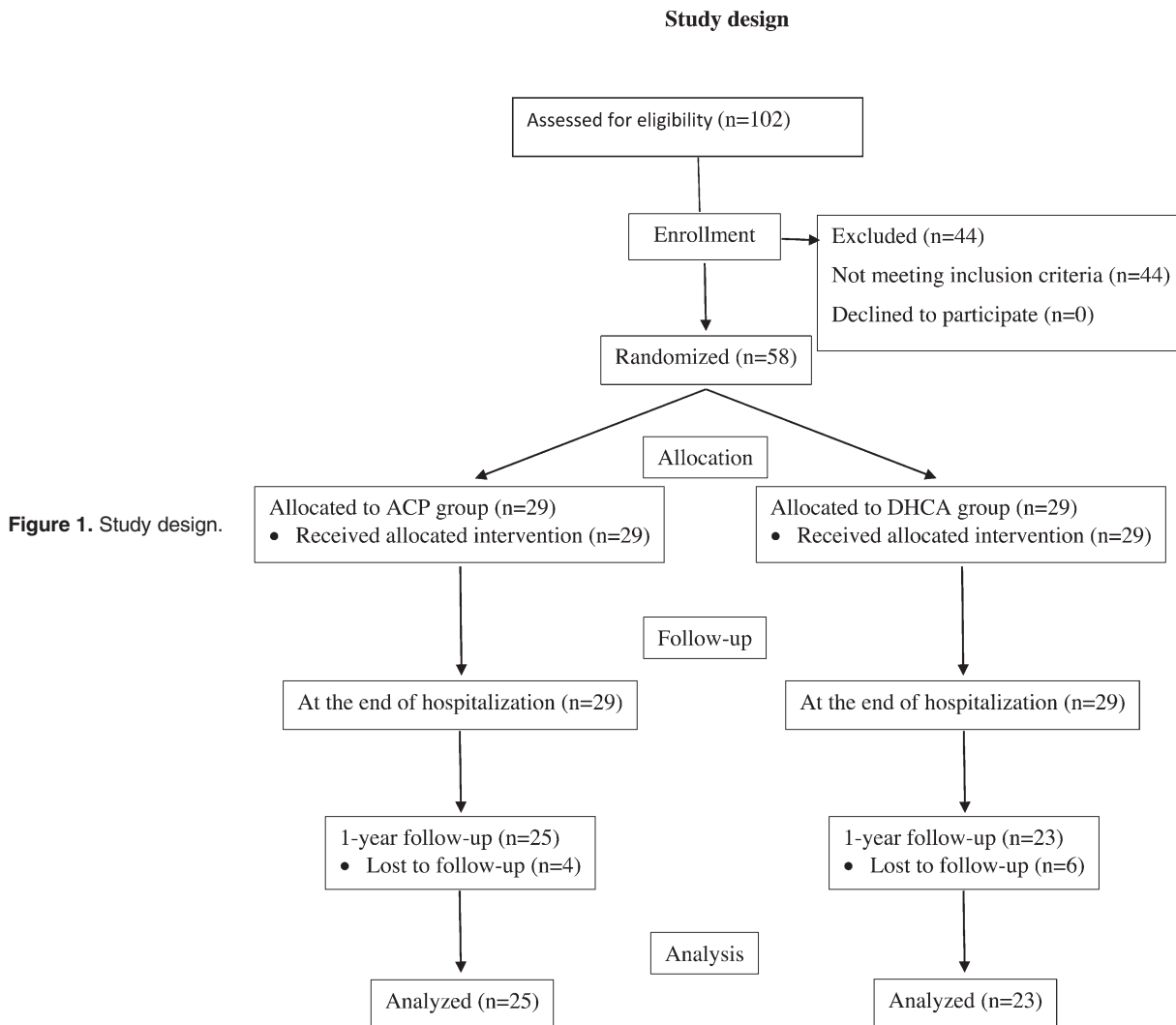
1. Patients with hemodynamically significant stenoses of brachiocephalic and intracranial arteries.
2. Patient with extension of dissection to brachiocephalic arteries.
3. Patients with hemodynamically significant stenoses of coronary arteries.
4. Patients with neurological disorders (including cerebral symptoms, disorders of higher mental functions, disturbances of motor activity, and focal abnormalities of cerebral tissue).
5. Patients with a history of brain trauma and neuroinfection.
6. Patients with diabetes mellitus.
7. Patients with a history of cardiovascular or major abdominal surgery.

The primary endpoint was detection of neurologic complications at the early postoperative period of aortic replacement surgery. The secondary endpoint was QoL assessment at the long-term postoperative period of aortic replacement surgery.

The first group included 29 patients, who underwent surgery under conditions of moderate hypothermia (23–24°C) combined with ACP (ACP group), performed using right subclavian artery cannulation during aortic surgery. The second group included 29 patients, who underwent surgery under conditions of DHCA group, performed with a decrease in body temperature to 18°C by perfusion and craniocerebral hypothermia established by packing the head with ice. The study design is presented in Figure 1.

## Operative and Anesthetic Techniques

All surgeries were performed using a standardized anesthetic technique. The anesthesia induction was performed with fentanyl (3.0–5.0 mg/kg) and midazolam (.1–.15 mg/kg). Muscle relaxation was achieved using pipecuronium bromide (.1 mg/kg). After undergoing tracheal intubation, the patients were ventilated to maintain normocapnia. A tidal volume of 8 mL/kg, respiratory rate of 12–14 breaths/min, and inspired oxygen content of 50% were used intraoperatively and postoperatively. Anesthesia was maintained before and after cardiopulmonary bypass (CPB) by an intermittent injection of fentanyl (total hourly dose, 2.5–3.5 mg/kg) and sevoflurane inhalation (1–2%). Fentanyl (2.5–3.5 mg/kg/h) and propofol (2–4 mg/kg/h) were used



during CPB. Pipecuronium bromide was added as necessary. The temperature was monitored in the nasopharynx and controlled throughout the intraoperative period.

Full median sternotomies were performed in all the patients. CPB was initiated after performing cannulation. The medical equipment included a membrane oxygenator (Affinity; Medtronic Inc., Minneapolis, MN) and a heart-lung machine (Stöckert™ SIII; Sorin Group, Munich, Germany). Nonpulsatile blood flow was maintained at 2.5 L/min/m<sup>2</sup>, mean arterial pressure was 50–70 mmHg. An initial dose of heparin (300 U/kg) was administered to achieve an activated coagulation time of 480 seconds.

After CPB initiation, the body temperatures were cooled to 24°C (nasopharynx) in the ACP group and to 18°C (nasopharynx) in the DHCA group. Body cooling was carried out with a thermal gradient of 7–8°C (heat-transfer agent body) (9). Cooling time is the time between start of CPB and moment when the nasopharyngeal temperature

reached minimum value. Blood gases were controlled in the course of cooling according to  $\alpha$ -stat strategy.

Myocardial protection was achieved by perfusion of the ascending aorta or coronary artery with a cold (5–8°C) crystalloid solution (Custodiol HTK-Bretschneider; Dr. Franz Köhler Chemie GmbH, Bensheim, Germany).

Patients underwent replacement of the ascending aorta and aortic arch with preservation of aortic valve where it was possible. The same surgery without preservation of aortic valve performed using valve/graft combination in cases of advanced fibrosis, calcinosis, and deformation of aortic valve leaflets combined with deterioration of closing function, due to impossibility to carry out the valve-sparing correction. In our study, we did not use multibranch grafts, and in case of total aortic arch replacement, entrances of brachiocephalic vessels were implanted on a single island.

The ascending aorta was replaced with a graft at the first stage of surgery. On reaching the requisite level of

hypothermia, surgery proceeded to the second stage, prosthetic aortic arch replacement. This stage of surgery was carried out in conditions of DHCA combined with craniocerebral hypothermia or partial circulatory arrest combined with support of cerebral perfusion under conditions of moderate hypothermia.

During the beginning of prosthetic aortic arch in the ACP group, when nasopharyngeal temperature decreased to 25°C, ACP was performed through right subclavian artery with volumetric flow rate 10 mL/kg/min to maintain the right radial arterial pressure within 55–100 mmHg. At the same stage of operation in the DHCA group, ACP was carried out in the conditions of deep hypothermia combined with craniocerebral hypothermia (cooling the patient's head by cloth helmet filled with ice that is put on immediately after anesthesia induction).

After the end of aortic replacement stage, patient started warming and carried out until the moment when the nasopharyngeal temperature reached 36°C. Termination of CPB was performed under control of invasive monitoring of central and peripheral hemodynamics. After the termination of CPB, the neutralization of heparin was achieved using protamine sulfate at a ratio of 1:1.

All patients received routine perioperative monitoring, including continuous pulse oximetry and recording of the electrocardiogram, heart rate, and arterial and central venous pressures.

After surgery, all patients were admitted to the intensive care unit (ICU). Patients were placed on mechanical ventilation according to a standardized protocol. The extubation criteria were clear consciousness, stable hemodynamics, an absence of signs of excessive drainage loss, and stabilization of electrolyte, acid–base, and respiratory parameters. The institution of inotropic support was guided by hemodynamic data. Patients were transferred from ICU to hospital ward when they met the following criteria: stable hemodynamics without inotropic support or vasoactive drugs, urine output >.5 mL/kg/h, and minimal drainage.

### Cerebral Oximetry

The regional hemoglobin oxygen saturation (rSO<sub>2</sub>) of the right and left hemispheres during the intraoperative period was assessed using bilateral near-infrared spectroscopy in the monitoring mode (cerebral oximeter INVOS 5100; Medtronic Inc.). Two sensors were placed on the forehead before induction of anesthesia. The rSO<sub>2</sub> of the left and right hemispheres was recorded at the following stages: 1) after anesthesia induction, 2) under conditions of CPB when the minimum temperature has been reached, 3) at the end of circulatory arrest (minimum value of rSO<sub>2</sub>), 4) 2 minutes after circulatory arrest, 5) warming before 36°C, 6) 15 minutes after CPB, and 7) at the end of surgery. Monitoring was performed by an independent anesthesiologist. Decrease of rSO<sub>2</sub> during circulatory

arrest was calculated by subtracting rSO<sub>2</sub> level at the stage 3 from rSO<sub>2</sub> level at the stage 2.

At the same stages, blood glucose and lactate levels were monitored. For future analysis, glucose and lactate levels were monitored after anesthesia induction and at 15 minutes after CPB.

### Neurological Status

All patients underwent neurological examinations according to the National Institutes for Health Stroke Scale (10) before surgery, on 5–6 days postoperatively and at the end of hospitalization by an independent trained neurological observer. Stroke outcome was defined as a focal neurological deficit persisting >24 hours and confirmed by MRI of the brain and EEG at the same stages. Encephalopathy after surgery was defined as a temporary nonfocal deficit. Neuropsychometric testing was examined with Mini-Mental State Examination (MMSE), 30-point questionnaire that was used extensively to measure state of cognitive functions and for screening of cognitive deterioration (11). The maximum score in that test is 30, which corresponds to high cognitive abilities. No neurological deficit was detected in any patient during the preoperative period; according to the MRI and EEG data.

We also recorded any other complications: new-onset atrial fibrillation, acute myocardial infarction, cardiac and pulmonary insufficiency, renal insufficiency, multiorgan dysfunction syndrome, need for cardiac pacing, and re-sternotomy for bleeding after aortic surgery. The mortality rate was determined by registered inhospital death.

### QoL Assessment

QoL was assessed using the Short-Form 36 Health Survey Questionnaire (SF-36) before the operation, and late after aortic surgery (1-year follow-up). Russian translation and testing methodology was conducted by the Institute of Clinical and Pharmacological Research (Saint Petersburg) (12). Testing was performed by blinded observer.

The SF-36 consists of 36 short questions reflecting QoL in eight different aspects:

1. Physical functioning (PF): the extent to which health limits physical activities, such as self-care, walking, climbing stairs.
2. Role functioning physical (RP): the extent to which physical health interferes with work or other daily activities.
3. Bodily pain (BP): the intensity of pain and the effect of pain on normal work, both inside and outside the home.
4. General health perceptions (GH): personal evaluations of current health, health outlook, and resistance to illness.
5. Vitality (VT): feeling full of energy rather than tired and worn out; social functioning.
6. Social functioning (SF): the extent to which physical health or emotional problems interfere with normal social activities.

7. Role functioning emotional (RE): the extent to which emotional problems interfere with work or daily activities.
8. Mental health (MH): general MH including depression, anxiety, behavioral–emotional control, and general positive affect.

These eight scales can be aggregated into two summary measures: the physical component summary (PCS) and mental component summary (MCS) scores. SF-36 scores are expressed on a scale that runs from 0 to 100, a higher score indicating a better QoL (13).

### Statistical Analysis

Based on the estimated event rate (neurological outcome) (14) and a significance level of 5%, a sample size of 58 was calculated to provide 80% power. Continuous data were presented as median and interquartile range; categorical data were described as the number and/or percentage. Comparative analyses of nonparametric characteristics were performed using the Mann–Whitney *U* test. For comparisons of related samples, the Wilcoxon test was used. The  $\chi^2$  test with Yates' correction or Fisher exact test was used for categorical variables, as appropriate. All correlation analyses were performed using the Spearman criterion. Correlation analysis data are presented as correlation coefficients (*r*) and 95% confidence intervals (CIs). Univariate logistic regression analysis was performed to determine the risk factors for neurological outcome. Odds ratios (ORs) were reported with 95% CIs. The receiver operating characteristic (ROC) curve analysis was drawn to determine the point of cutoff variables. The value on the ROC curve was determined with the maximum value of sensitivity and specificity as the point of parameter cutoff. Kaplan–Meier curves were obtained to

describe probability of freedom from neurological complications after surgical treatment in the study groups, which were compared by using the log-rank test. All *p* values <.05 were considered statistically significant. Statistical analyses were performed using Statistica 6.1 (StatSoft Inc., Tulsa, OK).

## RESULTS

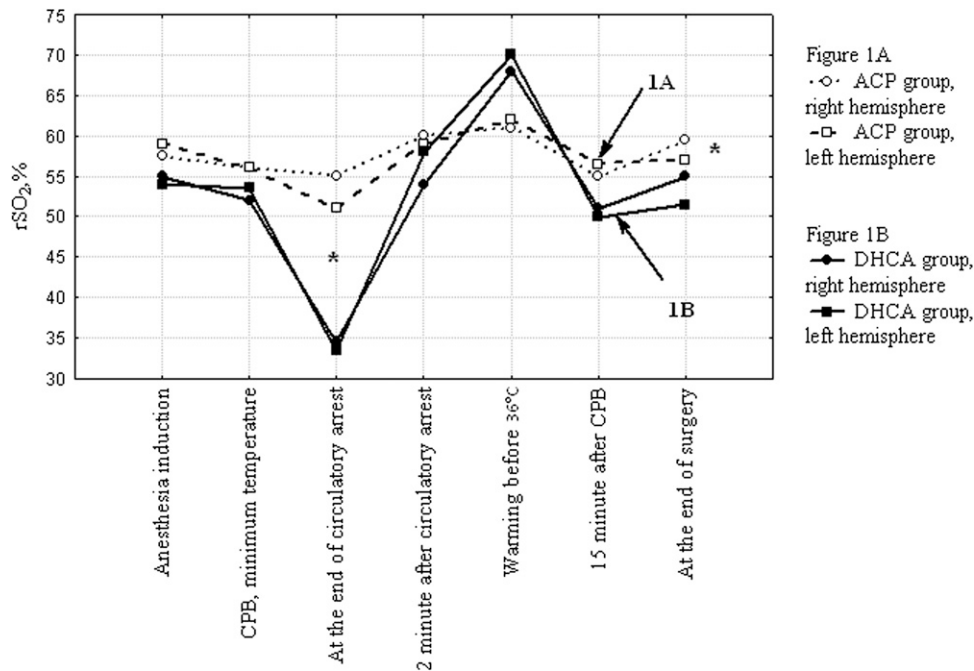
The clinical and functional characteristics of both groups of patients with chronic aortic dissection are shown in Table 1. According to the intraoperative data, patients in the DHCA group exhibited a longer cooling time compared with those in the ACP group (*p* = .003).

### Parameters of Cerebral Oxygenation

The changes in values of cerebral oxygenation for the right and left hemispheres in patients with chronic aortic dissection are shown in Figure 2 for both groups. During circulatory arrest in the DHCA group, a decrease of rSO<sub>2</sub> was 33 (24–41%) and 35 (25–43%) relative to previous values was observed in the right and left hemispheres, respectively. These changes were expected more pronounced than the changes observed in the ACP group, where rSO<sub>2</sub> values decreased by 11 (5–18%) and 17 (8–20%) in the right and left hemispheres, respectively. Differences between groups were statistically significant for both the right (*p* = .0001) and left (*p* = .0002) hemispheres, as well as absolute values of cerebral oxygenation for the right and left hemispheres (*p* = .0009) and (*p* = .0004), respectively. For the DHCA group, circulatory arrest was accompanied by a dramatic decrease in systemic arterial pressure that resulted in cerebral

**Table 1.** Clinical and functional characteristics of the patients with chronic aortic dissection.

Parameter (measurement units)	ACP Group ( <i>n</i> = 29)	DHCA Group ( <i>n</i> = 29)	<i>p</i> Value
<b>Demographics</b>			
Age (years)	52.0 (39–59)	54.2 (42–60)	.39
Male/female	22/7	23/6	.75
<b>Preoperative data</b>			
New York heart association class	2.7 (2.4–3.3)	2.8 (2.3–3.5)	.30
Body mass index (kg/m <sup>2</sup> )	29.2 (22.1–31.1)	27.8 (21.5–30.8)	.32
Hypertension (%)	23 (79.3)	25 (86.2)	.48
Aortic valve disease (%)	6 (20.6)	5 (17.2)	.73
Atrial fibrillation	4 (13.7)	5 (17.2)	.71
Chronic obstructive pulmonary disease (%)	3 (10.3)	2 (6.8)	.63
Chronic renal failure (%)	5 (17.2)	7 (24.1)	.51
Left ventricular ejection fraction (%)	64.1 (58–71)	62.8 (57–72)	.34
Right ventricular ejection fraction (%)	60 (54–65)	58 (50–64)	.41
<b>Intraoperative data</b>			
Cardiopulmonary bypass (minute)	213.4 (169.6–224.5)	241.3 (219.2–286.3)	.07
Cooling time (minute)	65.7 (48.0–74.0)	95.0 (79.0–127.3)	.003
Circulatory arrest time (minute)	—	51.0 (39.0–72.0)	
ACP time (minute)	55.0 (38.0–64.0)	—	
Warming time (minute)	81.7 (61.0–93.4)	87.6 (69.2–99.0)	.24
Aortic cross-clamp time (minute)	144.7 (118–196)	132.4 (110–185)	.34



**Figure 2.** Dynamics of cerebral oxygenation value of the right and left hemispheres during the ascending aorta and arch surgery, for both groups. ACP, antegrade cerebral perfusion; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; rSO<sub>2</sub>, %, regional hemoglobin oxygen saturation. \**p* < .05 was considered as statistical significance.

hypoperfusion, whereas in the ACP group cerebral circulation was supported by ACP.

As shown in Figure 2, at the reperfusion stage (2 minutes after circulatory arrest) in the DHCA group, a marked increase in rSO<sub>2</sub> values was observed because of an abrupt increase in cerebral perfusion pressure, and the maximum peak of rSO<sub>2</sub> values was achieved during the warming stage. In the ACP group, an abrupt increase in rSO<sub>2</sub> values was not significant after the end of circulatory arrest.

After the termination of CPB (15 minutes after CPB) in the DHCA group, a prominent decrease in rSO<sub>2</sub> values was observed due to an increment in brain metabolic activity when patient the was warmed. Therefore, two opposite peaks of rSO<sub>2</sub> values are marked on the Figure 2 at the end of circulatory arrest and warming stages, respectively. In the ACP group, opposite peaks of rSO<sub>2</sub> values at the abovementioned stages were smoother at the backdrop of cerebral perfusion and moderate hypothermia. At the end of surgery, significantly decreased rSO<sub>2</sub> values were detected for both hemispheres in the DHCA group, compared with the respective values in the ACP group.

Mean value of hematocrit at anesthesia induction was 40 (35–43%) for the ACP group, and 39 (33–44%) for the DHCA group; whereas, at the end of surgery, the values were 28 (25–32%) and 26 (23–31%) for the ACP and DHCA groups, respectively. No statistically significant difference in hematocrit level was detected between the groups. Furthermore, no packed red blood cells were transfused during CPB.

During the induction of anesthesia, glucose levels in the ACP and DHCA groups were 5.5 (4.9–5.9) and

5.3 (4.9–5.8) mmol/L, respectively. In the same period, lactate levels in the ACP and DHCA groups were 1.0 (.6–1.2) and .9 (.5–1.3) mmol/L, respectively.

Once patients were completely warmed up and after the termination of CPB (15 minutes after CPB), a statistically significant increase in blood glucose level was detected in the ACP and DHCA groups, to values of 9.0 (8.2–9.7) mmol/L (*p* = .001) and 11.1 (9.9–12.1) mmol/L (*p* = .003), respectively. In the DHCA group, the glucose level was significantly higher than that in the ACP group (*p* = .002). Moreover, a significant increase in blood lactate level was detected in the ACP and DHCA groups at this stage; levels increased to 5.3 (4.2–6.2) mmol/L (*p* = .004) and 8.5 (7.1–9.3) mmol/L (*p* = .0001), respectively. In the DHCA group, lactate levels after termination of CPB were significantly higher than that in the ACP group (*p* = .002). For the DHCA group, the highest level of blood lactate is indicative of the development of a more pronounced metabolic acidosis.

### Neurologic Complications

The results of univariate logistic regression analysis demonstrated that the risk of neurological complications in the early postoperative period of the ascending aorta and aortic arch replacement is dependent on the extent of rSO<sub>2</sub> decrease during circulatory arrest (Table 2). Other factors did not affect the development of neurological outcome in the early postoperative period. The threshold value for rSO<sub>2</sub> decrease in predicting of neurological outcome was 33% with a sensitivity of 82.7% and a specificity of 58.7% according to the ROC analysis. When rSO<sub>2</sub>

**Table 2.** Predictive value of indicators for neurological complications scores.

Variable	Neurological Complications		
	OR	95% CI	p Value
Age	1.02	.94–1.19	.18
Body mass index	1.01	.91–1.15	.32
Atrial fibrillation	1.19	.81–1.83	.16
Chronic obstructive pulmonary disease	1.05	.99–1.11	.23
Chronic renal failure	1.56	.45–3.48	.48
The duration of CPB	1.0	.99–1.04	.22
The duration of aortic cross-clamp	1.05	.96–1.15	.54
The absolute values of rSO <sub>2</sub> during aortic surgery less than 40%	1.49	.65–2.34	.21
Decrease of rSO <sub>2</sub> at the circulatory arrest	1.16	1.09–1.28	.03

decreased by >33% of the previous values, the probability of neurological complications increased 5.4-fold (OR = 5.4 [1.12–12.91], *p* = .03).

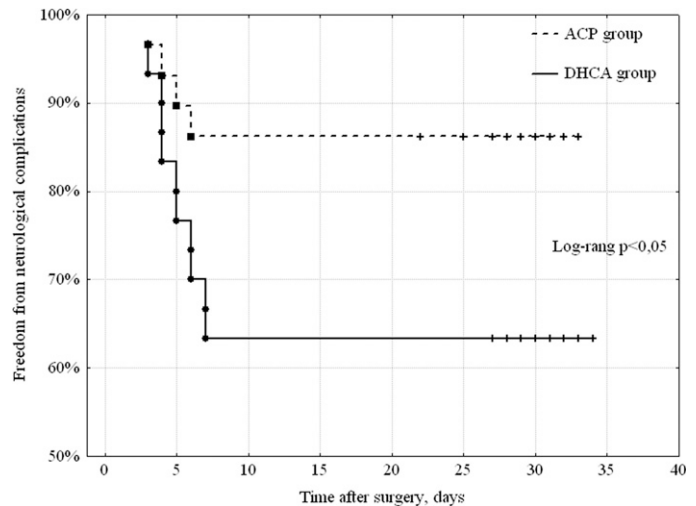
Details of the clinical outcomes are shown in Table 3.

Neurologic complications in the ACP group were observed in 13.8% of cases during the hospitalized period. Two patients were diagnosed with moderately expressed posthypoxic encephalopathy (composite scores of 25 and 26 respectively, according to the MMSE scale). Stroke was identified in two patients, in the left and right carotid arterial regions. For patients who developed stroke, a decrease in rSO<sub>2</sub> values within the range of 29–35% of the baseline was noted during aortic replacement surgery.

Neurologic complications in the DHCA group were observed in 37.9% of cases (significantly higher than in the ACP group). Six patients were diagnosed with moderately expressed posthypoxic encephalopathy, according to the MMSE scale for this patient group, with a mean composite score of 25 (23–27). Stroke was detected in five patients, specifically in the left and right carotid arterial regions

**Table 3.** Postoperative complications and clinical course.

	ACP Group ( <i>n</i> = 29)	DHCA Group ( <i>n</i> = 29)	<i>p</i> Value
Neurologic complications			
All (%)	4 (13.8)	11 (37.9)	.03
Encephalopathy (%)	2 (6.9)	6 (20.6)	.12
Acute stroke (%)	2 (6.9)	5 (17.2)	.22
Acute myocardial infarction (%)	1 (3.4)	0	.31
New-onset atrial fibrillation (%)	5 (17.2)	4 (13.7)	.71
Cardiac and pulmonary insufficiency (%)	3 (10.3)	5 (17.2)	.44
Renal insufficiency (%)	4 (13.7)	5 (17.2)	.71
Multorgan dysfunction syndrome (%)	3 (10.3)	5 (17.2)	.44
Inotropic support (%)	8 (27.5)	10 (34.4)	.57
Resternotomy for bleeding after aortic surgery (%)	3 (10.3)	4 (13.7)	.68
Ventilation time (hour)	45.8 (24–58)	54.6 (38–62)	.33
ICU (days)	4.2 (3–6)	5.4 (4–8)	.12
Hospital stay (days)	30.5 (21–39)	31.2 (24–38)	.41
Inhospital mortality (%)	3 (10.3)	4 (13.7)	.68



**Figure 3.** Kaplan–Meier curves for cumulative freedom for neurologic complications, according to the method of cerebral protection during aortic replacement. ACP, antegrade cerebral perfusion; DHCA, deep hypothermic circulatory arrest.

(*n* = 4) and the vertebral basilar basin (*n* = 1). These patients exhibited a reduction in rSO<sub>2</sub> values during circulatory arrest in the range of 29–46% of the baseline. Figure 3 shows freedom from neurologic complications according to the method of cerebral protection used during aortic replacement surgery.

Following aortic replacement surgery, cumulative freedom from neurologic complications at 30.7 (22–39) days, which was the mean duration of hospitalization for all patients, was 86.2 and 65.6% for patients in the ACP and DHCA groups, respectively. Significant differences were detected between the curves for freedom from neurologic complications.

Three deaths were observed in the ACP group during the early postoperative period. One fatal outcome of a 48-year-old patient occurred as a consequence of multiple organ failure combined with stroke in the left and right carotid arterial territories. For this patient, rSO<sub>2</sub> values decreased by 33% and 35% for the right and left hemispheres, respectively, during aortic replacement surgery. For the remaining two cases (45 and 52 years), the fatal outcome was the consequence of uncontrollable bleeding and cardiopulmonary failure requiring resternotomy. For these patients, the decrease in rSO<sub>2</sub> values during aortic replacement surgery was demonstrated to be in the range of 23–32% of the baseline.

Four deaths were noted in the DHCA group. Two women, 36 and 48 years, and one man, 52 years, succumbed because of progression to multiple organ failure. For these patients, a decrease in rSO<sub>2</sub> values during circulatory arrest was detected in the range of 30–48% of the baseline. Mortality between the study groups did not differ significantly.

A lethal complication was demonstrated in one male patient, 45 years, who had bleeding due to disseminated

intravascular clotting. For this patient, rSO<sub>2</sub> values decreased by 12% and 18% for right and left hemispheres, respectively, during circulatory arrest.

### QoL Assessment

Table 4 presents the QoL data for patients from both groups, before surgery and for a long-term period after aortic replacement surgery (1-year follow-up).

For the ACP group in the long-term period after surgery, four patients were lost for follow up as three patients died in hospital and one death was registered within 6 months of surgery. For the DHCA group in the long-term period after surgery, six patients were excluded from the QoL assessment as four patients died in hospital and two patients died within 8 months of surgery.

Comparing SF-36 scores between the ACP and DHCA groups did not demonstrate any statistically significant differences prior to surgery or in the long-term period following surgery. Preoperative values of patients were  $\leq 52$  for most scales excluding PF and SF, which indicates a very poor QoL.

For the ACP group, a statistically significant increase in the scores of seven subscales and two summary measures was detected during the long-term period after surgery: RP ( $p = .001$ ), BP ( $p = .0002$ ), GH ( $p = .02$ ), VT ( $p = .005$ ), SF ( $p = .02$ ), RE ( $p = .003$ ), MH ( $p = .01$ ), PCS ( $p = .03$ ), and MCS ( $p = .01$ ). For the DHCA group, a statistically significant increase in the scores of four subscales and one summary measure was detected: BP ( $p = .005$ ), VT ( $p = .02$ ), SF ( $p = .001$ ), RE ( $p = .0002$ ), and MCS ( $p = .01$ ). Therefore, no statistically significant positive differences in following subscale scores were demonstrated in the DHCA group, as compared with the ACP group: RP, GH, MH, and PCS. In both groups, PCS and MCS subscale scores remained reduced.

According to the results of correlation analysis, GH and MH subscale scores in the long-term period after surgery was inversely correlated with the total length of CPB during aortic replacement surgery:  $r = -.43$ ,  $p = .002$  and  $r = -.48$ ,  $p = .001$ , respectively. Furthermore, an

inverse correlation between the GH score in the long-term postoperative period after surgery and intraoperative cooling time was detected ( $r = -.51$ ,  $p = .003$ ). Therefore, it was demonstrated that the assessment of the overall health and psychological wellbeing of patients in the long-term period after aortic replacement surgery is dependent on intraoperative settings. Notably, the DHCA group exhibited a tendency for prolonged total CPB time, and the cooling time was significantly increased during the course of surgery, compared to the ACP group (Table 1).

### DISCUSSION

The main finding of the present study was that the use of ACP in the setting of moderate hypothermia during the surgical treatment of the aorta demonstrated higher qualities of cerebral protection, as evidenced by reduced neurologic complications during the early postoperative period compared to patients who underwent DHCA during surgery. Another notable finding of the study was that QoL during the long-term period after aortic replacement improved, but it is not dependent on the methods of cerebral protection during the course of surgery; rather they are inversely correlated with the length of CPB (which tended to increase for the DHCA group, compared with the ACP group), and with cooling time, which was extended in the DHCA group.

During the surgical treatment of DeBakey type I aortic dissection, technical difficulties that have arisen are associated not only with the duration of surgical intervention and CPB, but also with the necessity to protect the central nervous system during circulatory arrest, as the patient's QoL may be affected by these factors (15,16).

According to a recent meta-analysis, the risk of postoperative stroke depends on the method of cerebral protection and significantly reduced by the use of moderate hypothermic circulatory arrest with ACP (17). This is consistent with our results of significant differences in neurological outcome in the study groups, and increasing the number of neurological complications when used DHCA.

**Table 4.** Results of the SF-36 health survey in patients of both groups before and late postoperative periods.

SF-36 Subscales	Pre-operative QoL			Post-operative QoL		
	ACP Group ( $n = 29$ )	DHCA Group ( $n = 29$ )	$p$ Value	ACP Group ( $n = 25$ )	DHCA Group ( $n = 23$ )	$p$ Value
PF	70.0 (55.0–90.0)	85.0 (80.0–95.0)	.23	75.0 (50.0–95.0)	95.0 (50.0–100.0)	.41
RP	25.0 (0.0–50.0)	50.0 (0.0–50.0)	.77	75.0 (50.0–100.0)	75.0 (50.0–100.0)	.83
BP	51.0 (22.0–64.0)	41.0 (22.0–51.0)	.78	84.0 (68.0–100.0)	84.0 (62.0–84.0)	.87
GH	30.0 (15.0–50.0)	30.0 (15.0–45.0)	.39	50.0 (20.0–62.0)	25.0 (25.0–42.0)	.45
VT	35.0 (25.0–50.0)	35.0 (25.0–40.0)	.90	50.0 (40.0–55.0)	45.0 (40.0–55.0)	.56
SF	87.5 (62.5–100.0)	75.0 (50.0–75.0)	.40	100.0 (87.5–100.0)	100.0 (81.5–100.0)	.75
RE	33.3 (0.0–66.2)	33.3 (33.3–66.6)	.46	100.0 (66.6–100.0)	100.0 (100.0–100.0)	.49
MH	52.0 (40.0–58.0)	52.0 (36.0–56.0)	.76	64.0 (60.0–72.0)	60.0 (56.0–72.0)	.85
PCS	38.1 (30.8–46.0)	41.6 (33.0–43.0)	.83	57.1 (46.2–63.6)	50.4 (28.0–52.4)	.92
MCS	38.2 (33.6–42.6)	36.5 (35.1–37.0)	.69	50.0 (44.2–51.8)	51.1 (41.5–51.2)	.87



It is necessary to elucidate the pathophysiological aspects of alterations emerging during circulatory arrest and brain tissue hypoperfusion. In the hypoxic setting, anaerobic glycolysis is activated, which leads to the accumulation of lactate as one of the end products. Excess lactate results in tissue acidosis. Activation of anaerobic glycolysis is typically observed during circulatory arrest (18). Because of the lack of oxygen and glucose transport to the brain tissue, neurons are significantly damaged because of the accumulation of neurotoxic metabolites. Parts of neurons are committed to cellular death, which is reflected in the deterioration of the neurological status of patients in the postsurgery period (18). In the present study, a significant increase in lactate levels was demonstrated in both groups after the termination of CBP relative to the anesthesia induction stage. Furthermore, in the DHCA group, lactate concentrations were significantly elevated, as compared with the ACP group, suggesting more pronounced metabolic alterations.

Constant maintenance of arterial pressure within the range of 60–140 mmHg is essential for normal brain functioning. Sharp decreases in arterial pressure during circulatory arrest typically induce temporary shifts in cerebral blood flow levels. Notably, when brain temperature is 20°C, the autoregulatory system supports cerebral blood flow in the range of 30–100 mmHg, and when brain temperature decreases to 12°C, autoregulation is terminated (19). Impairments in these mechanisms may be aggravated by prolonged vasospasm in the conditions of craniocerebral hypothermia, and length of circulatory arrest. In the present study, the length of circulatory arrest was 51 minutes in the DHCA group, which exceeded the “safe” limit of 40 minutes as determined by a previous study (20).

All these factors should be considered when providing cerebral protection. Consequently, during vascular stiffness, a reduction in the volume of cerebral perfusion during circulatory arrest with subsequent reperfusion can induce ischemia-reperfusion injury of brain tissue and defects in cerebral blood flow autoregulation (21,22).

In the present study, changes in the cerebral perfusion are reflected in the sharp decrease of rSO<sub>2</sub> values during circulatory arrest (>30% from the baseline) and the development of a steep rSO<sub>2</sub> gradient (34–70%) at the reperfusion stage in the DHCA group, compared with the ACP group. Based on our findings, it was demonstrated that a decrease of rSO<sub>2</sub> values >33% from the baseline increases the probability of neurological complications 5.4-fold during the early postoperative period.

The length of CBP is an independent risk factor for the dysfunction of the central nervous system in the postoperative period (23). In the present study, due to an extended cooling time, length of CPB tended to increase in the DHCA group, compared with the ACP group. Furthermore, the results of correlation analysis demonstrated

that GH and MH subscale scores in the long-term postoperative period were inversely associated with the duration of CPB. Similarly, GH subscale scores in the long-term postoperative period were inversely correlated with the cooling time during surgery. These findings indicated that the patient’s general well-being and mental status in the long-term period following aortic replacement surgery is dependent on intraoperative conditions.

The wider range of methods of cerebral perfusion in the course of aortic replacement, including retrograde and ACP, should be investigated in future studies, as should a combination of these methods with various conditions of temperature, to elucidate the optimal approach to protect both the central nervous system and visceral organs.

The present study had several limitations. First, the dynamics of the levels of neural markers associated with cerebral tissue injury were not analyzed. Second, the limited number of patients per group may restrict the elucidation of a wider range of predictors for various postoperative complications. Moreover, we did not evaluate neurological complications during the long-term period following aortic replacement.

The present study demonstrated that the use of moderate hypothermia with ACP during aortic replacement demonstrated higher qualities of cerebral protection, as evidenced by the reduced incidence of neurologic complications observed during the early postoperative period, compared with the patients who underwent surgery with DHCA. The risk of neurological complications is associated with the extent of rSO<sub>2</sub> decrease during circulatory arrest, and the most profound decrease in rSO<sub>2</sub> values was detected in the DHCA group. According to our data, the risk of neurological complications was not associated with the following factors: age, body mass index, presence of atrial fibrillation, or chronic obstructive pulmonary disease. Furthermore, neurological complications were demonstrated to be independent of intraoperative conditions, which included the duration of CPB and aortic cross-clamp time.

QoL parameters during the long-term period following aortic replacement do not depend on the methods of cerebral protection during surgery; rather they are inversely correlated with the duration of CPB, which tended to increase in the DHCA group as compared with the ACP group, and with cooling time, which was more extended in the DHCA group.

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