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# PRETRANSPLANT RECONSTRUCTIVE SURGERY ON DONOR HEART

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**Aim:** to evaluate the immediate results of reconstruction of the valve heart apparatus and the great vessels of the heart graft before implantation. **Materials and methods.** The analysis included 24 cardiac transplants with pathology of the valve apparatus and the great vessels, as well as 24 recipients who needed emergency heart transplantation and were in the clinic under UNOS status code 1A and 1B. **Results.** Before performing heart transplantation, the valve apparatus and great vessels were corrected. **Conclusion.** With a shortage of donor organs for recipients requiring emergency care, cardiovascular transplantation from "suboptimal" donors is one of the most affordable ways. Given the possibility of reconstructive operations on the valve apparatus and the great vessels of the donor heart, and evaluating satisfactory immediate results of demonstrated observations, it can be argued that the above way out would reduce urgent waitlist mortality, achieve satisfactory survival results in the early postoperative period, increase the donor resource and optimize the transplant program.

*Keywords: heart transplantation, donor organ, heart failure, heart valve repair.*

Despite widespread adoption of effective drugs for the heart failure treatment, the annual survival rate of patients with terminal heart failure (THF) remains extremely low and is conditioned by progressive myocardial dysfunction [1; 25]. Besides pharmacological therapy the following surgical methods are currently widely used in patients with THF: 1) myocardial revascularization, 2) resynchronization therapy, 3) partial ventriculoplasty (Batista surgery), 4) implantation of the elastic mesh stent, 5) valvular heart disease treatment. These techniques could be effective in the early stages of heart failure and stored myocardial reserves, but they have no effect at the terminal stage of the disease [2; 3].

Moreover, despite the successful development and implementation of implantable systems of long-term mechanical circulatory support (MCS), heart transplantation (HT) remains the most effective method of treatment for patients with THF characterized with more than 90% survival rate within 1 year and an average life expectancy within 10 years after the surgery. Besides, post-HT patients have no significant physical activity limitations [4]. The desire to reduce the recipients' lethality due to the decompensation in THF during the organ waiting period led to mechanical circulatory support application as a "transfer" to HT by extracorporeal membrane oxygenation (ECMO), as well as transplantation from "suboptimal donors".

During the period from 1997 to 2017 36,340 adult patients aged 18 to 64 years underwent the HT surgery in the USA [5]. Currently, the USA waiting list consists of approximately 3000 candidates waiting for heart transplantation with waiting list annual mortality rate of nearly 15% [6]. According to Eurotransplant data, as of 2017 in Europe the active line of recipients in the waiting list consists of 1141 persons. During the same period, only 548 recipients underwent the HT surgery, taking into account that only 817 heart donors have been considered [7]. For the last several years the program of heart transplantation in Russia, in particular, in the FSBU [Federal State Budgetary Institution] "V.I. Shumakov. Shumakov National Medical Research Medical Center of Transplantology and Artificial Organs" of the Ministry of Health of Russia has been characterized by active and successful development. During the period from 2006 to 2017, the number of heart transplantation centers had increased by 14 (sevenfold). The number of patients in the heart transplant waiting list has reportedly increased in the Russian Federation from 2012 to 2017, while the time of heart transplantation waiting has been gradually decreasing. The heart transplant waiting list during 2017 included 645 potential recipients, where 405 were included into the waiting list for the first time in 2017. In Moscow, 304 potential recipients were in the heart transplant waiting list (47.1% from the national waiting list). The death rate during the heart transplantation waiting period in Russia during this period was 42 patients [8–13].

The first successful heart transplantation in our country was performed by Academician V.I. Shumakov on March 12, 1987. Back then, the HT development show-

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ed that the need for heart transplantation was not accompanied by a proportional increase in the number of transplants due to the lack of donors with the standard criteria. Currently, the number of heart transplantations is increasing year after year due to the raising of new donor programs efficiency. Therefore, during the period from 2006 to 2008, in total 56 heart transplantations were performed in the Russian Federation, 35 transplantations were conducted in Shumakov National Medical Research Center of Transplantology and Artifical Organs. Furthermore, in the period from 2014 to 2017, 813 heart transplantations were performed, 492 of them took place in our center. In 2017, from a total of 252 heart transplantations conducted in the Russian Federation 63.9% (161) corresponding procedures were performed in Shumakov National Medical Research Center of Transplantology and Artificial Organs. Besides new programs, the successful program of heart transplantation in our center enables increasing the number of heart transplantations in the country. In 2018 the number of HT in Shumakov National Medical Research Center of Transplantology and Artificial Organs made 196 [8–13].

The discrepancy between the need and the availability of donor organs is the most significant limiting factor of the heart transplantation program worldwide [4].

A rather great amount of donor hearts are left unused for transplantation due to the valvular heart apparatus pathology, atherosclerotic affection of the coronary arteries, lesion of the heart transplant ascending aorta, therefore, such organs are subject to "utilization" [14–18].

In the context of the heart donors with standard criteria deficit, the issue of the relevance of HT from donors with extended criteria or the so-called "suboptimal donors" has emerged [19].

A heart donor is regarded as optimal if the next criteria are fulfilled: equivalence or compatibility of donor and recipient according to the AB0 blood type system, donor's age under 40 years old, left ventricle ejection fraction more than 50%, cardiotonic or/and angiotonic [vasopressor] support (dopamine/dobutamine minimum dose below 10 um/kg/min or norepinephrine below 100 ng/kg/min), left ventricle cardiac muscle thickness below 12 mm, absence of coronary arteries stenosis, cardiac muscle contractility function local disorders and heart valvular apparatus and great vessels pathologies, as well as presumptive transplant ischemia being less than 4 hours [19].

Recently, the significant increase of heart transplantations from donors aged 60 years and above is observed. In literary sources cases of trials on HT from elderly donors can be found, in which cases no verifiably significant difference in HT surgeries results from donors under 40 years old had been determined [Drinkwater D.C. et al., 1996; Mulvagh S. et al., 1989; Pflugfelder P.W. et al., 1991; Menkis A.H. et al., 1991; Zuckermann A., Kocher P. et al., 1997]. The great attention in the heart transplantation program is paid to HT with myocardial hypertrophy more than 1.4 cm, with an ejection fraction of the left ventricle below 50% [19]. Rarely, but there are reports regarding valvular and coronary pathology correction of the heart transplant. Observations of plastic, mitral valve prosthetics, aortic valve prosthetics, aortocoronary bypass grafting of donor hearts are also described [16–18; 20; 21; 23; 24].

Goland et al (2008) consider that in the context of donor organs deficit the heart transplantation is justified in case of strict principle "suboptimal donor – suboptimal or urgent patient" maintenance.

In the Shumakov National Medical Research Center of Transplantology and Artificial Organs, during the period from 2012 to 2019, various pretransplantational reconstructive surgeries of valvular apparatus and great vessels were performed on donor organs for 24 recipients.

This work aims at evaluating the direct results of this procedure type.

## METHODS AND RESULTS

24 heart donors were included in the analysis, including 14 (58.4%) males and 10 (41.6%) females aged 27 to 63, with the mean age of 48.8 ± 7.6. Among the causes that led to brain death in a heart donor, there were: traumatic (traumatic brain injury) in 5 and hemorrhagic and ischemic strokes in 15 and 4, respectively. Donor body weight varied from 55 to 115 kg, on average: 83.5 ± 14.4 kg, body mass index ranged from 19.03 to 42.24 mg/m$^2$, averaging 27.93 ± 4.21 kg/m$^2$. Donor blood type: 0 (I) – n = 6, A (II) – n = 13, B (III) – 5. No periods of hypotension were observed during "donor conditioning". The donor "conditioning" period lasted from 1 to 4 days, on average: 1.7 ± 0.7 days.

The blood flow stagnation in the cerebral vessels leads to neurocirculatory regulation disorder and serves as a driving force for homeostasis disorder [Howlett T.A. et al., 1989]. In case of brain death, the endocrine system reaction is characterized by pronounced hormones release, which is manifested with clinical picture of the so-called "vegetative storm" [Bucker A.I., Shute Yu., 1981; Shemie S.D. et al., 2006]. Donor conditioning includes restoration and support of the blood circulation, stable arterial pressure, anemia, acidosis, hypernatremia, hypoproteinemia and polyuria correction, body temperature maintenance [Sergiyenko S.L. et al., 2010]. Hemodynamic parameters stability after donor brain death was supported using combined or isolated infusion of angiotonic and cardiotonic drugs (norepinephrine, dopamine). Due to pharmacological therapy correction at the stage of donor "conditioning", it became possible to achieve the maximum decrease of cardiotonic and angiotonic drugs dosage, in particular, of norepinephrine from 600 ng/kg/min to 80 ng/kg/min, on average: 253.4 ± 105.9 ng/kg/min; dopamine dosage ranged from 2 to 6 mg/kg/min, on average: 4.2 ± 1.4 ng/kg/min, in four cases

the drugs were used in combination, but in one case the donor "conditioning" was performed without any sympathomimetic support. Cardiovascular resuscitation was conducted to one of the donors at the observation stage on the background of the blood circulation arrest followed by effective hemodynamics restoration.

Adequate conditioning resulted in all donors being compensated by their blood electrolytes balance and having normal biochemical and clinical blood counts by the time of heart transplantation. During the clinical-instrumental examination of a potential heart donor, a transthoracic and/or transesophageal echocardiography were performed to evaluate the ejection fraction of the left ventricle, measure the size of the heart chambers and wall thickness, and the function of the valvular apparatus of the heart, assess the presence or absence of local contractility disorders, specifically hypokinesis, akinesis, dyskinesis. Among the examined heart donors, left ventricular hypertrophy (LVH) was detected in 13 patients. The thickness of the interventricular septum (IVS) ranged from 1.2 to 1.8 cm, averaging 1.29 ± 0.24 cm, the thickness of the posterior wall of the left ventricle (LVPW) was within the range of 1.2 to 1.5 centimeters, averaging 1.27 ± 0.16 cm.

During the EchoCG study in the examined group, the following was diagnosed: aneurysm of the ascending aorta above the sinotubular junction with aortic valve insufficiency in bicuspid aortic valve with stenosis revealed in one donor, complex aortic valve defect in two donors, mitral valve insufficiency in 17 donors. In one case, a combined defect of the mitral valve with insufficiency predominance was detected. Mitral valve stenosis was detected in 1 donor.

Stage 2 and 3 pulmonary hypertension was diagnosed in 6 and 1 donor, respectively.

According to electrocardiographic monitoring data aimed at detection of cardiac muscle and rhythm disorders in 9 donors arrhythmias were detected: atrial fibrillation in one donor, sinus arrhythmia with HR of 107 ± 4.8 bpm on average in 5 donorss, sinus bradycardia with HR of 53 bpm in 1 donor, stage 1 atrioventricular blockade in one donor, and in one case the rhythm was generated from atrioventricular connection. Sinus tachycardia and acute atrial fibrillation were, probably, driven by the heart donor brain death and electrolyte balance disturbance.

For the heart transplant storage, the method of cold pharmacological cardioplegia was applied using the following solutions: "Bretschneider-HTK" in two cases and "Kustodiol" in the others. The storage solution volume of 3000 ml was administered into the aortic root after the aortic clamping. During the intraoperative visual assessment of the cardiac transplant, signs of heart contusion associated with cardiac pulmonary resuscitation were observed.

After explantation, the visual and palpatory transplant examination was performed by the cardiac surgeon. During this examination, in accordance with the ultrasound findings, the mitral valve affection was revealed: cusps degeneration (n = 3), cusps thickening with calcification foci and fish-mouth mitral stenosis (concretion along commissures) (n = 2), fibrotic changes of cusps (n = 11), and mitral valve posterior cusp cleavage up to fibrous ring, anterior cups cleavage along the A2–3 margin of and posterior cusp cleavage along P2–3 margin in one patient. At the revision of aortic valve, the following lesions were visualized: bicuspid aortic valve with massive cusps calcification (n = 1), fibrous alterations of cusps calcification (n = 1). Aneurysm of ascending aorta associated with the aortic valve insufficiency was identified in two patients. The valves lesion was combined in one case: mitral valve cusps degeneration and massive calcinosis of the aortic valve cusps.

Moreover, at the revision of the heart septum, the patent foramen ovale was revealed in one donor and sutured during heart transplant processing.

24 recipients were prepared for transplantation including 17 (71%) males and 7 (29%) females aged from 16 to 64, on average 47.5 ± 11.4. At admission, the most common recipients' complaint was breathlessness at rest (n = 13) and minimal physical exertion (n = 10). Swelling in the ankles and feet were identified in 13 recipients, in particular, only feet edema in 6 and edema up to thighs in 1 recipient.

The primary disease leading to the development of terminal heart insufficiency and the need in HT conduction in 24 recipients was the DCMP [dilated cardiomyopathy] in 13 patients and cardiomyopathy as result of myocarditis in one recipient, ischemic cardiomyopathy in 7 recipients, hypertrophic cardiomyopathy in one case, postradiation anthracycline cardiomyopathy in 1 recipient and heart transplant dysfunction at 3$^{rd}$ year after orthotopic heart transplantation in 1 recipient.

All recipients (n = 24) required cardiotonic dopamine therapy, the dosage ranged from 3.3 to 8.4 μg/kg/min, the average dose made 4.9 ± 1.14 μg/kg/min or dobutamine, with the minimal dose of 3 μg/kg/min and the maximum dose of 10.3 μg/kg/min, the average dose made 5.3 ± 1.62 μg/kg/min, to maintain the adequate hemodynamics while waiting for HT. 6 recipients were under mechanical circulatory support during the pretransplantation period using extracorporeal membrane oxygenation with peripheral connection method lasting for 1 to 9 days (averaging 3.6 ± 2.2 days) and a productivity of 3.5 to 4.5 l/min, averaging 3.8 ± 0.26 l/min.

All recipients requiring urgent HT were under permanent intravenous infusion therapy only or/and a combination of cardiotonic drugs, hemodynamics mechanical support was used, patients' status according to the UNOS classification was 1A–B. In the study group, 1 patient was waiting for heart re-transplantation.

Average systolic BP was 95 (±6.8) mm Hg, diastolic BP = 62.6 (±5.7) mm Hg.

The results of pretransplantation EchoCG are shown in table 1.

Table 1

**Pretransplantation echocardiography parameters of recipients**

| Parameter | Mean values |
|---|---|
| Aorta at the level of fibrous ring, cm | 2.4 ± 0.37 |
| Aorta at the level of the ascending segment, cm | 3.2 ± 0.46 |
| LV anteroposterior dimension, cm | 5.2 ± 0.82 |
| RV, cm | 3.4 ± 0.65 |
| EDD, cm | 7.1 ± 1.2 |
| ESD, cm | 6.4 ± 0.96 |
| EDV, ml | 298.5 ± 101.76 |
| ESV, ml | 234.1 ± 89.96 |
| SV, ml | 70.3 ± 17.88 |
| LVEF, % | 22.8 ± 4.78 |
| IVS thickness, cm | 1.1 ± 0.22 |
| PW thickness, cm | 1.0 ± 0.14 |
| Pulmonary artery pressure, mm Hg | 51.6 ± 12.24 |

*Note.* Here and in the table 2: LV – left ventricle; RV – right ventricle; EDD – end-diastolic dimension of left ventricle; ESD – end-systolic dimension of left ventricle; EDV – end-diastolic volume of left ventricle; ESV – end-systolic volume of left ventricle; EF – ejection fraction; LVEF – left ventricle ejection fraction; IVS – interventricular septum; PW – posterior wall.

Stage 3 mitral valve regurgitation was revealed in n = 15, stage 2 in n = 8.1, stage 1 in n = 1 of recipients. Stage 3 tricuspid valve regurgitation was diagnosed in 12 recipients, stage 2 in 11 recipients and stage 4 in one observed patient.

Transplantation surgery was performed using the following methods:

1) atrial (Lower R.R., Stofer R.S., Shumway N.N., 1961) in 3 recipients;
2) cava-caval (Yacoub M., 1990; Dreyfus G., 1991) in 16 recipients;
3) complex in 1 recipient, during which the tissue "bridge" was formed from the right atrium wall with the purpose of the superior and inferior vena cava connection (Shumakov V.I., 2006) [22].

Due to the state severity of recipients in HT waiting list, the decision was made regarding heart transplantation from "suboptimal donors".

During transplantation, taking into account the valvular apparatus and great vessels changes of the heart transplant, the following surgeries were performed:

1) supracoronary ascending aorta replacement with prosthesis "Vascutec-28" and "Gelewave-28" (n = 2);
2) aortic valve replacement with mechanical valve "Medinge-25" and "Medinge-23" (n = 2);
3) mitral valve replacement with mechanical valve "Medinge-29" (n = 2);
4) mitral valve annuloplasty with supporting ring (n = 4), "Medinge-28", "Medinge-34", "Medinge-30" (n = 2);
5) mitral valve annuloplasty with supporting ring "MedtronicProfile 3D-28", suturing of MVPC and MVAC cleavage (n = 1);
6) mitral valve annuloplasty with supporting ring "Medinge-32" in combination with Alfieri mitral valve cusps plasty;
7) mitral valve annuloplasty with supporting ring with chorda replacement using PTFE fiber in 3 patients. Supporting rings "Medinge-28" (n = 2) and "Medinge-30" (n = 1) were used;
8) mitral valve annuloplasty with supporting ring "Medinge-30" with chorda replacement using PTFE fiber, MVAC cleavage suturing (n = 1);
9) mitral valve annuloplasty with supporting ring "Medinge-30" with chorda replacement using PTFE fiber, MVPC cleavage suturing and Boyd's tricuspid valve plasty;
10) mitral valve annuloplasty with supporting ring and tricuspid valve annuloplasty with supporting ring (n = 4), rings for mitral valve: "Medinge-28" (n = 3) and "Medinge-30" (n = 1), for HT "Medinge-28" (n = 2), "Medinge-30" and "Medinge-34";
11) mitral valve annuloplasty with supporting ring and deVega and Boyd tricuspid valve plasty (n = 2). Supporting rings: "Medinge-30" (n = 2);
12) mitral valve annuloplasty with supporting ring "Medinge-28" with chorda replacement using PTFE fiber and aortic valve replacement with "Medinge-21" mechanical prosthesis.

Intraoperative photos with notes are provided in Fig. 1–4.

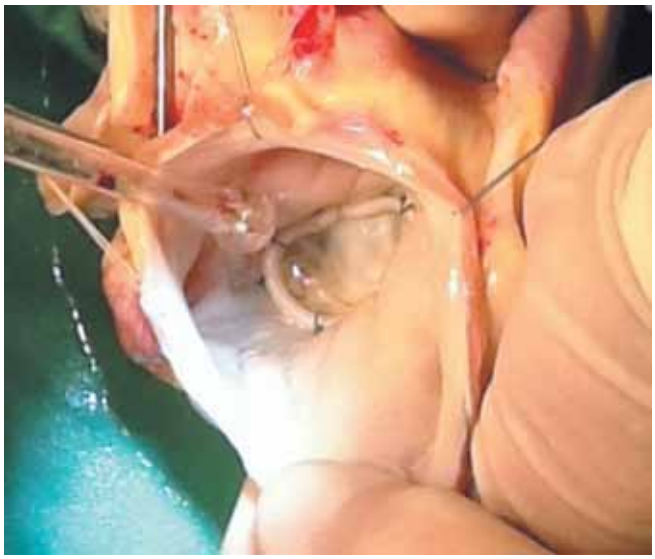

Fig. 1. Donor S., 47 years old, with brain death due to ischemic stroke with preserved pumping function of the heart, having fibrous changes in mitral valve. Hydraulic test after implantation of the support ring

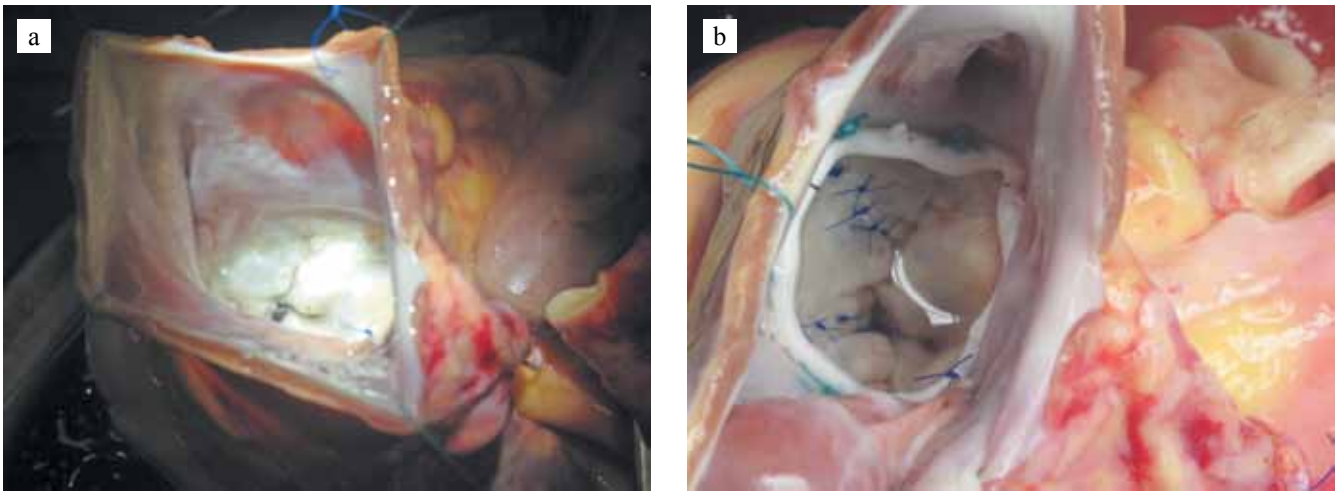


Fig. 2. Donor U., 49 years old, with brain death due to intracerebral hemorrhage, mitral valve posterior flap cleavage: a – the splitting of the mitral valve leaflets of the donor heart, unsatisfactory co-optation; b – annuloplasty of the mitral valve by the support ring and valvuloplasty of the mitral valve

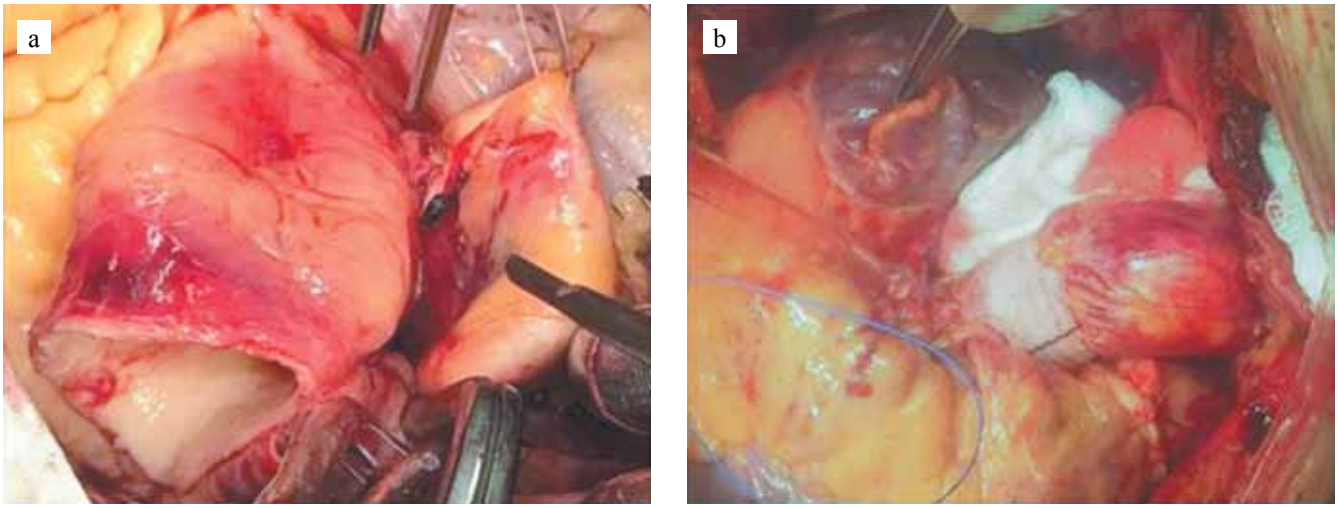


Fig. 3. Donor E., 57 years old, with brain death due to intracerebral hemorrhage, ascending aortic aneurysm and aortic valve insufficiency: a – aneurysm of the ascending part of the donor heart, mismatch of the donor and recipient aortic diameters; b – supracoronary aortic prosthetics of an implanted heart

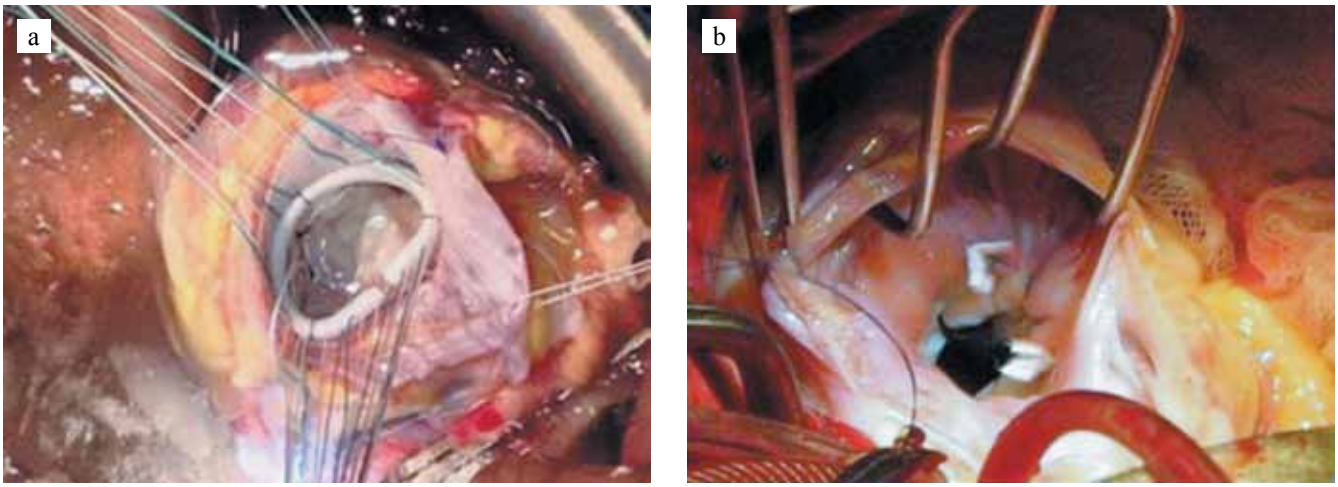


Fig. 4. Donor Z., 52 years old, with brain death due to intracerebral hemorrhage, mitral insufficiency and tricuspid valve insufficiency: a – implanted support ring in mitral position; b – Plastic tricuspid valve by De Vega

The duration of the surgery was 160 to 432 minutes, with an average of 298.23 ± 54.39 minutes. The time of artificial blood circulation ranged from 56 to 210 minutes, averaging 131 ± 30.9 minutes. Heart transplant ischemia averaged 195.1 ± 40 min. The duration of myocardial ischemia for more than 3 hours was recorded in 13 (54%) recipients. The level of hypothermia during the procedure of artificial blood circulation ranged from 35.2 to 27.9 °C, averaging 33.08 ± 10 °C.

In two (8%) patients the cardiotonic therapy was not applied in the early pre-transplantation period. In 92% of patients complex multicomponent cardiotonic support was applied.

From 6 recipients previously being under mechanical circulatory support by venoarterial ECMO [extracorporeal membrane oxygenation] before HT, the post-transplantation venoarterial peripheral ECMO was required in 5 patients and 1 recipient was disconnected from the ECMO apparatus due to the early heart transplant dysfunction. Apart from these patients, 3 recipients required post-transplantation mechanical circulatory support by veno-arterial central ECMO . The volume speed of extracorporeal blood flow was on average 2.36 ± 1 l/min. The duration of mechanical circulatory support ranged from 2 to 9 days, on average 4.5 ± 2.6 days.

In 8 patients, mechanical circulatory support was combined with sympathomimetic therapy, including epinephrine, dobutamine, and/or dopamine, the dose made on average 0.05 ± 0.03 μg/kg/min, 4.75 ± 3.5 μg/kg/min and 5.75 ± 0.37 μg/kg/min, respectively. After early transplant dysfunction regression, recipients with peripheral ECMO were disconnected from the mechanical circulatory support.

In 62.5% recipients, the functioning of the heart transplant was restored after circulatory support. In 3 patients the repeated HT was performed in three recipients with central ECMO due to irreversible heart transplant dysfunction.

In 14 recipients, not requiring mechanical circulatory support, the efficacy of pumping ability of the transplant was provided by cardiotonic therapy, including epinephrine, dobutamine and/or dopamine. Dopamine dose ranged from 2 to 15 μg/kg/min, on average – 8 ± 3.73 μg/kg/min. Dopamine dose ranged from 2 to 15 μg/kg/min, averaging 8 ± 3.73 μg/ kg/min. Dobutamine dose ranged from 3 to 8 μg/kg/min, with an average of 4.58 ± 1.5 μg/kg/min, the Adrenaline dose ranged from 0.01 to 1.2 μg/kg/min, averaging 0.41 ± 0.39 μg/kg/min.

The early postoperative period associated with renal dysfunction in 5 patients required the application of the replacement renal therapy. Antibody-related transplant failure after HT was detected in 5 recipients, therefore the immunosuppressive therapy was corrected. Furthermore, hydrothorax was among the most common postoperative period complications (n = 11).

After coronary angiography of the transplanted heart, no hemodynamically significant atherosclerotic lesions of coronary arteries were detected. Findings of the post-transplantation EchoCG are shown in table 2.

Table 2

**Echocardiography findings in recipients after heart transplantation**

| Parameter | Mean value |
|---|---|
| Aorta at the level of fibrous ring, cm | 2.52 ± 0.37 |
| Aorta at the level of ascending segment, cm | 3.09 ± 0.14 |
| LV, cm | 4.12 ± 0.91 |
| RV, cm | 2.42 ± 0.33 |
| EDD, cm | 4.35 ± 0.32 |
| ESD, cm | 2.62 ± 0.3 |
| EDV, ml | 84.31 ± 17.31 |
| ESV, ml | 26.31 ± 8.31 |
| EF, ml | 59.13 ± 11.39 |
| LVEF, % | 67.56 ± 4.6 |
| IVS, cm | 1.27 ± 0.13 |
| LVPW, cm | 1.23 ± 0.11 |
| PA pressure (mm Hg) | 36.47 ± 7.89 |

Stage 1 mitral valve regurgitation was detected in n = 14, stage 2 in n = 1 of recipients. Stage 3 tricuspid valve regurgitation was revealed in 1 recipient, stage 2 in 2 recipients and stage 1 in 12 of the observed patients. Despite these parameters, we have not revealed any residual insufficiency impact on the central hemodynamics parameters which were stable.

Hospital death rate after heart transplant valvular apparatus reconstructive surgeries with further HT was 12.5% (3 from 24 recipients). According to the post-mortem examination findings and results of autopsy material examination, the death of two recipients occurred on the 7$^{th}$ and 8$^{th}$ day, respectively, after the heart transplantation, due to progressive heart failure. The death of the third patient occurred on the 108$^{th}$ day due to multiple organ failure.

21 (87.5%) from 24 recipients with the HT from "suboptimal" donors did not require any repeated surgical interventions and were discharged. Bed days after surgery made on average 28.94 ± 14.14 days.

## CONCLUSION

In the context of the donor organs global deficit, the cardiac transplantation from the so-called "suboptimal" donors is regarded as one of the most effective ways to increase availability and number of surgeries, first of all, in recipients needing urgent medical help. Hemodynamically significant defects of the valvular apparatus and great vessels of the heart served as contraindications to the selection of the cardiac transplant. Given the possibility of reconstructive operations on the heart valve apparatus, a significant number of donor hearts can be used effectively [23; 14]. Evaluating the satisfactory

direct results in the described patients, it seems fair to say that the implementation of the above project will reduce the hospital death rate of recipients, improve the immediate HT results and allow for the most efficient use of the valuable donor resource.

*The authors declare no conflict of interest.*

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