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STRATEGY FOR PROPHYLACTIC APPLICATION OF PERIPHERAL VA-ECMO IN TRANSPLANTATION INVOLVING EXPECTED EXTREMELY PROLONGED ISCHEMIA TIME

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Heart transplantation (HT) with extremely prolonged (>6 hours) graft ischemia is associated with severe cardiac graft dysfunction. The high efficiency of prophylactic (preoperative initiation) veno-arterial extracorporeal membrane oxygenation (VA-ECMO) to prevent severe hemodynamic disorders during cardiac surgery has been demonstrated. **Objective:** to determine the effect of prophylactic VA-ECMO on the perioperative period in HT with an expected graft ischemia >6 hours. **Materials and methods.** Thirty-eight recipients (33 (86.8%) males and 5 (13.2%) females), age 11–66 (44.7 ± 12.0) years (median 48.0 years) were examined. Pre-transplant mechanical circulatory support (MCS) using peripheral VA-ECMO was applied in 15 (39.5%) recipients, in 6 of whom by prophylactic technique. The recipients (n = 38) were divided into 3 groups: 1) "no pre-HT VA-ECMO" (n = 23); 2) "pre-HT VA-ECMO" (n = 9) – pre-transplant VA-ECMO as a bridge to HT; 3) "prophylactic VA-ECMO" (n = 6). **Results.** In "prophylactic VA-ECMO" group, extracorporeal circulation (ECC) (94.0 [85.5; 102.8] min) and reperfusion time (20.0 [18.3; 27.6] min) were shorter ($p < 0.05$) compared to "no pre-HT VA-ECMO" (161.0 [122; 191.5] and 60.0 [55.3; 70.5] min) and "pre-HT VA-ECMO" (127.0 [117; 150.3] and 35.0 [27.8; 48.8] min) groups. The vasoactive-inotropic score was lower ($p < 0.05$) in "pre-HT VA-ECMO" and "prophylactic VA-ECMO" groups compared to recipients in "no pre-HT VA-ECMO" group, 12.1 [11.2; 14.0] and 12.5 [11.7; 14.8] *vs.* 16.0 [15.0; 18.5], respectively. The groups did not differ in terms of incidence of severe primary dysfunction. The "pre-HT VA-ECMO" and "prophylactic VA-ECMO" groups were characterized by shorter duration of mechanical ventilation (MV) compared with "no pre-HT VA-ECMO" group (11.7 [10.0; 16.5] and 12.7 [11.3; 18.4], respectively, *vs.* 14.5 [13.0; 19.3]). The "no pre-HT VA-ECMO" and "prophylactic VA-ECMO" groups did not differ in the need for postoperative MST, 21.7% and 16.7%, respectively. The groups did not differ in terms of length of stay in the intensive care unit (ICU) and in-hospital mortality – 0% ("prophylactic VA-ECMO") and 8.7% ("no pre-HT VA-ECMO") and 11.1% ("pre-HT VA-ECMO"), respectively. **Conclusion.** Prophylactic VA-ECMO in HT with extremely prolonged cardiac graft ischemia reduces ECC duration, reperfusion period, postoperative mechanical ventilation period, and the need for inotropic therapy.

Keywords: heart transplantation, prolonged ischemia time, prophylactic VA-ECMO.

INTRODUCTION

Suspected prolonged donor heart ischemic time is one of the criteria for expanded heart donation [1]. Although the limits of acceptable duration of donor heart ischemia have not yet been defined and continue to be the subject of scientific research, international guidelines state that the cardiac graft ischemia should not exceed 4 hours [2, 8]. Earlier studies have shown that ischemic time >4 hours significantly increases the risk of severe primary graft dysfunction requiring mechanical circulatory support (MCS) [3]. Some successful transplantations with cardiac graft ischemic time lasting for 4–6 hours and more demonstrates the possibility of effective transplantation with cold storage duration exceeding the recommended threshold (≤4 hours) [1, 4–7].

Prophylactic application of VA-ECMO during cardiac surgery is considered as one of the promising directions for improving surgical outcomes in patients with high surgical risk [9, 10].

The prerequisite for this study was the assumption that HT with an expected excessively long (>6 hours) cardiac graft ischemia under prophylactic VA-ECMO will contribute to the maintenance of systemic hemodynamics in the pre-perfusion period, reduce the reperfusion time (time interval between aortic clamp removal and end of ECC), total duration of ECC, reduce the dosage of cardiotonic drugs, and provide a timely transition from artificial to assisted circulation in case of severe early graft dysfunction.

The **objective** of the study was to determine the effect of prophylactic VA-ECMO on the course of the periope-

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rative period in HT with an expected duration of cardiac graft ischemic time >6 hours.

MATERIALS AND METHODS

The study included 38 recipients (33 (86.8%) males and 5 (13.2%) females) aged 11 to 66 (44.7 ± 12.0, median 48.0 years) who underwent primary (n = 37 (97.4%)) or repeat (n = 1 (2.6%)) HT (retransplantation) from January 1, 2011 to December 31, 2021) with cardiac graft ischemia lasting for more than 6 hours, which made up 2.5% of the total number of HT (n = 1500) during the analyzed period. In all observations, transplantation with extremely prolonged (≥6 hours) ischemia was due to the distance of the donor base from the transplant center.

The main heart pathology leading to chronic heart failure (CHF) and the need to perform HT were dilated cardiomyopathy (n = 20, 52.6%), coronary heart disease (CHD) (n = 16, 42.1%), restrictive cardiomyopathy (n = 1, 2.6%), and long-term irreversible cardiac graft dysfunction (n = 1, 2.6%)). CHF severity corresponded to stage IIA (n = 2, 5.3%), IIB (n = 25, 65.8%), and III (n = 11, 28.9%)) according to the Strazhesko–Vasilenko classification or to NYHA functional class 3 (n = 4, 10.5%)) and 4 (n = 34, 89.5%)) (3.8 ± 0.4). HT urgency corresponded to IA (n = 18, 47.4%), IB (n = 5, 13.2%)) or 2 (n = 15, 39.4%)) status according to the United Network for Organ Sharing (UNOS) algorithm.

Short-term pre-transplant MCS using peripheral VA-ECMO was applied in 15 (39.5%)) recipients, in 6 of them according to the **prophylactic technique**, in 4 (10.5%)) – long-term MCS by implantable left ventricular bypass method. VA-ECMO by pre-transplant MCS technique lasted for 1–6 (2.1 ± 0.8) days (n = 9), by prophylactic technique for 22–73 (44 ± 12) minutes (n = 6).

Patients were divided into 3 groups according to the absence or use of pre-transplant short-term MCS using peripheral VA-ECMO: (1) The "No pre-HT VA-ECMO" group (n = 23) consisted of those without pre-transplant VA-ECMO; (2) the "Pre-HT VA-ECMO" group (n = 9) comprised of those with pre-transplant VA-ECMO as a bridge to HT; (3) the "Prophylactic VA-ECMO" group (n = 6) included those with pre-transplant VA-ECMO using prophylactic VA-ECMO application technique.

For transplantation, we used hearts from brain-dead donors, whose condition was diagnosed in strict accordance with regulatory documents.

For VA-ECMO, we used the following perfusion devices for extracorporeal circulation: Medtronic BioConsole, RotaFlow Console, Cardiohelp-i, Medos. To fill the extracorporeal circuit, we used official balanced electrolyte solutions, up to 2000 mL with the addition of 5000 units of unfractionated heparin.

Peripheral femoral cannulation technique was used in all cases. Single-lumen, reinforced peripheral venous cannulas of 21–26 F size were used for blood drainage into the extracorporeal circuit depending on the recipient's anthropometric parameters. The venous cannula was installed at a depth of 30–35 cm from the skin surface and was determined by the recipient's growth parameters. The depth of this cannula location in the inferior vena cava was controlled using transesophageal echocardiogram to avoid competition with the venous cannula of the ECC circuit.

To return arterialized blood from the extracorporeal circuit to the systemic circulation, arterial peripheral femoral cannulas of 15–17 F size were used, depending on the recipient's anthropometric parameters, placed through the common femoral artery.

In prophylactic application of VA-ECMO, ECMO volumetric flow rate in the pre-perfusion period ranged from 1.2 to 1.5 L/min. In the postperfusion period, the flow rate depended on the initial function of the cardiac graft. With adequate graft functioning, ECMO volumetric flow rate was maintained at 1.0–1.5 L/min for no more than 3 days (protective mode). In cases of primary graft dysfunction, the volumetric flow rate and VA-ECMO duration depended on the nature and severity of its pumping dysfunction.

Study data was statistically processed using Microsoft Excel spreadsheets and application packages Statistica for Windows 7.0 (Start Soft Inc. USA), Biostat and SPSS. The obtained statistical data were combined into variation series according to the nature of distribution into research groups. The obtained data were presented in the form of quantitative (numerical) and categorical indicators. Normality of distributions was assessed using the Kolmogorov–Smirnov test. The values of numerical indicators are presented as mean with standard deviation (M ± σ), median (Me) with lower [Q1 (25%)] and upper [Q3 (75%)] quartiles. Categorical measures are presented as absolute values and percentages. Depending on the normality of distribution, the comparison of two groups by quantitative index was performed using Mann–Whitney U test or Student's t-test. A difference of $p < 0.05$ was considered significant. Pearson's chi-squared test and Fisher's exact test were used to compare categorical indicators.

RESULTS

A comparative analysis of the pre-transplant status of **recipients** in the 3 studied groups showed that with no differences in age, sex, anthropometric indices (weight, body surface area, BMI), nature of the underlying disease, and clinical manifestations of CHF were more ($p < 0.05$) pronounced in the recipients in whom VA-ECMO was used before HT ("Pre-HT VA-ECMO" and "Prophylactic VA-ECMO" groups) (Table 1). Pre-transplant impairments in systemic and central hemodynamics before MCS were more significant in "Pre-HT VA-ECMO" group, as expressed by significantly low mean blood pressure, PVR, CI and significantly high values of DPP, mPAP, PCWP compared to "No pre-HT VA-ECMO"

group or to both "No pre-HT VA-ECMO" and "Prophylactic VA-ECMO" groups. The pre-transplant laboratory results demonstrated significantly lower preoperative Hb, total protein, thrombocythemia and higher ($p < 0.05$) levels of urea, total bilirubin, AST, INR in "Pre-HT VA-ECMO" group compared to "No pre-HT VA-ECMO" group or both "No pre-HT VA-ECMO" and "Prophylactic VA-ECMO" groups, which reflected the severity of preoperative multi-organ dysfunction.

Donors for the recipients in "Prophylactic VA-ECMO" group were significantly older compared to those for "No pre-HT VA-ECMO" and "Pre-HT VA-ECMO" groups (Table 2). In addition, 83.3% of donors in "Prophylactic VA-ECMO" group were female and had significantly lower body weight and donor weight-recipient weight ratio. Donors in "No pre-HT VA-ECMO" group had a shorter ($p < 0.05$) duration of MV compared to "Pre-HT VA-ECMO" group. The groups did not differ significantly in the nature of causes of brain death, need and dosages of inotropic/vasopressor therapy, global echocardiographic parameters (except for interventricular septum (IVS) thickness), number of extended donor factors, marginalization score (assessment scales Eurotransplant Donor Heart Score, Donor Risk Index Model, RADIAL score).

Table 1

Pre-transplant clinical characteristics and laboratory and instrumental findings for transplantation with cardiac graft ischemia >6 hours in recipients with and without pre-transplant VA-ECMO (n = 38)

Indicator	Cardiac graft ischemia >6 hours (n = 38)			Statistical significance (p)		
	No pre-HT VA-ECMO	Pre-HT VA-ECMO	Prophylactic VA-ECMO	A	B	C
1	2	3	4	5	6	7
Number of observations	23	9	6			
Age (years) M ± σ Me [Q1; Q3]	 49.0 ± 9.9 48.0 [46.0; 57.0]	 48.8 ± 11.9 52.0 [39.5; 57.0]	 50.5 ± 8.7 49.0 [45.0; 54.0]	0.962	0.738	0.770
Gender Female (n/%)	 1/4.3	 2/22.2	 2/33.3	0.184	0.100	1.000
Weight (kg) M ± σ Me [Q1; Q3]	 81.4 ± 15.6 79.5 [70.0; 88.3]	 84.8 ± 18.6 91.0 [74.8; 97.5]	 84.8 ± 20.5 88.5 [74.5; 98.8]	0.603	0.659	1.000
Body surface area (m^2) M ± σ Me [Q1; Q3]	 1.92 ± 0.23 1.90 [1.79; 2.10]	 2.01 ± 0.26 2.1 [1.90; 2.10]	 1.95 ± 0.28 2.0 [1.89; 2.10]	0.345	0.787	0.678
BMI (kg/m^2) M ± σ Me [Q1; Q3]	 26.7 ± 4.4 26.4 [24.2; 28.4]	 28.5 ± 6.7 28.5 [23.9; 31.8]	 28.8 ± 7.4 28.9 [23.1; 34.7]	0.378	0.376	0.936
Underlying disease: DCM (n/%) CHD (n/%)	 10/43.5 11/47.8	 4/44.4 5/55.6	 2/33.3 4/66.7	 1.000 1.000	 1.000 0.651	 1.000 1.000
NYHA FC M ± σ Me [Q1; Q3]	 3.1 ± 0.3 3.0 [3.0; 3.0]	 3.8 ± 0.5 4.0 [3.8; 4.0]	 3.9 ± 0.2 4.0 [4.0; 4.0]	**0.001**	**0.001**	0.652
RAP (mmHg) M ± σ Me [Q1; Q3]	 7.8 ± 3.8 7.0 [5.0; 10.0]	 12.6 ± 5.1 13.5 [8.8; 18.0]	 6.5 ± 2.3 6.0 [4.8; 7.8]	**0.007**	0.434	**0.017**
mPAP (mmHg) M ± σ Me [Q1; Q3]	 24.7 ± 8.1 24.0 [19.0; 27.0]	 31.2 ± 7.7 31.0 [26.8; 36.0]	 26.0 ± 4.8 26.5 [25.3; 27.5]	**0.047**	0.712	0.167
PCWP (mmHg) M ± σ Me [Q1; Q3]	 17.5 ± 4.9 15.0 [12.0; 18.0]	 22.0 ± 5.1 22.0 [18.0; 25.0]	 16.0 ± 2.8 15.0 [14.0; 17.0]	**0.028**	0.481	**0.022**

End of table. 1

1	2	3	4	5	6	7
CI (L/min/m^2) M ± σ Me [Q1; Q3]	1.95 ± 0.39 2.0 [1.7; 2.3]	1.61 ± 0.34 1.6 [1.2; 1.7]	1.88 ± 0.50 2.0 [1.8; 2.1]	**0.029**	0.714	0.232
TPG (mmHg) M ± σ Me [Q1; Q3]	7.2 ± 2.8 7.0 [5.0; 8.6]	8.5 ± 2.5 8.0 [7.5; 9.3]	8.5 ± 3.3 7.5 [6.0; 10.0]	0.234	0.037	1.000
PVR (Wood units) M ± σ Me [Q1; Q3]	2.1 ± 0.8 1.6 [1.3; 3.1]	2.8 ± 0.9 2.6 [2.1; 3.7]	2.5 ± 0.4 2.5 [2.3; 2.7]	**0.040**	0.250	0.460
LVEF (%) M ± σ Me [Q1; Q3]	25.7 ± 8.1 24.0 [18.0; 29.0]	20.1 ± 8.9 18.0 [13.0; 22.5]	17.5 ± 7.0 18.8 [12.3; 23.5]	0.097	0.032	0.559
Mitral regurgitation (grade) M ± σ Me [Q1; Q3]	1.9 ± 0.7 2.0 [1.7; 2.3]	2.8 ± 0.3 2.7 [2.4; 2.9]	2.3 ± 0.5 2.3 [2.2; 2.6]	**0.001**	0.202	**0.030**
Tricuspid regurgitation (grade) M ± σ Me [Q1; Q3]	1.8 ± 0.5 2.0 [1.0; 2.0]	2.7 ± 0.5 2.6 [2.3; 3.0]	2.2 ± 0.3 2.2 [2.1; 2.7]	**0.001**	**0.074**	**0.048**
Hb (g/dL) M ± σ Me [Q1; Q3]	13.4 ± 3.4 13.7 [12.1; 15.9]	11.0 ± 1.8 11.0 [9.8; 11.8]	14.9 ± 4.1 14.8 [14.5; 15.3]	**0.055**	0.487	**0.024**
Platelets (×10^9/L) M ± σ Me [Q1; Q3]	202.2 ± 73.5 194.0 [144.0; 240.0]	77.6 ± 36.4 74.0 [60.2; 85.4]	221.8 ± 39.7 232.0 [204.5; 249.3]	**0.001**	**0**.538	**0.001**
Total protein (mmol/L) M ± σ Me [Q1; Q3]	74.7 ± 6.0 76.3 [70.9; 78.5]	68.2 ± 5.5 66.0 [65.1; 72.0]	73.3 ± 2.5 73.1 [71.6; 74.7]	**0.009**	0.585	**0.055**
Urea (mmol/L) M ± σ Me [Q1; Q3]	8.2 ± 2.5 7.5 [6.3; 9.2]	10.5 ± 2.6 10.0 [8.2; 13.0]	8.1 ± 1.3 7.9 [7.2; 8.7]	**0.028**	0.926	**0.058**
Creatinine (μmol/L) M ± σ Me [Q1; Q3]	99.5 ± 29.9 91.9 [80.2; 121.8]	106.8 ± 25.2 103.5 [84.3; 125.4]	84.9 ± 23.7 85.7 [75.7; 94.9]	0.523	0.279	0.115
Total bilirubin (μmol/L) M ± σ Me [Q1; Q3]	26.9 ± 20.2 20.7 [13.7; 35.0]	46.5 ± 18.9 41.2 [20.8; 62.0]	23.1 ± 7.9 20.8 [17.1; 26.7]	**0.018**	0.659	**0.014**
INR M ± σ Me [Q1; Q3]	1.19 ± 0.11 1.20 [1.10; 1.30]	1.46 ± 0.48 1.40 [1.20; 1.64]	1.25 ± 0.23 1.30 [1.10; 1.40]	**0.015**	0.359	0.340

Note. A, p-value of "No pre-HT VA-ECMO" and "Pre-HT VA-ECMO"; B, p-value of "No pre-HT VA-ECMO" and "Prophylactic VA-ECMO"; C, p-value of "Pre-HT VA-ECMO" and "Prophylactic VA-ECMO"; BMI, body mass index; CHF, chronic heart failure; DCM, dilated cardiomyopathy; CHD, coronary heart disease; FC, functional class; RAP, right atrial pressure; mPAP, mean pulmonary artery pressure; PCWP, pulmonary artery wedge pressure; CI, cardiac index; TPG, transpulmonary pressure gradient; PVR, pulmonary vascular resistance; LVEF, left ventricular ejection fraction; Hb, hemoglobin; INR, international normalized ratio.

Analysis of the course of the **perioperative period** showed that in "Prophylactic VA-ECMO" recipients, the duration of ECC and reperfusion period ("aortic clamp removal-to-end of ECC" interval) were shorter ($p < 0.05$) compared to "No pre-HT VA-ECMO" and "Pre-HT VA-ECMO" groups (Table 3). Recipients in "Pre-HT VA-ECMO" and "Prophylactic VA-ECMO" groups had lower doses of cardiotonic/vasopressor therapy medications ($p < 0.05$) compared to those in "No pre-HT VA-ECMO" group. Recipients in the study groups did not differ in the incidence of severe primary graft dysfunction requiring post-transplant VA-ECMO. Due to the development of severe primary dysfunction, 4 recipients in "No pre-HT VA-ECMO" group needed to be connected to the peripheral VA-ECMO system in the early postperfusion period. In all, "Pre-HT VA-ECMO" recipients ($n = 9$) and in 5 of 6 "Prophylactic VA-ECMO" recipients, MCS was continued in the posttransplant period in a safety mode (blood flow rate <1.2–1.5 L/min). ECMO volumetric flow rate and duration of posttransplant VA-ECMO were significantly lower in "Prophylactic VA-ECMO" group. Recipients from "Prophylactic VA-ECMO" group and from "No pre-HT VA-ECMO" group did not differ in terms of volume of intra- and postoperative blood loss and the need for transfusion therapy. Accordingly, the values of these parameters were higher ($p < 0.05$) in "Pre-HT VA-ECMO" group compared to "Prophylactic VA-ECMO" and "No pre-HT VA-ECMO" groups. The duration of postoperative MV was shorter ($p < 0.05$) in "Pre-HT VA-ECMO" and "Prophylactic VA-ECMO" groups. Renal replacement therapy (RRT) was used more frequently ($p < 0.05$) in "Pre-HT VA-ECMO" group, 66.7%. Recipients from "No pre-HT VA-ECMO" and "Prophylactic VA-ECMO" groups did not differ in the need for postoperative RRT, with the frequency of use being 21.7% and 16.7%, respectively. The groups were not statistically different in terms of duration of postoperative ICU treatment and in-hospital mortality. There was no mortality in "Prophylactic VA-ECMO" group.

DISCUSSION

HT with prolonged graft ischemia is characterized by longer reperfusion period (≥1 hour) and, accordingly, ECC duration, which is associated with gradual, slow restoration of myocardial contractility and pumping function of the heart transplant. Prolonged ECC is an important factor in the development of multi-organ dysfunction and the cause of eventful postoperative period in heart recipients [11]. In addition, HT with expected prolonged cardiac graft ischemia is associated with increased risk of impaired pumping function of the cardiac graft at the early stages of its functioning up to development of severe primary dysfunction due to severe manifestations of ischemia-reperfusion injury (IRI) [12]. Gradual, delayed recovery of myocardial contractility of the transplanted heart makes it necessary to use sympathomimetic drugs in high doses, which negatively affects early and long-term recipient survival [13]. In the absence of restoration of adequate pumping function of the cardiac graft, transition from ECC to different variants of assisted circulation is indicated. Excessive prolongation of ECC in an attempt to wait for rapid resolution of transplanted heart dysfunction and, accordingly, delay in timely withdrawal of ECC and initiation of assisted circulation increases the risk of unfavorable outcome after HT [3, 14]. Peripheral VA-ECMO is currently considered as the leading method of MCS in recipients with severe primary cardiac graft dysfunction [15].

Our previous experience with VA-ECMO as a short-term method of pre-transplant MCS has shown its versatility and efficacy both before and after HT in cases of severe primary graft dysfunction [16, 17].

Table 2

Results of anthropometric, anamnestic, laboratory, and echocardiographic findings of the heart donor for transplantation with cardiac graft ischemia >6 hours in recipients with and without pre-transplant VA-ECMO (n = 38)

Indicator	Cardiac graft ischemia >6 hours (n = 38)			Statistical significance (p)		
	No pre-HT VA-ECMO	Pre-HT VA-ECMO	Prophylactic VA-ECMO	A	B	C
1	2	3	4	5	6	7
Number of observations	23	9	6			
Age (years) M ± σ Me [Q1; Q3]	 42.6 ± 7.5 44.0 [37.8; 51.8]	 41.0 ± 6.2 43.5 [35.5; 46.3]	 49.0 ± 6.3 48.0 [44.5; 52.5]	0.575	0.066	0.030
Gender Female (n/%)	 0.0/0.0	 0/0.0	 5/83.3	–	0.001	0.002
Weight (kg) M ± σ Me [Q1; Q3]	 81.5 ± 12.0 80.0 [71.3; 89.3]	 77.9 ± 10.8 77.5 [70.0; 86.3]	 66.5 ± 15.8 60.0 [59.0; 67.5]	0.440	0.016	0.085

End of table. 2

1	2	3	4	5	6	7
Donor-to-recipient weight ratio M ± σ Me [Q1; Q3]	1.00 ± 0.16 1.00 [0.92; 1.10]	0.92 ± 0.26 1.0 [0.70; 1.06]	0.80 ± 0.19 0.8 [0.70; 0.93]	0.297	0.014	0.351
Causes of brain death: Stroke (n/%)	20/87.0	8/77.8	6/100.0	1.000	1.000	1.000
ICU/MV (days) M ± σ Me [Q1; Q3]	1.9 ± 0.9 2.0 [1.0; 2.0]	3.7 ± 2.7 3.0 [2.0; 4.5]	2.3 ± 0.9 2.5 [1.8; 3.0]	0.007	0.343	0.351
VIS (points, max) M ± σ Me [Q1; Q3]	35.4 ± 27.6 29.8 [20.0; 59.8]	29.9 ± 32.3 24.0 [11.4; 29.0]	36.7 ± 16.3 35.0 [22.5; 47.5]	0.632	0.914	0.644
IVS (cm) M ± σ Me [Q1; Q3]	1.20 ± 0.24 1.20 [1.00; 1.30]	1.29 ± 0.21 1.2 [1.0; 1.5]	1.10 ± 0.08 1.1 [1.0; 1.1]	0.332	0.329	0.056
LVEDV (mL) M ± σ Me [Q1; Q3]	103.0 ± 27.6 100.0 [87.3; 121.0]	95.6 ± 18.3 91.0 [82.5; 101.5]	94.8 ± 15.4 92.5 [85.8; 101.5]	0.465	0.494	0.931
LVEF (%) M ± σ Me [Q1; Q3]	63.2 ± 6.3 64.0 [59.0; 67.0]	61.5 ± 3.7 61.0 [59.8; 64.3]	64.0 ± 1.2 64.0 [63.0; 65.0]	0.456	0.7862	0.137
Blood Na^+ (mmol/L) M ± σ Me [Q1; Q3]	144.8 ± 8.6 140.0 [139.0; 150.0]	145.8 ± 11.9 144.0 [138.5; 150.0]	144.5 ± 4.9 145.5 [142.8; 146.3]	0.793	0.915	0.806
Hb (g/dL) M ± σ Me [Q1; Q3]	12.4 ± 2.8 12.3 [10.5; 14.0]	11.9 ± 2.4 11.8 [9.7; 13.6]	9.7 ± 1.9 9.7 [9.1; 10.3]	0.641	0.035	0.083
Total protein (g/L) M ± σ Me [Q1; Q3]	61.5 ± 13.4 66.5 [55.0; 67.8]	63.8 ± 9.6 66.0 [56.6; 70.0]	60.5 ± 13.8 65.5 [60.8; 70.3]	0.643	0.702	0.592
Expanded heart donation factor (n), M ± σ Me [Q1; Q3]	2.1 ± 0.3 2.0 [1.8; 2.1]	2.1 ± 0.4 2.0 [1.9; 2.1]	2.2 ± 0.5 2.1 [1.8; 2.3]	1.000	0.534	0.674
Eurotransplant Donor Heart Score (points) M ± σ Me [Q1; Q3]	18.6 ± 5.6 18.0 [16.3; 20.5]	19.7 ± 6.2 19.1 [17.3; 22.0]	22.8 ± 7.4 20.6 [18.2; 23.5]	0.631	0.429	0.395
Donor Risk Index Model (points) M ± σ Me [Q1; Q3]	6.4 ± 1.9 6.0 [5.0; 7.2]	6.9 ± 2.5 6.5 [5.2; 8.0]	7.4 ± 2.7 7.2 [5.8; 8.5]	0.545	0.302	0.719
RADIAL score (points) M ± σ Me [Q1; Q3]	2.7 ± 0.7 2.6 [2.4; 3.0]	2.8 ± 0.9 2.6 [2.5; 3.2]	3.1 ± 0.7 3.0 [2.6; 3.4]	0.740	0.223	0.504

Note. A, p-value of "No pre-HT VA-ECMO" and "Pre-HT VA-ECMO"; B, p-value of "No pre-HT VA-ECMO" and "Prophylactic VA-ECMO"; C, p-value of "Pre-HT VA-ECMO" and "Prophylactic VA-ECMO"; TBI, traumatic brain injury; CPR, cardiopulmonary resuscitation; ICU, intensive care unit; MV, mechanical ventilation; min, minimum; max, maximum; VIS, vasoactive inotropic score; IVS, interventricular septum; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; Hb, hemoglobin.

In this regard, it was assumed that HT, under prophylactic MCS using peripheral VA-ECMO, will provide hemodynamic stability not only in the pre-perfusion period, but also in the early posttransplant period when restoring the pumping function of the transplanted heart. A scheduled transition from ECC to posttransplant MCS by peripheral VA-ECMO can reduce reperfusion time and ECC duration, use of sympathomimetic cardiotonics in lower doses and maintain adequate level of systemic circulation in cases of gross impairment of pumping function of the heart transplant due to severe primary dysfunction.

The study demonstrated that patients in whom VA-ECMO was used in the pre-transplant period, regardless of its technique (therapeutic (bridge to HT) or prophylactic) had more severe manifestations of CHF, impaired central and systemic hemodynamics, which justified the use of preoperative MCS. Accordingly, the most severe pre-transplant hemodynamic impairments were in patients in whom VA-ECMO was used as a mechanical short-term bridge to HT [18]. Transplant centers with a high volume of HT have clinical and organizational opportunities to use VA-ECMO as a method of short-term MCS before HT with guaranteed survival to heart transplantation in optimal time (up to 10–14 days) [17]. However, it should be taken into account that patients with pre-transplant VA-ECMO belong to the most severe category of heart recipients with high risk of perioperative complications and early post-transplant survival rates lower than in recipients without preoperative MCS [19, 20].

One of the developing directions of perioperative MCS in cardiac surgery is the strategy of prophylactic application of VA-ECMO in patients at high risk of intraoperative life-threatening hemodynamic impairments of various genesis or development of postcardiotomy acute heart failure (AHF) [21–23]. International guidelines on prophylaxis and treatment of postcardiotomy AHF consider the prophylactic application of VA-ECMO as one of the highly effective measures for early correction of hemodynamic impairments caused by this critical complication [24].

We assumed that prophylactic connection of the patient to a VA-ECMO circuit immediately before HT surgery would ensure guaranteed maintenance of systemic hemodynamics both in the pre-perfusion and early post-transplant periods. The increased risk of hemodynamic destabilization in patients with severe manifestations of CHF due to progression of myocardial failure and/or life-threatening cardiac arrhythmias at the most critical stages of surgical intervention before ECC – sternotomy, isolation and placement of purse-string sutures on the vena cava, vena cava cannulation – was taken into account. There is increased risk of such an unfavorable scenario in patients in whom HT is a repeated surgical intervention and prolonged and traumatic cardiolysis is required due to severe adhesions in the pericardial cavity. Since HT with expected prolonged ischemia may be accompanied by severe IRI and primary graft dysfunction, prophylactic use of VA-ECMO guarantees the maintenance of systemic hemodynamics in the event of this complication.

In addition, preoperative initiation of VA-ECMO provides rapid timely transition to assisted circulation, reducing reperfusion and ECC time, as well as the intensity of sympathomimetic cardiotonic therapy, reducing the risk of severe multi-organ failure [25].

The study demonstrated that when VA-ECMO was started preemptively immediately before HT, the transplant cardiac surgery itself proceeded with significantly less blood loss and transfusion therapy compared to recipients in whom VA-ECMO was used as a pre-transplant MCS (bridge to transplant). In addition, recipients with and without preoperative VA-ECMO did not differ in these parameters. It was also noted that recipients with postoperative VA-ECMO had a shorter duration of postoperative MV, which is due to the possibility of safe transfer to spontaneous breathing under extracorporeal circulation and gas exchange [26]. Thus, the study demonstrated the possibility of effective application of VA-ECMO as a prophylactic measure aimed at preventing intra- and postoperative life-threatening hemodynamic impairments when performing HT with excessively long (>6 hours) cardiac graft ischemia.

Table 3

Perioperative period for graft transplantation with cardiac graft ischemia >6 hours in recipients with and without pre-transplant VA-ECMO (n = 38)

Indicator	Cardiac graft ischemia >6 hours (n = 38)			Statistical significance (p)		
	No pre-HT VA-ECMO	Pre-HT VA-ECMO	Prophylactic VA-ECMO	A	B	C
1	2	3	4	5	6	7
Number of observations	23	9	6			
Graft ischemia (min) M ± σ Me [Q1; Q3]	 424.4 ± 48.9 414.0 [390.0; 449.5]	 413.4 ± 57.9 395.0 [364.0; 428.0]]	 426.5 ± 46.1 419.5 [405.8; 440.3]	0.591	0.925	0.651

End of table. 3

1	2	3	4	5	6	7
ECC (min) M ± σ Me [Q1; Q3]	173.3 ± 38.9 161.0 [122.0; 191.5]	121.3 ± 30.5 127.0 [117.0; 150.3]	94.3 ± 12.4 94.0 [85.5; 102.8]	**0.001**	**0.001**	**0.062**
"Aortic clamp removal/end of ECC" interval M ± σ Me [Q1; Q3]	66.3 ± 14.7 60.0 [55.3; 70.5]	35.3 ± 11.9 35.0 [27.8; 48.8]	22.3 ± 7.9 20 [18.3; 27.6]	**0.001**	**0.001**	**0.036**
Dopamine (max, μg/kg/min) M ± σ Me [Q1; Q3]	9.6 ± 2.9 8.5 [7.5; 10.3]	7.1 ± 2.4 7.0 [5.5; 9.0]	6.9 ± 1.0 8.0 [7.5; 8.0]	**0.029**	**0.035**	0.851
Adrenaline (max, μg/kg/min) M ± σ Me [Q1; Q3]	73.8 ± 25.9 65.0 [50.0; 80.0]	47.6 ± 17.8 40.0 [35.0; 55.0]	46.5 ± 15.2 42.5 [38.3; 60.0]	**0.009**	**0.021**	0.903
VIS (max) M ± σ Me [Q1; Q3]	16.5 ± 4.1 16.0 [15.0; 18.5]	12.3 ± 3.6 12.1 [11.2; 14.0]	12.0 ± 4.3 12.5 [11.7; 14.8]	**0.042**	**0.025**	0.886
Severe primary dysfunction (n/%)	4/17.4	0/0.00	1/16.7	0.303	1.000	0.400
MV (hours) M ± σ Me [Q1; Q3]	17.9 ± 7.1 14.5 [13.0; 19.3]	12.3 ± 5.4 11.7 [10.0; 16.5]	11.3 ± 5.8 12.7 [11.3; 18.4	**0.042**	**0.046**	0.736
Post-HT VA-ECMO (n/%)	4/14.5	9/100.0	6/100.0			
Post-HT VA-ECMO, (L/min) M ± σ Me [Q1; Q3]	3.3 ± 0.4 3.1 [3.3; 3.5]	2.3 ± 0.2 2.2 [2.0; 2.4]	1.8 ± 0.4 2.1 [1.6; 2.0]	**0.001**	**0.001**	**0.007**
VA-ECMO (hours) M ± σ Me [Q1; Q3]	116.6 ± 23.5 110 [105; 130.0]	63.6 ± 13.5 55.0 [50.0; 65.7]	47.4 ± 8.9 42.7 [38.7; 52.1]	**0.001**	**0.001**	**0.023**
VA-ECMO (>3 days) n/%	4/14.5	0/0.00	1/16.7	0.303	1.000	0.400
Blood loss (mL) M ± σ Me [Q1; Q3]	1081.3 ± 324.5 1010 [860.0; 1350.0]	3671.4 ± 849.8 3200 [2750.0; 5200.0]	835.0 ± 448.0 555.0 [465.0; 825.0]	**0.001**	0.137	**0.001**
Erythromass (mL) M ± σ Me [Q1; Q3]	570.4 ± 181.3 500.0 [350.0; 825.0]	1847.3 ± 643.2 1800.0 [1016.0; 3160.0]	610.5 ± 98.3 380.4 [320.3; 550.5]	**0.001**	0.609	**0.001**
FFP (mL) M ± σ Me [Q1; Q3]	1020.4 ± 427.1 950.0 [700.0; 1300.0]	3040.8 ± 744.3 2830.0 [2450.0; 4270.0]	960.7 ± 340.5 880.3 [800.5; 1150.4]	**0.001**	0.756	**0.001**
RRT (%)	5/21.7	6/66.7	1/16.7	**0.035**	1.000	0.119
ICU (days) M ± σ Me [Q1; Q3]	5.3 ± 3.2 5.0 [4.2; 6.0]	6.5 ± 3.8 6.0 [5.5; 7.8]	5.0 ± 2.9 4.7 [4.1; 6.2]	0.372	0.837	0.426
In-hospital mortality (n/%)	2/8.7	1/11.1	0/0.00	1.000	1.000	1.000

Note. A, p-value of "No pre-HT VA-ECMO" and "Pre-HT VA-ECMO"; B, p-value of "No pre-HT VA-ECMO" and "Prophylactic VA-ECMO"; C, p-value of "Pre-HT VA-ECMO" and "Prophylactic VA-ECMO"; ECC, extracorporeal circulation; VIS, vasoactive inotropic score; MV, mechanical ventilation; max, maximum; FFP, fresh frozen plasma; RRT, renal replacement therapy; ICU, intensive care unit.

CONCLUSION

Prophylactic VA-ECMO in HT with extremely prolonged ischemic time reduces ECC duration, reperfusion period, and postoperative MV period, and decreases the need for inotropic therapy.

The authors declare no conflict of interest.

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