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Selective cerebral perfusion during total hypothermic circulatory arrest in surgical treatment of acute thoracic aortic dissection

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Abstract

Background. *Surgical treatment of acute thoracic aortic dissection is often associated with the need for selective cerebral perfusion at the stage of total hypothermic circulatory arrest.*

Objective. *To establish the preferred method and mode of selective cerebral perfusion (SCP) during complete hypothermic circulatory arrest in surgical treatment of acute thoracic aortic dissection.*

Material and methods. *Study design: prospective, cohort, single-center. Inclusion criteria: surgical intervention using cardiopulmonary bypass, confirmed diagnosis of acute aortic dissection type A according to Stanford, age > 18 years. The study included 112 patients: 77 men and 32 women aged 31 to 75 years, M±SD=54.79±11.33. All patients (n=112) were treated between 2019 and 2023 and were divided into 3 groups depending on the method of selective cerebral perfusion: antegrade unilateral perfusion (n=51), antegrade bilateral perfusion (n=49), and retrograde perfusion (n=12). The endpoints of the study* *were cerebrovascular accident (CVA) in the early postoperative period and 30-day in-hospital mortality.*

Results. *In the bilateral antegrade cerebral perfusion group (biACP), the incidence of CVA in the early postoperative period (p=0.002) and 30-day in-hospital mortality (p=0.006) were statistically significantly lower. Acute cerebral circulatory failure in the postoperative period increases the risk of death by 7.977 times. The volumetric rate of selective perfusion in biACP is a statistically significant predictor of death, and biACP >12.5 ml/kg/min when calculated for the true body weight according to Broc is associated with an increased risk of hospital mortality.*

Conclusions. *Bilateral antegrade cerebral perfusion is the preferred technique for selective cerebral perfusion as part of the cardiopulmonary bypass procedure in the surgical treatment of acute thoracic aortic dissection. Restrictive biACP tactics can reduce the risk of 30-day hospital mortality.*

Keywords: cardiopulmonary bypass, aortic dissection, total hypothermic circulatory arrest, deep hypothermia, selective cerebral perfusion

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CPB, cardiopulmonary bypass
CVA, cerebrovascular accident
biACP, bilateral antegrade cerebral perfusion
BMI, body mass index
BSA, body surface area
CI, confidence interval
ICU, Intensive Care Unit
OR, odds ratio
RCP, retrograde cerebral perfusion

SCP, selective cerebral perfusion
SOFA, Sequential Organ Failure Assessment
SPVR, selective perfusion volumetric rate
THCA, total hypothermic circulatory arrest
uACP, unilateral antegrade cerebral perfusion

Introduction

Reconstructive interventions on the aortic arch represent one of the most complex areas of cardiovascular surgery, not only in terms of surgical tactics, but also in terms of cardiopulmonary bypass (CPB) [1]. Providing CPB during surgical interventions on the aortic arch is complicated by the need to ensure selective blood supply to the brain during total hypothermic circulatory arrest (THCA) [2]. So far, many methods of cerebral perfusion have been described, opinions on the choice of method and technique differ, and agreement has only been reached regarding the necessity of this procedure [3]. Methods of technical implementation of the technique of selective cerebral perfusion are subdivided into retrograde, antegrade unilateral, and antegrade bilateral perfusion defined in the order of increasing complexity of the connection. Each method has its advantages and disadvantages, but in the setting of emergency surgical intervention for acute aortic dissection, the clinical presentation is further complicated by the changes in the acute period of the disease over time and often preceding cerebral malperfusion. Available publications on this topic are few and indicate comparable effectiveness of all methods of cerebral perfusion [4–6], but, as a rule, they discuss the problem within the framework of aortic surgery in general and do not allow for the development of a practical approach to this category of patients, agreeing only on the need for selective perfusion [7].

Objective. The aim of our study was to establish the preferred method and regimen of selective cerebral perfusion during total hypothermic circulatory arrest in surgical treatment for acute thoracic aortic dissection.

Material and methods

A single-center prospective cohort study was performed to investigate the treatment outcomes of patients with acute thoracic aortic dissection.

Patient inclusion criteria were the following: surgery performed under cardiopulmonary bypass, a confirmed diagnosis of acute Stanford type A aortic dissection, emergency hospital admission, and age over 18 years. Exclusion criteria were as follows: a SOFA score of over 12 at hospital admission, a body mass index (BMI) of over 40, and the age over 80 years old.

The endpoints of the study were the occurrence of cerebrovascular accident (CVA) in the early postoperative period and a 30-day hospital mortality rate.

In accordance with the inclusion and exclusion criteria, 112 patients were enrolled in the study: 77 (68.8%) men and 35 (31.2) women aged from 31 to 75 years, M±SD = 54.79±11.33.

In all cases, CPB was performed under conditions of THCA with the selective cerebral perfusion (SCP), including antegrade unilateral perfusion in 51 patients, antegrade bilateral perfusion in 49, and retrograde perfusion in 12 patients. The unilateral cerebral perfusion was performed by connecting the main arterial line with a 3/8-3/8 inch adapter to a 10 mm diameter linear vascular graft; the vascular graft was also connected to the subclavian artery by an end-to-side anastomosis. To provide bilateral antegrade cerebral perfusion (biACP), additional 3/8 and 1/4 inch arterial lines were used, as well as 3/8-3/8-3/8, 3/8-1/4-1/4, 3/8-1/4 adapters, and 1/4- LL (Luer Lock adapter); 15 Fr retrograde cannulas with an inflatable cuff were also used. The retrograde perfusion was performed through the cannula (28/30/32 Fr) of superior vena cava. The cerebral perfusion was monitored using cerebral oximetry with an Invos 5100C device (Medtronic, USA), avoiding a decrease in tissue oxygenation (rSO_2) of more than by 20% from baseline within the range of 55–75%. The myocardial protection was provided retrogradely with Custodiol solution.

CPB was used in the treatment of 112 (100%) patients with acute Stanford type A aortic dissection. CPB was ensured by using Stockert devices. C5, S5 (“Sorin”, USA). For venous drainage, separate cannulation of the superior and inferior vena cava was performed (cannulas of sizes 32, 34, 36 Fr were used); and depending on the level of dissection, the cannulation of the femoral arteries, aorta, right subclavian artery, right axillary artery or brachiocephalic trunk was performed (using cannulas of sizes 17, 19, 20, 21, 22, 23, 24 Fr) for blood return. Systemic blood flow velocity was calculated with a perfusion index of 2.7. Ideal weight was calculated using the original Broca formula (1871) without corrections: Ideal weight [kg] = height [cm] – 100 [8]. Body surface area (BSA) was calculated using the Dubois formula (1916): BSA $[m^2]=0.007184\times height[cm]^{0.725}\times weight[kg]^{0.425}$. The selective perfusion volumetric rate (SPVR) was calculated based on ideal weight.

Data on the anthropometric parameters of patients and perioperative clinical parameters are presented in Table 1, which shows that, despite the hypothermia depth, all patients had been warmed up to normal values by the end of surgery, which increased the duration of CPB.

Table 1. Descriptive characteristics of perioperative data

Patient parameters, n=112	M±SD / Me	95% [CI]/(Q_1; Q_3)
Age, years, M±SD	54.79±11.33	[52.66–56.91]
BMI, kg/m², Me	28.65	(25.70;31.23)
BSA, m², Me	2.09	(1.87;2.20)
Height, cm, M±SD	173.92±10.10	[172.03–175.81]
Weight, kg, M±SD	88.62±18.49	[85.16–92.09]
Ideal weight, kg, M±SD	73.92±10.10	[72.03–75.81]
Ideal BMI, kg/m², Me	24.49	(23.88;24.70)
Ideal BSA, m², M±SD	1.88±0.20	[1.85–1.92]
CPB duration, minutes, Me	180.00	(153.00;230.00)
Cross clamping duration of, minutes, Me	98.50	(79.75;141.25)
THCA, minutes, Me	29.00	(23.00;38.00)
T THCA, C°, Me	25.45	(23.95;26.60)
SPVR, mL/kg/min, M±SD	11.40±3.00	[10.83–11.96]
Diuresis, ml, M±SD	2108.33±1245.76	[1827.46–2389.21]
Blood loss, ml, Me	2000.00	(1500.00;2500.00)
Hemoglobin upon transfer to the Intensive Care Unit, g/L, M±SD	92.96±11.24	[89.93–96.00]
Albumin level at transfer to the Intensive Care Unit, g/L, M±SD	30.65±4.63	[29.62–31.68]
T when transferred to the Intensive Care Unit, C°, Me	36.50	(35.70;36.90)
Length of stay in the Intensive Care Unit, days, Me	6.00	(4.00;12.25)
Hospital length of stay, days, Me	15.50	(10.00;21.00)

Notes: BMI, body mass index; BSA, body surface area; CPB, cardiopulmonary bypass; THCA, total hypothermic circulatory arrest; T, temperature; SPVR, selective perfusion volume rate; ICU, intensive care unit; M, mean value; SD, standard deviation; Me, median; Q, quartile; n, number of cases; CI, confidence interval

Acute cerebrovascular accidents were diagnosed based on neurological examination, electroencephalography, and magnetic resonance imaging (MRI) or computed tomography (CT) scans. On the first postoperative day, after patients' condition had stabilized, sedation was withdrawn to assess their level of consciousness. If neurological deficits were detected, instrumental investigations were performed. Data on the incidence of acute cerebrovascular accidents and in-hospital mortality are presented in Table 2, demonstrating that the treatment outcomes are comparable with international practice.

Table 2. Descriptive characteristics of complications and treatment outcomes

Parameters	Categories	n	%	95% [CI]
CVA	Present	41	36.6	[27.7–46.2]
	Absent	71	63.4	[53.8–72.3]
Outcome	Discharge	81	72.3	[63.1–80.4]
	Death	31	27.7	[19.6–36.9]

Statistical analysis was performed using StatTech v. 4.8.3 software (the developer: StatTech LLC, Russia). Quantitative variables were assessed for compliance with a normal distribution using the Shapiro–Wilk test (for fewer than 50 subjects) or the Kolmogorov–Smirnov test (for more than 50 subjects). Quantitative variables with a normal sampling distribution were described using mean values (M) and standard deviations (SD). The 95% confidence interval (95% CI) limits were specified as a measure of representativeness for mean values. In the absence of a normal distribution, the quantitative data were described using the median (Me) and the lower and upper quartiles (Q1;Q3). Categorical data were described using absolute values and percentages; 95% CIs for percentages were calculated using the Clopper-Pearson method. Comparison of three or more groups by a quantitative variable, which distribution in each of the groups corresponded to the normal distribution, was performed using one-way analysis of variance; post-hoc comparisons were performed using the Tukey test (under the condition of equal variances) and the Games-Howell test (in case of unequal variances). Comparison of three or more groups by a quantitative variable, which distribution differed from the normal distribution, was performed using the Kruskal-Wallis test; post-hoc comparisons were performed using the Dunn test with Holm correction. Comparison of percentages in the analysis of multifield contingency tables was also performed using the Pearson χ^2 test. Post-hoc comparisons were performed using the Pearson χ^2 test with Holm correction. As a quantitative measure of the effect when comparing relative variables, the odds ratio (OR) with 95% CI [OR; 95% CI] was calculated. The direction and strength of the correlation between two quantitative variables were assessed using the Spearman's rank correlation coefficient (for variables with a non-normal distribution). A predictive model characterizing the relationship of a quantitative variable from factors was also developed using the linear regression method. Comparison of two groups by a quantitative variable, which distribution in each group corresponded to a normal distribution, under the condition of equal variances, was performed using Student's t-test. To assess the discriminatory ability of quantitative variables in predicting a specific outcome, the ROC curve analysis was also used. The separating value of a quantitative variable at the cut-off point was determined by the highest value of the Youden Index. Differences were considered statistically significant at $p<0.05$.

Results

In this study, a comparative assessment of patient groups was made depending on SCP method: antegrade unilateral perfusion (uACP), antegrade bilateral perfusion (biACP) and retrograde cerebral perfusion (RCP). The presented parameters of patients of the three groups (Table 3) did not have statistically significant differences in values of most parameters, which indicated the comparability of intraoperative treatment tactics, however, in the retrograde cerebral perfusion (RCP) group, the THCA temperature, and SPVR were statistically significantly lower, which was due to the peculiarities of the RCP technique ($p<0.001$).

Table 3. Comparative characteristics of groups depending on the method of selective cerebral perfusion

Parameters	Selective cerebral perfusion			p
	Antegrade unilateral, n=51	Antegrade bilateral, n=49	Retrograde, n=12	
Age, years, M (SD)	54.22 (10.87)	55.14 (12.56)	55.75 (8.17)	0.878
BMI, kg/m², Me (Q_1;Q_3)	28.70 (25.35;30.95)	29.30 (25.70;32.20)	28.35 (26.90;29.85)	0.882
BSA, m², M (SD)	2.03 (0.25)	2.06 (0.28)	2.13 (0.13)	0.164
Height, cm, M (SD)	172.94 (9.70)	173.84 (11.30)	178.42 (4.36)	0.101
Weight, kg, Me(Q_1;Q_3)	87.00 (72.50;98.00)	90.00 (70.00;101.00)	90.00 (86.50;95.00)	0.688
Ideal weight, kg, M (SD)	72.94 (9.70)	73.84 (11.30)	78.42 (4.36)	0.113
Ideal BMI, kg/m², Me (Q_1;Q_3)	24.49 (23.88;24.69)	24.44 (23.88;24.78)	24.63 (24.49;24.76)	0.212
Ideal BSA, m², M (SD)	1.86 (0.18)	1.89 (0.22)	1.87 (0.08)	0.091
CPB duration, minutes, Me(Q_1;Q_3)	178.50 (151.25;229.25)	179.00 (153.00;216.00)	216.00 (176.75;245.25)	0.275
Cross clamping duration of, minutes, Me(Q_1;Q_3)	100.00 (79.50;155.00)	98.00 (79.00;133.00)	105.00 (82.00;129.25)	0.965
THCA, minutes, Me (Q_1;Q_3)	30.00 (23.00;41.00)	29.00 (23.00;38.00)	24.00 (21.50;28.25)	0.138
T THCA, C°, Me (Q_1;Q_3)	25.50 (24.05;26.55)	26.00 (24.90;27.20)	18.85 (18.38;20.10)	<0.001 * antegrade unilateral vs. retrograde $p<0.001$ antegrade bilateral vs. retrograde $p<0.001$
SPVR, mL/kg/min, M (SD)	11.56 (2.75)	11.95 (2.88)	8.44 (3.08)	<0.001 * antegrade bilateral vs. retrograde $p<0.001$ antegrade unilateral vs. retrograde $p=0.003$
Diuresis, ml, Me(Q_1;Q_3)	2000.00 (1425.00;2800.00)	1675.00 (950.00;2525.00)	3300.00 (1675.00;3850.00)	0.091

Blood loss, ml, Me (Q_1;Q_3)	2000.00 (1500.00;2500.00)	2000.00 (1525.00;2500.00)	2000.00 (1725.00;2625.00)	0.945
Hemoglobin, g/L, M (SD)	91.43 (9.55)	93.73 (11.66)	91.25 (14.93)	0.775
Albumin, g/L, M (SD)	30.33 (4.40)	30.38 (5.02)	33.34 (3.22)	0.226
T when transferred to the Intensive Care Unit, C°, Me (Q_1;Q_3)	36.70 (36.02;37.60)	36.45 (35.50;36.60)	36.90 (36.40;37.05)	0.059
Length of stay in the Intensive Care Unit, days, Me (Q_1;Q_3)	5.00 (4.00;14.00)	7.00 (4.00;12.00)	6.00 (5.00;7.50)	0.959
Hospital length of stay, days, Me (Q_1;Q_3)	17.00 (11.00;21.00)	14.50 (9.75;21.00)	18.00 (10.00;22.50)	0.856

Notes: M, mean; SD, standard deviation; Me, median; Q, quartile; n, number of cases; p, significance level; * significance level of multiple comparisons

A comparative analysis of the groups (Table 4) revealed a statistically significant difference in the number of diagnosed episodes of stroke in the postoperative period (p=0.002). In the biACP group, the stroke incidence was statistically significantly lower than in the uACP group (p=0.004) and the RCP group (p=0.010). In-hospital mortality was also statistically significantly lower in the biACP group (p=0.006), indicating the advantages of the biACP technique.

Table 4. Comparative characteristics of complications and treatment outcomes depending on the method of selective cerebral perfusion

Parameters	**Categories**	**Selective cerebral perfusion**			**p**
		Antegrade unilateral	Antegrade bilateral	Retrograde	
CVA, abs. (%)	Present	25 (49.0%)	9 (18.4%)	7 (58.3%)	0.002* antegrade unilateral vs. antegrade bilateral p=0.004 antegrade bilateral vs. retrograde p=0.010
	Absent	26 (51.0%)	40 (81.6%)	5 (41.7%)	
Outcome, abs. (%)	Discharge	31 (60.8%)	43 (87.8%)	7 (58.3%)	0.006*
	Death	20 (39.2%)	6 (12.2%)	5 (41.7%)	

					antegrade unilateral vs. antegrade bilateral p=0.006 antegrade bilateral vs. retrograde p=0.035

Notes: abs., absolute value; p. significance level, * significance level of multiple comparisons

Using the Pearson χ^2 test with Holm's correction, we established a statistically significant relationship between the stroke factor and the treatment outcome (Table 5, Fig. 1). The odds of discharge in the group with stroke were 7.977 times lower compared to the group without stroke; the differences in odds were statistically significant (OR=0.125; 95% CI [0.049–0.318]).

Table 5. Analysis of outcome with consideration of cerebrovascular accident

Parameter	**Category**	**CVA**		**p**
		Absent	Present	
Outcome	Death	9 (12.7)	22 (53.7)	<0.001
	Discharge	62 (87.3)	19 (46.3)	

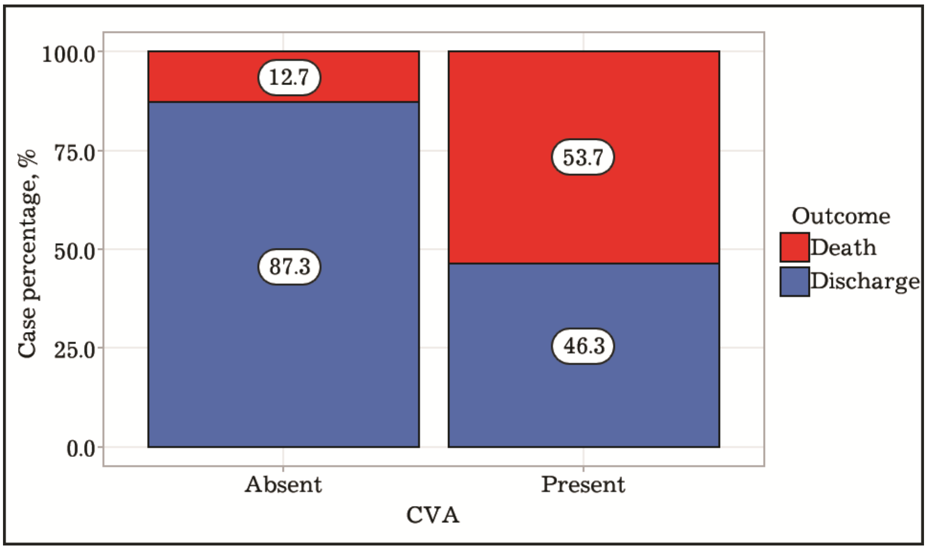

Fig. 1. Analysis of the outcome with consideration of cerebrovascular accident

At the next stage of the study, after having received data on the benefits of biACP, we analyzed the patient treatment outcomes in the biACP group (n=49).

Using the Student's t-test, statistically significant differences (p=0.013) were established when analyzing the treatment outcome in relationship from the SPVR (Table 6).

Table 6. Analysis of the relationship of the outcome from the selective perfusion volumetric rate

Parameter	Categories	SPVR, mL/kg/min			p
		M±SD	95% [CI]	n	
Outcome	Discharge	11.57±2.66	[10.75–12.39]	43	0.013
	Death	14.64±3.19	[11.29–17.99]	6	

When assessing the discriminatory ability of fatal outcome prediction, using ROC analysis, the following curve was obtained (Fig. 2). The resulting area under the ROC curve (AUC=0.789) indicated good (0.7–0.8) model quality.

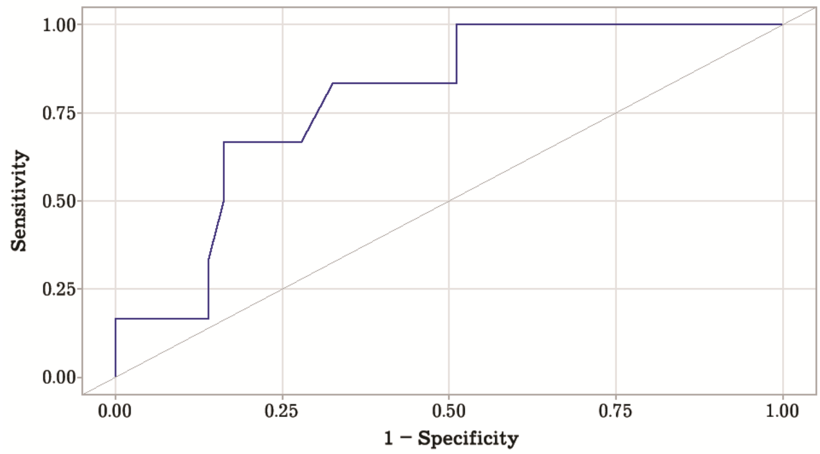

Fig. 2. ROC curve characterizing the discriminatory ability of the selective perfusion volumetric rate in predicting the outcome

Using Youden's J statistic made it possible to calculate the threshold value of the SPVR (Table 7, Fig. 3) when providing biACP at the stage of THCA.

Table 7. Analysis of the discriminatory ability of the selective perfusion volumetric rate

Threshold	Sensitivity (Se), %	Specificity (Sp), %
12.50	83.3	67.4

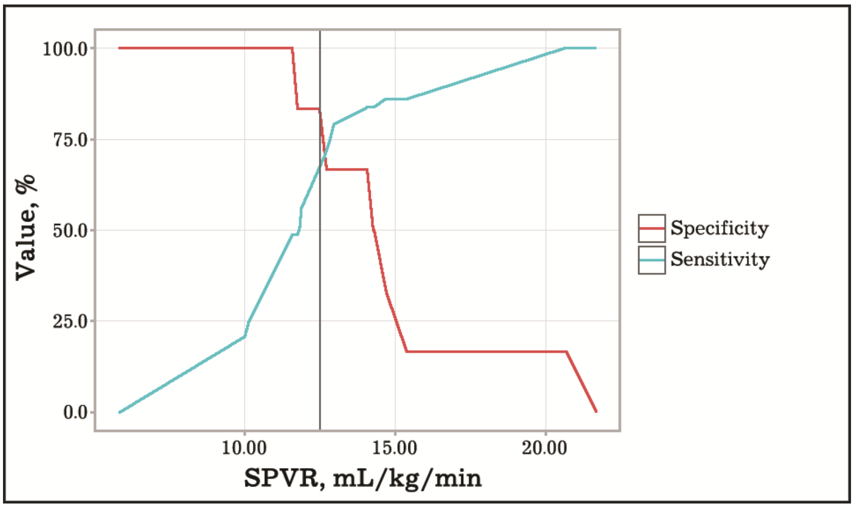

Fig. 3. Analysis of sensitivity and specificity of the model depending on the threshold values of death probability estimates

The SPVR was found to be a statistically significant predictor of mortality (AUC=0.789; 95% CI [0.564–0.998], p=0.023). The threshold value of the SPVR at the cut-off point, which corresponded to the highest value of the Youden index, was 12.50. Mortality was predicted at SPVR above this value. The sensitivity and specificity of the resulting predictive model were 83.3% and 67.4%, respectively.

Discussion

The data obtained during the study allowed us to establish the presence of a statistically significant difference in the incidence of complications (CVA), and the treatment outcomes between the groups of using different SCP tactics, which indicates the advantages of using biACP at the stage of total hypothermic circulatory arrest during surgical treatment of patients with acute thoracic aortic dissection. Data from existing publications indicate the absence of statistically significant differences when using different SCP techniques, but indicate a lower incidence of postoperative CVAs with biACP [9, 10]. The uACP technique, in turn, requires a preoperative assessment of the circle of Willis anatomy, which is not always possible in emergency surgery for vital indications [11]. A potential advantage of the RCP technique is the washout of emboli from the arteries by retrograde blood flow, but a major limitation is the uneven distribution of the perfusion volume due to the pressure-limited volumetric flow rate [12, 13]. Thus, in our study, statistically significant differences in the minimum temperature and cerebral volumetric perfusion rate in the RCP group are due to the limitation of the perfusion rate by the pressure in the superior vena cava; and a deeper level of hypothermia was intended to compensate for the reduced SCP rate from the point of organ protection. The established relationship between the CVA factor and the treatment outcome showed an expected higher risk of death in patients with stroke CVA in the postoperative period when compared with their uncomplicated category. Cerebral SPVR has been a subject of discussion for a long time, since it requires an individual balance to avoid hemorrhage, edema, and ischemic damage to the brain [14, 15]. According to the available literature, in antegrade SCP, the cerebral SPVR value of 10-15 mL/kg/min at a pressure of 40-80 mmHg in the right radial artery serves as a guideline; and the one with retrograde SCP the guideline is 100-500 mL/min with a pressure limit of 20 mmHg in the internal jugular vein [3, 16-18]; however, these values are not tied to the type of cannulation and SCP technique, do not point to the method for calculating the patient's weight, meanwhile the actual and ideal body weight of patients differ significantly. This complicates the choice of cerebral perfusion mode in actual clinical conditions. Having obtained the best results using biACP, compared to other methods, we considered it appropriate to evaluate the relationship between the SPVR and treatment outcomes. A detailed study revealed that the SPVR is a significant predictor of treatment outcome, and a ROC analysis allowed us to establish a threshold SPVR value of 12.5 ml/kg/min for biACP based on the ideal body weight; above this threshold, the risk of death increased.

The obtained data indicate the need for continued research and additional data analysis, taking into account all aspects of intraoperative treatment and individual patient characteristics to improve treatment outcomes in acute thoracic aortic dissection.

Conclusions

1. Bilateral antegrade cerebral perfusion as part of the cardiopulmonary bypass procedure in the surgical treatment for acute thoracic aortic dissection provides a statistically significantly lower

incidence of acute cerebrovascular accident in the early postoperative period (18.4%, p=0.002) and the lowest 30-day hospital mortality (12.2%, p=0.006).

2. Acute cerebrovascular accident in the postoperative period increases the risk of death by 7.977 times (OR=0.125; 95% CI [0.049–0.318], p<0.001).

3. An increase in the selective perfusion volumetric rate above 12.5 mL/kg/min (Se=83.3%, Sp=67.4%) during bilateral antegrade cerebral perfusion leads to an increased risk of 30-day hospital mortality (AUC=0.789; 95% CI [0.564–0.998], p=0.023), which indicates the advisability of restrictive cerebral perfusion tactics.

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