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Perfusion module for extracorporeal anti-ischemic protection of a donor heart in experiment

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Abstract

Introduction. *Extracorporeal perfusion of transplants is proposed as one of the areas to expand the pool of donor hearts. Important aspects are the establishment of optimal perfusion parameters, which is of particular importance in prolonged perfusion.*

Objective. *To present the results of the development of a perfusion module for extracorporeal anti-ischemic protection of donor hearts.*

Material and methods. *A perfusion module for extracorporeal anti-ischemic protection of donor hearts was developed on mature outbred male rats. After 12-hour hypothermic extracorporeal perfusion of the heart in the perfusion module with +8°C oxygenated HTK solution, its function was studied.*

Results. *In the hypothermic perfusion group on the module, sinus rhythm was observed with a heart rate of 268.5 (256.2;279.0) beats/min; the* left *ventricle-developed pressure (LVDP) was 65.5 (65.0;70.7) mm Hg, by the*

end of the 1st hour, the LVDP was 73.0 (70.5;75.0) mm Hg, after 90 minutes the LVDP was 82.0 (80.5;83.5) mm Hg, by the end of the 2nd hour, the LVDP was 82.5 (80.5;84.0) mm Hg, which indicated the cardioprotective potential of hypothermic perfusion. The hearts of the control group had sinus bradycardia with a heart rate of 113.5 (90.0;124.7) beats per minute. The LVDP was 27.5 (25.5;30.0) mm Hg by the end of the 30-minute cardiac stabilization period; by the end of the 1st hour, LVDP was 22.0 (20.5;23.7) mm Hg; by the 90th minute the contractile function of the hearts was absent, which indicated the development of myocardial damage.

Conclusion. *Obtained data indicate that the module can maintain the viability of the donor heart for 12 hours by hypothermic perfusion with +8°C oxygenated HTK solution at flow rate of 0.3 ml/min and pressure of 10 cm H_2O and pO_2 600-700 mm Hg, which is accompanied by heart rate of 325.0 beats/min and LVDP of 82.5 mm Hg, compared to non-perfusion conservation.*

Keywords: perfusion module, extracorporeal perfusion, donor heart, hypothermia

Conflict of interests. The authors declare no conflicts of interests.

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Compliance with ethical standards: The study involving experimental animals was conducted in compliance with the humanity principles set out in the Directive of European Community (86/609/EEC) and the Declaration of Helsinki, and was approved by the Ethics Committee of Omsk State Medical University, (Protocol No. 4 of 07.02.2021)

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HR, Heart rate

LVDP, left ventricle-developed pressure

Introduction

Currently, donor heart transplantation remains the only definitive treatment option for patients with end-stage chronic heart failure [1]. Static cold preservation remains the primary, generally accepted method for preserving the viability of donor hearts. This organ preservation method combines cardioplegic cardiac arrest and hypothermic storage of grafts in a preservative solution, which significantly reduces the myocardial demand for metabolites and energy substrates [2]. It has been shown that cold ischemia time exceeding 4–6 hours and subsequent warm reperfusion in the recipient's body are closely associated with a high risk of graft rejection [3]. The ongoing shortage of optimal-quality donor hearts remains one of the main limiting factors in clinical transplantology.

The use of dynamic preservation, namely controlled machine perfusion of grafts, is being actively considered as a promising technology both to expand the donor pool and to increase the use of donor organs. The effectiveness and safety of this approach has been demonstrated using machine cold oxygenated perfusion of liver, kidney, and lung grafts from extended criteria donors in both experimental and clinical studies [4–6]. Theoretically, continuous machine perfusion can meet the metabolic needs of the myocardium and thereby minimize irreversible ischemic damage to cardiomyocytes and prevent organ death. To date, Organ Care System (TransMedics, Inc., USA) is the only one commercially available and extremely expensive cardiac perfusion system for clinical use, which, however, is not universal and has not yet become widespread [7]. In addition, the current approach to expanding the criteria for the use of grafts is to more actively use organs obtained

from donors after irreversible circulatory arrest (Donors after Circulatory Death, DCD) [8]. For such donor hearts, machine perfusion may provide a technological platform for maintaining their viability, as well as dynamically assessing their morphofunctional state and, potentially, even restoring a reversibly impaired cardiac function (heart "revitalization") before planned transplantation.

Despite the existing encouraging results on the effectiveness of machine perfusion for anti-ischemic protection of donor hearts, it should be noted that this technology has not yet passed the experimental stage and has not been implemented into clinical practice [9, 10]. There is evidence that long-term machine perfusion of donor organs can lead to a number of adverse effects, such as hemolysis when using blood components as part of the perfusion solution, accumulation of end products of metabolism in the perfusate, as well as the development of intracellular edema of cardiomyocytes, which is manifested in the form of a significant graft dysfunction [11]. The important aspects requiring further experimental studies are both the establishment of optimal parameters of the perfusion per se (the duration, pressure, and the preservative solution temperature), and the creation of a perfusion solution having a physiological composition, which is of particular importance during prolonged extracorporeal perfusion and autonomous transportation of a container with a donor heart over long distances.

The aim of this study is to present the results of the development and experimental testing of a perfusion module for extracorporeal anti-ischemic protection of the donor heart in small laboratory animals as a methodological basis for preclinical studies of prolonged graft preservation.

Material and methods

The development of a perfusion module for extracorporeal anti-ischemic protection of donor hearts in small laboratory animals was undertaken as part of an innovative Project at the Department of Topographic Anatomy and Operative Surgery of Omsk State Medical University, and the Department of Theoretical Electrical Engineering of Omsk State Transport University. Experimental testing of the perfusion module was performed in the Operating Room of the Department of Topographic Anatomy and Operative Surgery of Omsk State Medical University. All stages of the study were conducted in compliance with the humane principles set forth in the European Community Directives (86/609/EEC) and the Declaration of Helsinki. The study was approved by the University Ethics Committee; Protocol No. 4 dated November 24, 2023.

Within the study framework, a perfusion module was developed for extracorporeal anti-ischemic protection of donor hearts in small laboratory animals using a closed circuit, which volume matched the capacity of the animal's vascular bed. To solve the experimental design problem, the components of the extracorporeal circuit for ensuring the perfusion of the donor heart were selected and modeled into a single compact structure taking into account the anatomical and physiological parameters of the heart of outbred rats according to the basic device (Fig. 1) based on our previously obtained patent for the invention [12].

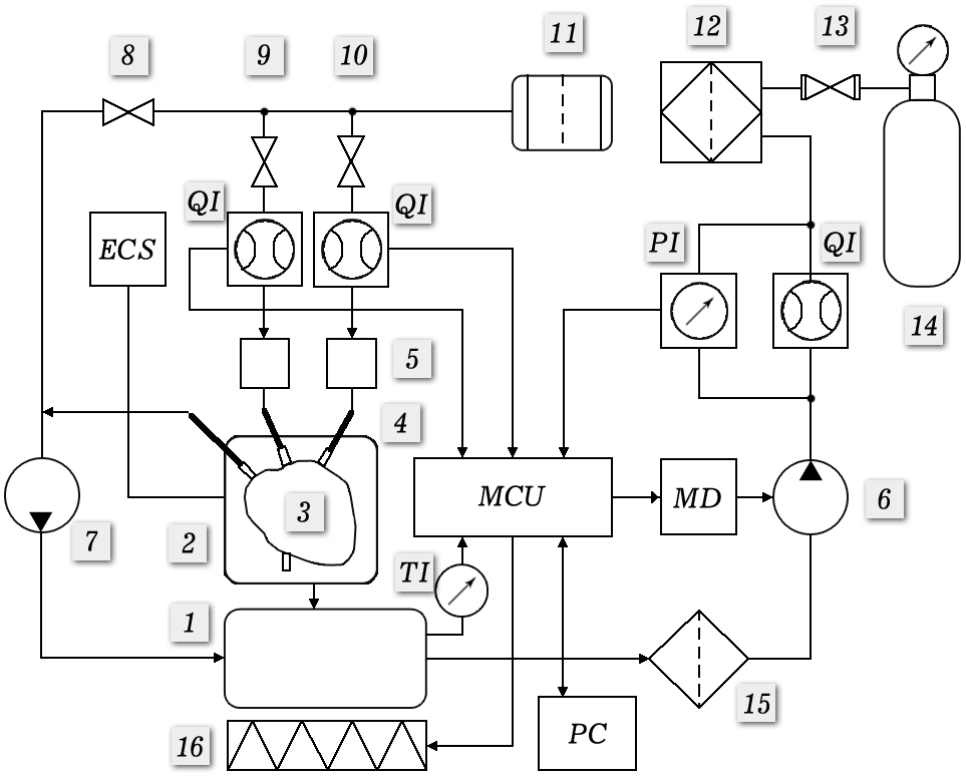

Fig. 1. Schematic representation of perfusion module for extracorporeal anti-ischemic protection of the donor heart, where 1, return reservoir; 2, thermostatic chamber; 3, donor heart; 4, cannula; 5, perfusion column; 6 and 7, peristaltic pumps; 8, 9, and 10, three-way valves; 11, foam trap; 12, gas saturation unit; 13, oxygenator; 14, gas cylinder; 15, filter; 16, induction thermostat; PI, pressure indicator; TI, temperature indicator, QI, quantity indicator, MCU, microcontroller unit

The explanted donor heart **(3)** was placed in a sterile thermostatic chamber (**2)**, and the aorta was connected to the perfusion column (**5)** using a cannula (**4)**. The perfusion column was sequentially connected via lines to peristaltic pumps (**6)** and (**7)**, which provided circulation of the perfusion solution. A pressure indicator (PI), temperature indicator (TI), and the perfusate flow rate quantity indicator (QI) were introduced into the circulation circuit, which signals were transmitted to the input of the microcontroller unit (MCU). Laboratory work stations of the NI type or Elvis II + (National Instruments, USA) or compact NI mioDAQ USB modules (National Instruments, USA) connected to a personal computer

were used as a microcontroller. Virtual tools developed in the LabView environment (National Instruments, USA) were used as control software. The feed-in peristaltic pump **(6)** (MD motor driver) was controlled in the software mode, maintaining the required pressure and flow rate of the preservative solution. Then, using the outflow peristaltic pump **(7),** the extracorporeal circuit was closed by connecting it to the return reservoir (**1)** and the thermostatic chamber **(2)** using three-way valves **(8), (9)** and **(10)**. Maintaining the temperature of the isolated heart and perfusion solution in the range specified by the experimental conditions was ensured by placing the lines in the thermal insulation "jacket" of the induction thermostat **(16)** of the temperature control unit. The perfusion solution was saturated with carbogen, for which purpose the perfusion column was connected to the gas cylinder **(14)**, foam trap **(11)** and oxygenator **(13)** of the gas saturation unit **(12)**. Control of the heart rhythm function, coping with bradycardia and ventricular fibrillation were exercised by means of an ECS pacemaker (Boston Scientific, USA) with a defibrillation function, connected to the ventricular myocardium using needle electrodes.

The design of the perfusion module (Fig. 2, Table 1) provided the ability to regulate the main parameters of extracorporeal perfusion of the donor heart in small laboratory animals in the ranges corresponding to physiological ones.

Fig. 2. External appearance of the perfusion module for extracorporeal anti-ischemic protection of the donor heart

Table 1. Main parameters of the perfusion module for extracorporeal anti-ischemic protection of the donor heart

Module parameter	Characteristics
Functioning	Autonomous, up to 24 hours
Circuit	Closed
Pump	Peristaltic
Perfusion pressure	Adjustable in the range from 0 to 80 mm Hg
Volumetric perfusion rate	Adjustable from 0 to 20 mL/min
Perfusion parameter control	Automatic adjustment within a given range
Return reservoir capacity	20 0 mL
Thermostating	Circulation thermostat, temperature range from +4° to +40°C
Power supply	Autonomous, direct current 12 V
Dimensions *	220×250×310 mm
Weight	1.8 kg
Transportation	In an insulated thermal container

* The prototype perfusion module also includes a 2-liter gas cylinder and a personal computer of a laptop type (not shown in Table 1)

During technical testing of the designed perfusion module, its components demonstrated stable operation over a 12-hour observation period at an operating room temperature of 15 to 25°C. No malfunctions of individual module components or design defects were identified during testing. Actual perfusion parameters (the pressure and volumetric perfusion rate, solution temperature, oxygenation level) remained stable, without significant changes within the specified range. The module's functionality criterion was defined as its ability to ensure the viability of the donor heart during dynamic preservation.

Experimental protocol. The required sample size for the two-sided alternative hypothesis was calculated based on a power of 80%, a Type I error rate of 5%, and an assumption that the standardized effect size (Cohen's d) was is 0.9. The estimated required sample size: n=12.

Due to this the efficacy study of the developed perfusion module for extracorporeal anti-ischemic protection of the donor heart was conducted in an experiment on 24 mature outbred male rats weighing 250–300 g. Considering the well-known high sensitivity of the myocardium to anoxia and the complexity of implementing technical solutions related to ensuring continuous normothermic perfusion of the isolated heart, it was decided to test the module using the method of prolonged hypothermic myocardial perfusion.

Animals in the experimental group (n=12) were anesthetized with ether, given artificial ventilation, and had their hemodynamics monitored and were subjected to the model of brain death using the method we developed earlier [13]. One hour after the brain death had been confirmed, a bilateral thoracotomy was performed, the main vessels were transected, the donor heart was explanted, and it was washed in a HTK preservative solution (Custodiol, Dr. F. KOHLER CHEMIE, GmbH, Germany) cooled to +8°C, until cardioplegia was achieved.

After aortic cannulation, the explanted hearts were placed in a thermostatic chamber of the perfusion module and the retrograde perfusion of the hearts was performed through the aorta using the Langendorff method, using the oxygenated NTK solution at +8°C for 12 hours with a volume flow rate of 0.3 mL/min under a pressure of 10 cm H_2O. The perfusate oxygenation was provided continuously; the perfusate pO_2 level was monitored hourly and maintained in the target range of 600–700 mm Hg. After the expiry of the hypothermic perfusion period, the isolated hearts were reperfused for 2 hours with Krebs–Henseleit solution saturated with carbogen at a constant pressure of 70 mm Hg at a temperature of 37°C and pH=7.33–7.36. The Krebs–Henseleit solution prepared ex tempore included the following components: NaCl 118 mmol/L, $NaHCO_3$ 25 mmol/L, KCl 4.7 mmol/L, $MgSO_4$ 1.2 mmol/L, KH_2PO_4 1.2 mmol/L, $CaCl_2$ 2.5 mmol/L, glucose 11 mmol/L.

The control group (n=12) consisted of animal hearts that were explanted 1 hour after confirming the brain death and were subjected to static pharmacological cold preservation according to the standard method in a NTK solution at +4°C for 12 hours and the subsequent normothermic reperfusion was performed under the same conditions as the experimental group hearts. To assess the functional status of the donor heart after reperfusion for 2 hours, the heart rate (HR) and left ventricle-developed pressure (LVDP) were determined.

Statistical processing of the study results was performed on a computer using the StatTech v.4.6.3 software (StatTech LLC, Russia). The nonparametric Mann–Whitney U-test was used to compare two groups by parameter. When comparing three or more dependent populations, the nonparametric Friedman test was used, with post hoc comparisons using the Conover–Iman test with Holm's correction. The critical significance level for testing statistical hypotheses was set at 0.05.

Results

The baseline HR and LVDP data in laboratory animals of both groups did not differ and were comparable to data reported in literature, HR was 350 (326; 372) beats/min, LVDD was 90.5 (86.8; 92.0) mm Hg. [14].

Table 2 and Fig. 3 present the data of the heart rate dynamics during a 2-hour reperfusion of hearts after hypothermic perfusion with oxygenation and in the control group. In the hypothermic perfusion group, in all hearts, during the 30-minute stabilization period from the onset of normothermic reperfusion, the restoration of uniform blood filling of the heart muscle was visually observed (Fig. 4A), as well as sinus rhythm with a heart rate of 268.5 (256.2;279.0) beats/min ($p<0.001$ when compared with the control group); by the end of the 1st hour of reperfusion the heart rate was 321.0 (297.5;330.5) beats/min ($p<0.001$ when compared with the control group); at 90 minutes after the reperfusion start, the heart rate was 315.0 (301.2;330.0) beats/min ($p<0.001$ when compared with the control group), by the end of the 2^{nd} hour of reperfusion, the heart rate was 325.0 (322.7;333.2) beats/min ($p<0.001$ when compared with the control group). No reperfusion-related rhythm or conduction disturbances were observed in the hearts of the hypothermic perfusion group. The data obtained indicated the rhythm function restoration, and the elimination of the reversible donor heart dysfunction caused by the brain death, the explantation procedure, and hypothermic perfusion.

Table 2. Analysis of the heart rate changes over time depending on the method of heart preservation

Preservation method	Stages of reperfusion				p
	30 min, Me (Q_1;Q_3)	60 min, Me (Q_1;Q_3)	90 min, Me (Q_1;Q_3)	120 min, Me (Q_1;Q_3)	
Controls (Static cold preservation)	113.5 (90.0;124.7)	85.0 (69.0;95.0)	0.0 (0.0;0.0)	0.0 (0.0;0.0)	<0.001* $p_{30\ min–90\ min} = 0.001$ $p_{30\ min–120\ min} = 0.001$ $p_{60\ min–90\ min} = 0.023$ $p_{60\ min–120\ min} = 0.023$
Perfusion (Perfusion hypothermic preservation)	268.5 (256.2;279.0)	321.0 (297.5;330.5)	315.0 (301.2;330.0)	325.0 (322.7;333.2)	<0.001* $p_{30\ min–60\ min} = 0.016$ $p_{30\ min–90\ min} = 0.019$ $p_{30\ min–120\ min} = 0.003$
p	<0.001*	<0.001*	<0.001*	<0.001*	–

* – differences in parameters are statistically significant (p<0.05)

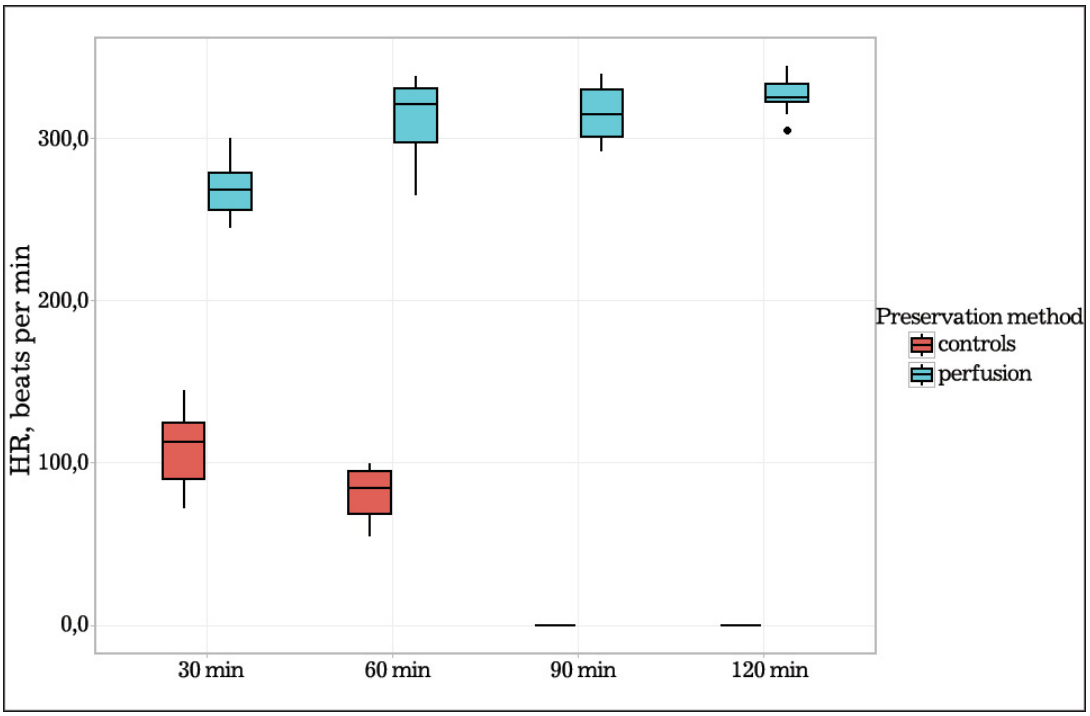

Fig. 3. Analysis of the heart rate changes over time depending on the method of heart preservation

In the control group (n=12), 30 minutes after the onset of normothermic reperfusion, the hearts appeared cyanotic upon visual

assessment (Fig. 4B), the heart contractions being consistent with ischemic contracture.

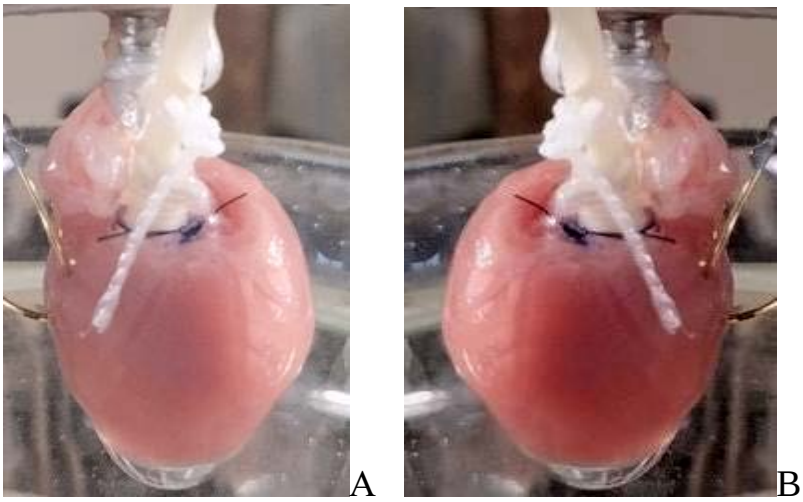
A B

Fig. 4. External view of the donor heart on reperfusion: A, after hypothermic perfusion; B, control group

During reperfusion, ventricular fibrillation was observed in seven hearts in the control group. Sinus rhythm was restored in two of these hearts after defibrillation, while ventricular fibrillation could not be coped with in five other hearts. This indicated the development of irreversible donor heart dysfunction due to brain death, the explantation procedure, and non-perfusion heart preservation. Therefore, to obtain statistically significant differences, eight additional animals were included in the control group. During reperfusion, ventricular fibrillation was observed in 12 hearts in the control group. Sinus rhythm was restored in four of these hearts after defibrillation, while ventricular fibrillation could not be coped with in eight hearts. As a result, 12 hearts in the control group showed pronounced sinus bradycardia with a heart rate of 113.5 (90.0;124.7) beats/min.

Table 3 and Fig. 5 present the data of LVDP dynamics during a 2-hour reperfusion of hearts after hypothermic perfusion with oxygenation

and in the control. In the hypothermic perfusion group, after 30 minutes of the heart function stabilization, LVDP was 65.5 (65.0;70.7) mm Hg ($p<0.001$ when compared to the control group); by the end of the 1st hour of reperfusion, LVDP was 73.0 (70.5;75.0) mm Hg ($p<0.001$ compared to the control group); at 90 minutes after the onset of reperfusion, LVDP increased to 82.0 (80.5;83.5) mm Hg. ($p<0.001$ compared to the control group), by the end of the 2nd hour of reperfusion, the LVDP was 82.5 (80.5;84.0) mm Hg ($p<0.001$ compared to the control group), which indicates the cardioprotective potential of hypothermic perfusion and the restoration of the donor heart contractile function.

Table 3. Analysis of the left ventricle-developed pressure dynamics depending on the method of heart preservation

Preservation method	Stages of reperfusion				p
	30 min, Me (Q_1;Q_3)	60 min, Me (Q_1;Q_3)	90 min, Me (Q_1;Q_3)	120 min, Me (Q_1;Q_3)	
Controls (Static cold preservation)	27.5 (25.5;30.0)	22.0 (20.5;23.7)	0.0 (0.0;0.0)	0.0 (0.0;0.0)	<0.001* $p_{30\ min–90\ min} < 0.001$ $p_{30\ min–120\ min} < 0.001$ $p_{60\ min–90\ min} = 0.035$ $p_{60\ min–120\ min} = 0.035$
Perfusion (Perfusion hypothermic preservation)	65.5 (65.0;70.7)	73.0 (70.5;75.0)	82.0 (80.5;83.5)	82.5 (80.5;84.0)	<0.001* $p_{30\ min–90\ min} = 0.017$ $p_{30\ min–120\ min} = 0.005$ $p_{60\ min–90\ min} = 0.036$ $p_{60\ min–120\ min} = 0.014$
p	<0.001*	<0.001*	<0.001*	<0.001*	–

* – differences in parameters are statistically significant ($p<0.05$)

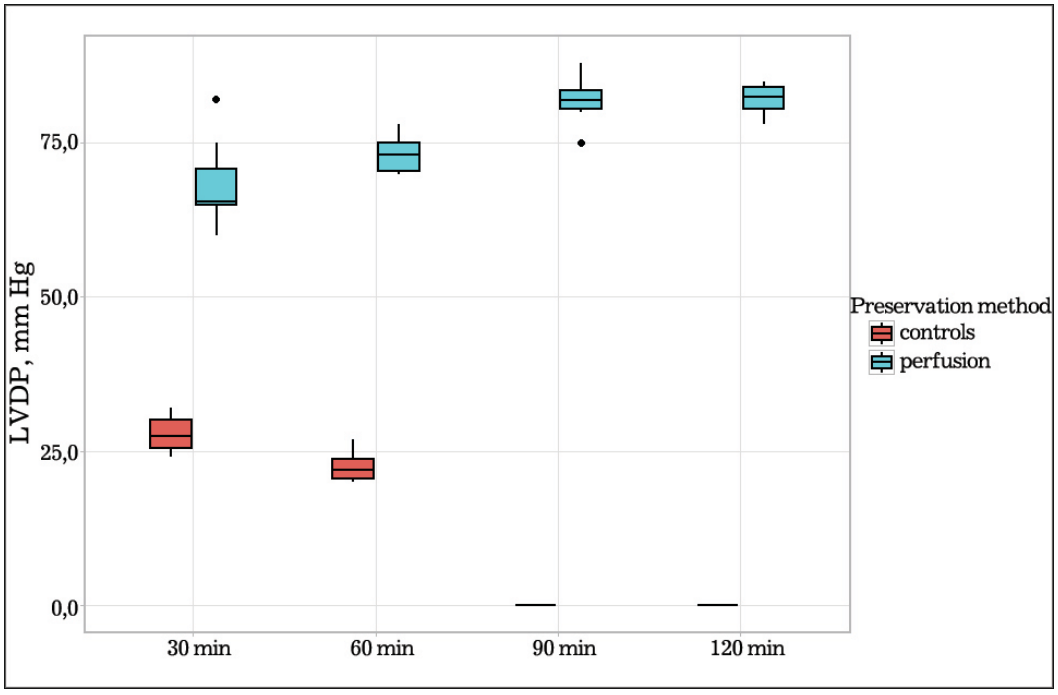

Fig. 5. Analysis of the left ventricle-developed pressure dynamics depending on the method of heart preservation

During reperfusion, the hearts of control group displayed post-ischemic contracture with a significant decrease in LVDP to 27.5 (25.5;30.0) mm Hg by the end of the 30-minute heart stabilization period; by the end of the 1st hour of reperfusion LVDP had no tendency to recovery and was 22.0 (20.5;23.7) mm Hg; subsequently progressive depression and further cessation of contractile function of the hearts was noted, and by the 90th minute of reperfusion, the contractile function in the hearts of the control group was absent, which indicated the development of irreversible myocardial damage during static pharmacological cold preservation/reperfusion, and the graft death.

Discussion

Currently, we must admit that the problem of long-term anti-ischemic protection of the donor heart is far from being fully resolved. The ischemic and reperfusion injury to the cardiac graft is typically

manifested through the induction of reperfusion arrhythmias, in particular the ventricular fibrillation, the development of microvascular dysfunction, and myocardial stunning, and the most dangerous manifestation of this damage is a primary graft non-function [15]. Initially, the short-term ischemic cell damage can be reversible, and reoxygenation leads to restoring the graft morphofunctional state. However, as the ischemia time increases, the reperfusion would no longer be accompanied by restoration, rather by additional damage to the graft cellular structures due to the no-reflow phenomenon and the hyperproduction of free radicals, the activation of pro-inflammatory cytokines, adhesion molecules and the complement system, and the initiation of pro-apoptotic signaling pathways [16], etc.

Despite the fact that a static cold preservation at +4°C significantly reduces the metabolic needs of the donor heart, within 4 hours hypothermia leads to the breakdown of up to 95% of intracellular adenosine triphosphate, which is accompanied by acidosis, lactate accumulation and subsequent activation of intracellular phosphorylases and proteases, initiating irreversible damage to cell membranes [17].

The hypothermic oxygenated perfusion, as an alternative method for preserving the viability of the donor heart, restores aerobic cellular metabolism, prevents the accumulation of toxic metabolic products, and promotes the clearance of formed element sludge from the graft microcirculation. The effect of hypothermic perfusion appears to be achieved through the continuous circulation of a preservative solution with an elevated partial oxygen pressure in the graft vascular bed, which, in turn, minimizes the risk of irreversible ischemic damage and organ death from reperfusion injury [18]. There are reasons to believe that pulsatile perfusate flow is capable of maintaining a balance of endothelial factors influencing microcirculatory bed tone. There is also evidence that

hypothermic oxygenated perfusion effectively reduces the concentration of proinflammatory cytokines (interleukin 1b, interleukin 2, and TNF-α), and diminishes the expression of caspase-3, inhibiting proapoptotic mechanisms [19]. It should be noted that the search for optimal technical and physiological parameters of extracorporeal perfusion of the donor heart is currently ongoing, since the advantages and disadvantages of performing cardiac perfusion under certain conditions have not been fully determined.

Our study presents the results of an experimental trial of a perfusion module for extracorporeal anti-ischemic protection of donor hearts. Experiments conducted on 24 donor hearts of outbred male rats demonstrated the high efficiency of cardiac conditioning in the designed module by using a low-flow (volumetric flow rate 0.3 mL/min) hypothermic oxygenated perfusion with NTK solution at +8°C for 12 hours at a pressure of 10 cm H_2O and a perfusate pO_2 level in the range of 600–700 mm Hg for 12 hours. As previously demonstrated in relation to donor liver and kidneys, it is low-flow perfusion under hypothermia conditions that has a more pronounced protective effect on the vascular endothelium and prevents the development of cellular edema [4, 6]. The parameters of the functional state of the donor heart that underwent hypothermic perfusion with oxygenation studied after the reperfusion were within the physiological range. Parameters of hypothermic cardiac perfusion, such as the temperature, pressure, and volumetric perfusion flow rate, and partial oxygen pressure in the perfusate were monitored and no significant changes were observed during the experiment.

Currently available data give reason to believe that the implementation of machine perfusion of donor hearts into clinical practice will ensure an increase in the availability of grafts by 15–20% through both prolonging the preservation period and restoring viability

(reconditioning) of initially ischemically damaged donor organs that were previously considered unsuitable for transplantation [20].

It is also clear that advances in the development of perfusion devices for dynamic organ preservation, particularly of the heart, and their subsequent implementation in clinical practice are closely linked to the organization of a consortium of medical and technical specialists, with co-financing and involving industrial partners. It should be noted that the developments of such medical equipment in our country would be significantly interesting for clinical transplantology in terms of improving access to transplant care.

Our experimental study confirmed demonstrated technical feasibility and effectiveness of prolonged hypothermic perfusion with oxygenation of the donor heart in the experiment by using the developed perfusion device. We will subsequently study in detail the impact of hypothermic perfusion on the functional, metabolic, and ultrastructural changes in the donor heart. The developed perfusion module is a multifunctional device that can be used for the preclinical evaluation of the effectiveness of anti-ischemic protection of the donor heart under various perfusion conditions. However, continued translational research is necessary for successful transfer of the technology for machine-assisted perfusion of donor hearts.

Conclusion

The conducted technical trials and the obtained experimental data have indicated that the proposed perfusion module ensures an effective maintenance of the donor heart viability for 12 hours by hypothermic perfusion through the aorta with an oxygenated NTK solution at +8°C with a volume flow rate of 0.3 mL/min under a pressure of 10 cm H_2O and a perfusate pO_2 level of 600–700 mm Hg, which is accompanied by

the restoration of sinus rhythm with a heart rate of 325.0 (322.7;333.2) beats/min and an increase in the left ventricle-developed pressure to 82.5 (80.5;84.0) mm Hg ($p<0.001$) by the end of the 2nd hour of reperfusion versus the static pharmacological cold preservation.

References

1. Chew HC, Macdonald PS, Dhital KK. The donor heart and organ perfusion technology. *J Thorac Dis.* 2019;11(Suppl. 6):S938–S945. PMID: 31183173 https://doi.org/10.21037/jtd.2019.02.59

2. Kounatidis D, Brozou V, Anagnostopoulos D, Pantos C, Lourbopoulos A, Mourouzis I. Donor heart preservation: current knowledge and the new era of machine perfusion. *Int J Mol Sci*. 2023;24(23):16693. PMID: 38069017 https://doi.org/10.3390/ijms242316693

3. Sicim H, Tam WSV, Tang PC. Primary graft dysfunction in heart transplantation: the challenge to survival. *J Cardiothorac Surg*. 2024;19(1):313. PMID: 38824545 https://doi.org/10.1186/s13019-024-02816-6

4. Novruzbekov MS, Balkarov AG, Anosova EYu, Dmitriev IV, Anisimov YuA, Zhuravel NS, et al. The role of oxygenation in kidney and liver machine perfusion. *Transplantologiya. The Russian Journal of Transplantation.* 2023;15(4):529-540. (In Russ.). https://doi.org/10.23873/2074-0506-2023-15-4-529-540

5. Fabrika AP, Tychina EP, Bayramkulov AM, Tarabrin EA. Ex vivo lung perfusion in lung transplantation. *Transplantologiya. The Russian Journal of Transplantation.* 2024;16(1):99-115. (In Russ.). https://doi.org/10.23873/2074-0506-2024-16-1-99-115

6. Reznik ON, Manukovskiy VA, Dayneko VS. Theoretical backgrounds of technology of preservation of donor organs. *The Journal*

of Emergency surgery of I.I. Dzhanelidze. 2022;1(6);60-64. (In Russ.). https://doi.org/10.54866/27129632_2022_1_60

7. Rojas SV, Avsar M, Ius F, Schibilsky D, Kaufeld T, Benk C, et al. Ex-vivo preservation with the organ care system in high risk heart transplantation. *Life (Basel)*. 2022;12:247. PMID: 35207534 https://doi.org/10.3390/life12020247

8. Schroder JN, Patel CB, DeVore AD, Bryner BS, Casalinova S, Shah A, et al. Transplantation outcomes with donor hearts after circulatory death. *N Engl J Med*. 2023;388(23):2121–2131. PMID: 37285526 https://doi.org/10.1056/NEJMoa2212438

9. Nilsson J, Jernryd V, Qin G, Paskevicius A, Metzsch C, Sjöberg T, et al. A nonrandomized open-label phase 2 trial of nonischemic heart preservation for human heart transplantation. *Nat Commun.* 2020;11(1):2976. PMID: 32532991 https://doi.org/10.1038/s41467-020-16782-9

10. Rojas SV, Ius F, Kaufeld T, Sommer W, Goecke T, Poyanmehr R, et al. Ex vivo heart perfusion for heart transplantation: a single-center update after 5 years. *Thorac Cardiovasc Surgeon.* 2020;68. https://doi.org/10.1055/s-0040-1705375

11. Sponga S, Ius F, Ferrara V, Royas S, Guzzi G, Lechiancole A, et al. Normothermic ex-vivo perfusion for donor heart preservation in transplantation of patients bridged with ventricular assist devices. *J Heart Lung Transplant.* 2020;39(4):S245. https://doi.org/10.1016/j.healun.2020.01.926

12. Ermolaev PA, Khramykh TP, Korpacheva OV. *Apparatus for perfusion preservation and reconditioning of a donor heart.* RF Patent 2754592 C1, applic. No 2020130330, stated September 15, 2020, published September 3, 2021. Bull. № 25. Available at:

https://patentimages.storage.googleapis.com/de/ed/f2/5e63aacf7aac41/RU2754592C1.pdf [Accessed December 22, 2025]. (In Russ.).

13. Ermolaev PA, Khramykh TP. *Method of modeling brain death in an experiment.* RF Patent 2798902 C1, applic. No 2023106577, stated March 21, 2023, published June 28, 2023. Bull. № 19. Available at: https://patentimages.storage.googleapis.com/4b/79/bd/6610040922b085/RU2798902C1.pdf [Accessed December 22, 2025]. (In Russ.).

14. Milani-Nejad N, Janssen PM. Small and large animal models in cardiac contraction research: advantages and disadvantages. *Pharmacol Ther*. 2014;141(3):235-249. PMID: 24140081 https://doi.org/10.1016/j.pharmthera.2013.10.007

15. D'Alessandro D, Pretorius VG, Louca JO, Large S, Bowles DE, Silvestry SC, et al. Current approaches to optimize the donor heart for transplantation. *J Heart Lung Transplant*. 2025;44(4):672-680. PMID: 39730081 https://doi.org/10.1016/j.healun.2024.12.001

16. Ughetto A, Roubille F, Molina A, Battistella P, Gaudard P, Demaria R, et al. Heart graft preservation technics and limits: an update and perspectives. *Front Cardiovasc Med*. 2023;10:1248606. PMID: 38028479 https://doi.org/10.3389/fcvm.2023.1248606 eCollection 2023.

17. Resch T, Cardini B, Oberhuber R, Weissenbacher A, Dumfarth J, Krapf C, et al. Transplanting marginal organs in the era of modern machine perfusion and advanced organ monitoring. *Front Immunol*. 2020;11:631. PMID: 32477321 https://doi.org/10.3389/fimmu.2020.00631 eCollection 2020.

18. Zhang Y, Fu Z, Zhong Z, Wang R, Hu L, Xiong Y, et al. Hypothermic machine perfusion decreases renal cell apoptosis during ischemia/reperfusion injury via the Ezrin/AKT pathway. *Artif Organs* 2016;40(2):129-135. PMID: 26263023 https://doi.org/10.1111/aor.12534

19. Qin G, Jernryd V, Sjöberg T, Steen S, Nilsson J. Machine perfusion for human heart preservation: a systematic review. *Transpl Int*. 2022;35:10258. PMID: 35401041 https://doi.org/10.3389/ti.2022.10258 eCollection 2022.

20. Javier MFDM, Delmo EMJ, Hetzer R. Evolution of heart transplantation since barnard's first. *Cardiovasc Diagn Ther*. 2021;11(1):171–182. PMID: 33708490 https://doi.org/10.21037/cdt-20-289

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