Despite growing progresses in long-term mechanical circulatory support (MCS) technology, mainly concerning implantable ventricle assist devices (VAD), heart transplantation (HTx) remains the treatment of choice for patients with end-stage advanced heart failure. In the last decades, the availability of HTx was limited due to low annual heart donation rates as a result of shortage of brain-dead heart donors presenting with standard criteria. So, survival of heart transplant candidates was poor. HTx from donors with extended criteria is one of the ways to increase the number of transplantations with the result of improvement of donor heart availability and reduction...
of waiting list mortality. Single- and multi-center studies demonstrate acceptable early and long-term survival of heart transplant recipients from donors with extended criteria. The prioritization on the transplant waiting list is made by the United Network for Organ Sharing (UNOS) and has been updated in 2018.

Left ventricular (LV) systolic dysfunction and LV regional wall motion abnormality are frequent echocardiographic findings in brain-dead patients frequently leading to declining of donor organs. HTx from brain-dead donors with abnormal LV systolic function especially LV ejection fraction of less than 40% is a most controversial approach that may potentially expand the heart donor pool. The absence of well-defined criteria for the non-reversibility of myocardial damage, the discrepancy between the severity of brain-dead echocardiographic abnormality and the morphological evidence of ischemic myocardial damage indicate that rejecting organs from donors with impaired systolic function and/or regional wall motion abnormalities may often be unreasonable. Previous studies demonstrated a rapid recovery to normal levels in the early post-transplant period of the initially compromised donor hearts with abnormal LV systolic function.

In the last few years, the Shumakov National Medical Research Center (Moscow, Russian Federation) performed on regular basis HTx from brain-dead donors with extended criteria with a total annual number of more than 125 HTx procedures. In 2016, the center commenced performing HTx from donors with abnormal LV systolic function (LVEF < 40%) with the view for improving donor heart availability because the growing heart transplant waiting list was more and more increasing (more than 230 heart transplantation candidates per year) and a large proportion of heart transplant candidates with temporary needed urgent HTx.

The aim of this study was to evaluate early and late outcomes of recipients after HTx from donors with abnormal LV systolic function (LVEF < 40%).

## 2 | MATERIAL AND METHODS

Four hundred eighty seven patients underwent HTx in our institution from January 2016 to December 2018. 27 (5.5%) patients had cardiac allografts from donors with LVEF <40%. Indications for HTx from donors with LVEF <40% were as follows: (1) need for urgent transplantation (UNOS status 1–3), especially patients supported with temporary mechanical circulatory support (MCS); (2) long waiting list time (especially patients with blood group O) and/or (3) high risk of life-threatening complications (left heart thrombosis, cardiac arrhythmias, impending multi-organ dysfunction, and other life-threatening conditions). Real-time consent was obtained from the patient when marginal organs were used.

Our cohort included 23 (85.2%) men and 4 (14.8%) women, with a mean age of 42.9 ± 5.7 (range, 29–63) years. The diagnosis was idiopathic cardiomyopathy in 14 (51.9%) patients, ischemic cardiomyopathy in 11 (40.7%) patients, and valvular heart disease in 2 (7.4%) patients. Table 1 shows patients’ demographic and pretransplant characteristics. Sixteen patients (59.3%) had blood group O. Twenty-five patients (92.6%) needed urgent HTx and management on ICU including 19 patients with pretransplant temporary MCS (paracorporeal centrifugal BiVAD (para-MCS)) and veno-arterial extracorporeal membrane oxygenation (vaECMO; n = 18, 66.7%), whereas six subjects (22.2%) needed on inotropic support. One patient (3.7%) was on mechanical ventilation on vaECMO. Three patients (11.1%) were on continuous veno-venous hemofiltration (CVVH) for the management of advanced renal dysfunction and diuretic resistance. In all cases, pretransplant vaECMO application was continued in early postoperative period. The reason why the biatrial approach was used in a third of our transplantations was surgeons’ preference.

Echocardiographic evaluation was conducted twice preoperatively within an interval of about 48 h and was regularly done until discharge of the patients. After surgery until discharge day, patients were regularly evaluated via echocardiography. In echocardiography, left ventricular function was evaluated as well as heart valve. Also, right ventricular function was compared to earlier examinations. Primary graft dysfunction was not seen more often in donors without reversibility of LV dysfunction during donor management.

Before starting the study, the study protocol was approved by the institutional Ethics Committee. Informed consent was obtained from each patient before heart transplant listing. Study was performed in accordance with the ethical statement of the 1975 Declaration of Helsinki.

### 2.1 | Surgical procedures and immunosuppression

In all cases, cold static storage of the donor heart was performed by custodiol preservation solution (3–4 L). All patients from this cohort underwent HTx using either bicaval or biatrial implantation techniques. Detailed surgical procedure has been described elsewhere.

For induction therapy, interleukin-2 receptor antagonist basiliximab was administered on postoperative day 0 and 4. Heart transplant recipients received standard immunosuppressant therapy with methylprednisolone, calcineurin inhibitor tacrolimus, and mycophenolate mofetil. Intraoperatively, patients received 10 mg/kg methylprednisolone immediately before cardiac allograft reperfusion. Postoperatively, patients received 125 mg methylprednisolone every 8 h (3 doses totally). Oral methylprednisolone was provided in tapered regimen. Mycophenolate mofetil was administered at 500–1000 mg twice daily. First, endomyocardial biopsy and coronary angiography were performed on postoperative day 5–9.

Diagnosis of primary allograft dysfunction (PGD) in patients without pretransplant vaECMO was performed according to ISHLT PGD definition. In cases with pretransplant vaECMO, the need for prolonged MCS in early postoperative period for more than 2 days and/or with extracorporeal blood flow more than 2.0 L/min a manifestation of PGD (definition from internal protocol of our transplant center) was assigned. Among patients with pretransplant vaECMO and without hemodynamic signs of PGD, circulatory support was maintained after HTx in “protective” mode for no longer than 1-2 days.
Data analysis

All data were analyzed using the Statistical Package for Social Sciences, version 16.0 (SPSS Inc) and are presented as continuous or categorical variables. Continuous variables were expressed as means ± standard deviation (SD). Continuous variables were analyzed with Mann-Whitney U test. Categorical variables were analyzed with the chi-square test. A p-value of less than .05 was considered statistically significant.

3 | RESULTS

Forty seven comatose patients with traumatic or non-traumatic brain injury, Glasgow Coma Scale score 3, apnea test and/or cerebral angiography diagnostic criteria of brain death and LVEF <40% were...
evaluated according to the protocol for potential heart donation. 14 patients with confirmed brain death diagnosis were recognized unacceptable for various reasons. Leading causes for heart donation refusal were as follows: (1) electrocardiographic/echocardiographic signs of cardiac contusion due to blunt chest trauma \( n = 2 \); (2) high dilatation of right and/or left heart (probably due to pre-existing pathology) \( n = 4 \); (3) severely high inotropic/vasopressor support (dopamine >20 \( \mu \)g/kg/min and/or norepinephrine >1.0 \( \mu \)g/kg/min \( n = 5 \)); (7) multiple coronary vessel disease \( n = 3 \)). The remaining 6 donor hearts were refused due to logistic problems, such as absence of suitable recipients \( n = 2 \); too long calculated transportation time (more 4 h; \( n = 2 \)) and due to family members refuse to organ donation \( n = 2 \).

Acceptable for heart donation were 27 (57.4%) among 47 patients with confirmed diagnosis of brain death and with LVEF <40%. This cohort of potential heart donors was assessed at least two times in terms of echocardiographic evaluation. This was immediately after brain death confirmation and before organ procurement.

The final decision to use the donor heart for subsequent transplantation was made after assessment of the results of the last echocardiographic evaluation (before procurement), inotropic/vasopressor support dosage, markers of cardiomyocyte injury (troponin I, CK-MB) values, visual evaluation of the heart during retrieval surgery and the presence and extent of palpable or angiographic coronary abnormalities.

Criteria for choosing dysfunctional heart donors were age (<63 years), LVEF (20% - 40%), LVH (<1.5 cm), and projected ischemic time average (152 min). Though age is a critical aspect, because young dysfunctional donors may be more likely to improve than older, we equally applied all hearts of donors up to 63 years. Not all criteria simultaneously met in each donor. No patient required re-transplant due to lack of recovery of LV function. Age of heart donors (19 (70.4%) men and 8 (29.6%) women) ranged from 22 to 63 (42.9 ± 5.7) years (Table 2). In 4 cases (14.8%), donor age was 45–55 years, in 2 (7.4%) more than 55 years. The oldest heart donor was 63 years old. The cause of brain death was either traumatic \( n = 5 \); 18.5% or non-traumatic \( n = 22 ; 81.5% \) brain injury. Prolonged out-of-hospital cardiopulmonary resuscitation (18 min) was needed in a single heart donor. Donors’ ICU stay was 2.1 ± 1.4 days. 92.6% of all heart donors received inotropic and/or vasopressor support. In 77.8% of cases (\( n = 21 \), heart donor procurement was performed under pulmonary artery catheterization with continuous cardiac output monitoring. The mean cardiac index was 2.4 ± 0.3 L/min/m². Only a single (3.7%) donor had a serum sodium level higher than 160 \( \mu \)mol/L. Serum cardiac troponin I (cTnI) and creatine kinase isoenzyme MB (CK-MB) levels accounted for 0.21 ± 0.13 ng/ml (10.5 times higher than the upper normal value) and 48.6 ± 22.2 ng/ml (10.7 times higher than the upper normal value). Two (7.4%) heart donors had cTnI levels higher than 1.0 ng/ml.

The data of both echocardiographic evaluations before diagnostics of brain death and before procurement of donor hearts are presented in Table 3. Before diagnosis of brain death and

### Table 2  Characteristics of cardiac donors (\( n = 27 \))

| Parameters                              | Value                  |
|-----------------------------------------|------------------------|
| **Sex**                                 |                        |
| Men                                      | 19 (70.4%)             |
| Women                                    | 8 (29.6%)              |
| **Age, years**                           |                        |
| <45 years                                | 21 (77.8%)             |
| 45–55 years                              | 4 (14.8%)              |
| >55 years                                | 2 (7.4%)               |
| **Weight, kg**                           |                        |
| 81.3 ± 11.3                              |                        |
| **Cause of brain death**                 |                        |
| Traumatic damage                         | 5 (18.5%)              |
| Non-traumatic damage                     | 22 (81.5%)             |
| **CPR**                                  |                        |
| 1 (3.7%)                                 |                        |
| **Out-hospital/in-hospital**             | 1/0                    |
| **Duration, min**                        | 18                     |
| **ICU stay, days**                       | 1–7 (2.1 ± 1.4)        |
| >3 days                                  | 5 (18.5%)              |
| **Inotropic/vasopressor support**        |                        |
| Dopamine only                            | 25 (92.6%)             |
| Norepinephrine only                      | 18 (66.7%)             |
| Norepinephrine and dopamine              | 6 (22.2%)              |
| **Norepinephrine**                       |                        |
| Before evaluation (ng/kg/min)            | 477 ± 257              |
| Before procurement (ng/kg/min)           | 320 ± 205              |
| \( P = .021 \)                           |                        |
| **Dopamine**                             |                        |
| Before evaluation (\( \mu \)g/kg/min)    | 6.9 ± 3.8              |
| Before procurement (\( \mu \)g/kg/min)   | 2.4 ± 1.8              |
| \( P < .0001 \)                          |                        |
| **Hemodynamic parameters in donors with pulmonary artery catheter monitoring** | 21 (77.8%) |
| HR, bpm                                  | 88.2 ± 11.7            |
| SAP, mm Hg                               | 124.1 ± 27.4           |
| MAP, mm Hg                               | 65.9 ± 16.7            |
| DAP, mm Hg                               | 73.2 ± 17.5            |
| RAP, mm Hg                               | 8.6 ± 2.9              |
| SPAP, mm Hg                              | 33.2 ± 5.7             |
| MPAP, mm Hg                              | 19.2 ± 5.2             |
| DPAP, mm Hg                              | 13.9 ± 4.1             |
| PAWP, mm Hg                              | 13.2 ± 3.6             |
| CI, L/min/m²                              | 2.4 ± 0.3              |
| **Laboratory data:**                     |                        |
| Hb, g/dl                                 | 131.5 ± 19.4           |
| Total protein, g/L                       | 72.2 ± 13.0            |
| Potassium, mmol/L                        | 3.9 ± 0.7              |
| Sodium, mmol/L                           | 143.8 ± 8.2            |
| Sodium >160 mmol/L                       | 1 (3.7%)               |

(Continues)
TABLE 2 (Continued)

| Parameters          | Value                  |
|---------------------|------------------------|
| Urea (mmol/L)       | 7.1 ± 2.6              |
| Creatinine (µmol/L) | 106.5 ± 27.3           |
| Total bilirubin (µmol/L) | 72.1 ± 14.5         |
| ALT, U/L            | 32.7 ± 6.9             |
| AST, U/L            | 38.5 ± 9.1             |
| Arterial pH         | 7.43 ± 0.05            |
| Base excess         | −1.9 ± 0.9             |
| Lactate, mmol/L     | 1.9 ± 0.9              |
| PaO₂, mm Hg         | 187.3 ± 37.4           |
| PaCO₂, mm Hg        | 38.2 ± 6.5             |
| cTnl, ng/ml         | 0.21 ± 0.13 (normal value <0.02 ng/ml) |
| cTnl >1.0 ng/ml     | 2 (7.4%)               |
| CK-MB, ng/ml        | 48.6 ± 22.2 (normal value 0.34-4.55 ng/ml) |

Note: Variables are presented as means ± SD or number of patients and percentages.

Abbreviations: ALT, alanine aminotransaminase; AST, aspartate aminotransaminase; CI, cardiac index; CK-MB, creatine kinase isoenzyme MB; CPR, cardiopulmonary resuscitation; cTnl, conventional troponin I; DPAP, diastolic pulmonary artery pressure; HR, heart rate; ICU, intensive care unit; MAP, mean arterial pressure; MPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; RAP, right atrium pressure; SAP, systolic arterial pressure; SPAP, systolic pulmonary artery pressure.

MCS. The recipients showed a CI of 2.7 L/min/m² at all stages of the study. Paracorporeal BiVAD in one recipient was discontinued immediately before the start of the CPB. Requirement of any mechanical circulatory support after heart transplantation was not necessary. In two out of 15 recipients with pretransplant vaECMO support, mechanical circulatory support was discontinued in the operating room immediately after the end of surgery. In terms of 13 recipients with pretransplant vaECMO, mechanical circulatory support was continued for 2 days after transplantation (32 ± 6 h) in preventive mode with extracorporeal blood flow of less than 2.0 L/min (1.3 ± 0.3 L/min). The highest doses of epinephrine were 65.3 ± 22.3 ng/kg/min, of dopamine 8.2 ± 3.5 µg/kg/min and dobutamine 7.2 ± 3.6 µg/kg/min. Epinephrine was used for 4–68 (28.6 ± 7.9) h. Until postoperative day 5, doses of inotropic support of dopamine or dobutamine were not exceeding 4 µg/kg/min. Total duration of inotropic support was 8.2 ± 3.9 days. Three of these recipients with acceptable primary cardiac graft function were extubated in operating room within 1 h after the end of surgery. In other recipients (n = 20), mechanical ventilation was continued until first postoperative day.

On the 1st postoperative day, in the cohort of recipients without early cardiac primary graft dysfunction the echocardiographic study demonstrated significant increase in LVEF (from 35 ± 4% to 55 ± 7%) and decrease in LVEDV (from 131 ± 33 ml to 104 ± 12 ml) compared to corresponding pre-procurement values. All recipients from this cohort were discharged home. At discharge, LVEF and LVEDV were 71 ± 3% and 93 ± 6 ml, respectively. The cohort of recipients without early cardiac allograft dysfunction revealed ICU and post-transplant hospital stay of 6.7 ± 1.7 and 22.1 ± 3.9 days, respectively.

Four (14.8%) recipients presented severe early allograft dysfunction, such as primary biventricular cardiac allograft dysfunction (n = 3) and right ventricle cardiac allograft dysfunction due to high pretransplant secondary pulmonary hypertension with PVR 4.6 Wood units (n = 1). This cohort of recipients required prolonged vaECMO support or initiation of MCS (vaECMO) in early post-transplant period (n = 1). Recipients were characterized by a delayed normalization of LV systolic function. All these patients, however, fully recovered from severe early allograft dysfunction. MCS was discontinued on 4th to 6th (5.0 ± 0.5) postoperative day. LVEF increased up to more than 50% on 4th to 7th (5.3 ± 0.8) postoperative day and up to more than 60% on the 11th to 18th (14.8 ± 2.3) postoperative day after the heart transplant. Three out of four recipients were discharged home on day 28, 37, and 46 after HTx and are alive. One recipient died on the 32nd postoperative day due to sepsis.

All recipients demonstrated early (85.2%) or delayed (14.8%) recovery of systolic function (LVEF > 60%) after HTx. In the majority of recipients, LVEF was 60% or higher during the first three days after HTx. Severe early cardiac allograft dysfunction treated by MCS occurred in 14.8% of patients. One transplanted patient died during hospital stay. Follow-up after HTx was 27.7 ± 9.7 months. During follow-up, no further patient died.
DISCUSSION

Out of all potential brain death donors only in 1/8 of cases, the heart is considered suitable for HTx. The shortage of donor hearts in the cardiac donor pool with standard criteria and the extreme discrepancy between the high demand and availability of donor hearts makes it necessary to consider hearts from donors with extended criteria, especially for heart transplant candidates with the need for urgent HTx. Acceptable early and long-term survival was obtained after HTx from donors with extended criteria, such as older age, left ventricular hypertrophy, prolonged ischemic time, high inotropic and vasopressor support, prolonged cardiopulmonary resuscitation, potentially correctable valvular disease, or coronary atherosclerosis.

One of the common reasons for the declining of heart offers is pathological echocardiographic findings, such as abnormal LV systolic function (low LVEF), ranging from 20% to 45% of all potential brain death donors. In terms of moderate (LVEF 30%–50%) or severe (LVEF < 30%), left ventricular systolic function dysfunction can be observed in 25% and 14% of potential brain death donors, whereas impaired LVEF is more frequently detected in young or female potential donors. Moreover, abnormal systolic LV function (LVEF less than 40%–50%) is considered to be the most “marginal” of extended heart donor criteria due to unpredictability of initial pump function of cardiac allograft, predictable high risk of severe PGD, higher need for post-transplant MCS, and poor survival outcomes.

Lack of experience and scientific knowledge with concerns in terms of HTx from donors with low LVEF does not allow justification of the use of donor hearts with abnormal LV systolic function to overcome organ shortage.

Impairment of LV systolic function is the result of myocardial injury following brain death or other unknown pre-existing reasons. Brain death is also accompanied by functional (potentially reversible) or histologic (irreversible myocardial necrosis) myocardial injury and may lead to various grades of PGD. Experimental and clinical studies suggest that severe brain injury, such as subarachnoid hemorrhage, is associated with LV motion abnormalities and global LV systolic dysfunction. This is controversially discussed and still not completely understood.

Unfortunately, there is no standard approach on the evaluation of donors for the reversibility of LV dysfunction. This is a real conundrum. Most US centers request coronary angiography in donors with LV dysfunction, particularly if the donor is >40 years of age because this would help to rule out ischemic heart disease caused by LV dysfunction. Other centers, such as in Italy, perform dobutamine stress echocardiography for assessment of myocardial viability in donors with LV dysfunction. We performed coronary angiography in all donors.

It is known that cardiomyopathy of brain death donors cardiomyopathy reveals similar pathogenesis as LV systolic dysfunction after

### Table 3: Echocardiographic evaluation of heart transplant donors

| Echocardiographic parameters | Before diagnosis of brain death | Before procurement |
|-----------------------------|---------------------------------|-------------------|
| Ascending aorta, cm         | 3.1 ± 0.7                       | 3.1 ± 0.5         |
| Left atrium, cm             | 4.2 ± 0.6                       | 4.1 ± 0.8         |
| Right ventricle, cm         | 2.5 ± 0.3                       | 2.4 ± 0.4         |
| Interventricular septum, cm | 1.23 ± 0.29                     | 1.23 ± 0.31       |
| Interventricular septum ≥1.5 cm | 5 (18.5%)                    | 5 (18.5%)         |
| Posterior wall, cm          | 1.19 ± 0.27                     | 1.20 ± 0.27       |
| LVEDD, cm                   | 5.08 ± 0.42                     | 4.93 ± 0.37       |
| LVEDV, ml                   | 120.9 ± 28.3                    | 115.2 ± 25.0      |
| Stroke volume, ml           | 40.1 ± 16.7                     | 43.1 ± 18.4       |
| LVEF, %                     | 33.1 ± 5.6                      | 37.5 ± 6.3        |
| 30–40                       | 24 (88.8%)                      | 26 (96.3%)        |
| 20–29                       | 3 (11.2%)                       | 1 (3.7%)          |
| Aortic regurgitation degree | 0.6 ± 0.4                       | 0.6 ± 0.3         |
| Mitral regurgitation degree | 1.4 ± 0.5                       | 1.3 ± 0.6         |
| Tricuspid regurgitation degree | 1.1 ± 0.2                 | 1.2 ± 0.2         |

**LV regional wall motion abnormality**

|                      | Before diagnosis of brain death | Before procurement |
|----------------------|---------------------------------|-------------------|
| Diffuse hypokinesia  | 12 (44.4%)                      | 9 (33.8%)         |
| Basal hypokinesia with apex (Takotsubo syndrome) | 13 (48.1%) | 16 (59.3%) |
| Hypokinesia of the apex | 1 (3.7%)                        | 1 (3.7%)          |
| Hypokinesis of the posterior wall | 1 (3.7%) | 1 (3.7%) |
| LVH ≥1.5 cm          | 5 (18.5%)                       | 5 (18.5%)         |

Note: Variables are presented as means±SD or number of patients and percentages; LVEDD, left ventricle end-diastolic diameter; LVEDV, left ventricle end-diastolic volume; LVEF, left ventricle ejection fraction.
underlying mechanisms of regional wall motion abnormalities may include combination of functional (potentially reversible) and/or morphological (irreversible) patterns of ventricular dysfunction: excessive local release of norepinephrine from sympathetic nerve terminals, intra-cellular edema, myocyte calcium overload, band myocardial necrosis, mitochondrial injury, and myocyte death. Pre-existing myocardial pathology with chronic regional wall motion abnormalities should also not be underestimated. Such conditions may also cause pre-existing abnormal LV myocardial contractility and even more deteriorating LVEF during brain death. Currently, there are no clear diagnostic criteria allowing for distinguishing between potentially reversible and irreversible LV dysfunction conditions during brain death. Causes of abnormal LV systolic function cannot always be identified during donor procurement resulting in the impossibility of making the correct decision at heart donation selection process.

The lack of precise criteria for the irreversibility of myocardial injury, the discrepancy between the severity of functional disorders, and histological findings of ischemic myocardial damage against brain death indicate that the refusal of organs for HTx from donors with impaired systolic function and/or local LV contractility is often a real problem. Studies have shown a rapid recovery of the pre-existing dysfunctional donor hearts to normal LVEF in the early post-transplant periods. On the one hand, hemodynamic parameters display patient’s constitution, and on the other hand, the echocardiographic assessment is important especially in patients after heart transplantation. Only the synopsis of all available information sums up to a sensible diagnosis.

Some successfully transplanted patients were stabilized with low-level ECMO support for 2 days after surgery. The strategy of low-level ECMO support of patients after heart transplantation might lead to further hemodynamic stabilization. However, this strategy has not already been scientifically recommended. In these patients, we individually decided to support these patients with low-level ECMO use. This strategy might be validated by future studies.

According to some studies, low LVEF of the donor’s heart does not directly affect results of HTx. Optimization and preconditioning process of a potential donor with brain death may significantly contribute to the improvement of LV systolic function as well as global and local contractility of its myocardium. The real lessons learned in this study are that hemodynamic parameters might be more important that ECHO parameters, and that good quality donors despite a poor echo can be safely used if given some support and allow time to recover.

A potential reverse remodeling pattern of brain death cardiac donors with LV dysfunction may lead to the improvement in LV systolic function over time after HTx. Average duration of dysfunctional donor heart recovery was described to be 1–2 weeks. Although clinical studies demonstrated that systolic LV dysfunction had transient patterns in brain death cardiac donors, this factor represents one of the reasons for contraindication of heart donation in most cases. Evidence of potential recovery based on mechanisms described above in a relatively short period after transplantation should be the reason for revising the practice of declining donor hearts with reduced LV systolic function with the view to increasing the numbers of HTx from traditionally unusable donor hearts. Recently, European and US transplant centers started liberalizing criteria for heart transplantation due to extremely limited and further declining numbers of usable donor hearts.

In the last few years, our transplant center increased the number of annual HTx from 0–14 (5.9 ± 3.0) per year (1995–2007) to 15–194 (88.3 ± 47.0) per year (2008–2018). In 2016, 2017, and 2018, annual rates of HTx were 132, 161, and 194, respectively. Such a rapid increase in annual rate of HTx was associated with the extending and liberalization of heart donation criteria and increasing the rate of HTx in recipients with temporary MCS (vaECMO). Annual rate of HTx from donors with extending criteria increased from 23.1% (2011) to 74.7% (2018). At the same time, number of HTx in recipients with pretransplant vaECMO increased from 5.1% (2011) to 35.6% (2018). This approach allowed us to improve HTx availability at the same time reducing mortality of recipients who would die due to long waiting time to acceptable early and long-term post-transplant survival rates.

Our study demonstrated that HTx from donors with low LVEF (less than 40%) may be a realistic approach to improve heart availability for transplantation. In our heart transplant center, the proportion of such HTx was about 5.5% in the last three years. The present study showed that in most cases (85.2%), recipients with reduced LV systolic function recovered to the level of LVEF >60% shortly after HTx (usually within the first 3 days). The rate of severe early cardiac graft dysfunction requiring post-transplant MCS was 14.8% which is comparable with early results of HTx from donors without systolic LV dysfunction.

Taking into account the possible high risk of severe early cardiac allograft dysfunction, in most cases HTx from donors with LVEF <40% was performed in recipients requiring an urgent heart transplantation (92.6%) and for this reason in recipients needing peripheral vaECMO (66.7%). In this clinical scenario, peripheral vaECMO has proven to be a reliable approach for providing temporary biventricular MCS used as a single device both before and after HTx. This approach allowed for safe and sufficient hemodynamic support in cases of severe early cardiac allograft dysfunction for the period required for recovery of dysfunctional donor heart.

### 4.1 Limitations

One of the limitations of the paper is the retrospective character of the data analysis. Moreover, a selection bias could be seen in the fact that ischemic times were short and that hearts with EF<40% with long ischemic times were rejected. Due to experienced cardiac surgeons, surgery times respectively ischemic times have been minimized. However, we do not regard this as selection bias. Further, our cohort is not generalizable to other donor and recipient populations.
Our cohort consisted of a very high use of pretransplant vaECMO which was routinely postoperatively continued.

5 | CONCLUSION

Due to extreme shortage of donor hearts with acceptable criteria, the use of dysfunctional donor hearts with impaired LV systolic function may be a realistic approach for expanding the donor pool and improving HTx availability. However, the absence of clear predictors of post-transplant reversibility of dysfunctional donor hearts, organs from such donors, should only be used for recipient cohorts requiring an urgent HTx, particularly for those with pretransplant MCS allowing for hemodynamic support both before HTx and during the early vulnerable post-transplant period to overcome temporary severe cardiac allograft dysfunction.

ACKNOWLEDGEMENTS
Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTERESTS
The authors have declared no conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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### TABLE 4 Echocardiographic assessment of donor heart cohort before and from recipients after HTx without early cardiac allograft dysfunction (n = 23)

| Parameters                  | Timing of assessment | Before harvesting | 1st day | 3rd day | Hospital discharge |
|-----------------------------|----------------------|-------------------|---------|---------|--------------------|
| RV, cm                      |                      | 2.4 ± 0.4         | 2.7 ± 0.3 | 2.6 ± 0.2 | 2.6 ± 0.1          |
| IVS, cm                     |                      | 1.2 ± 0.2         | 1.3 ± 0.2 | 1.3 ± 0.2 | 1.2 ± 0.3          |
| PW, cm                      |                      | 1.2 ± 0.3         | 1.3 ± 0.2 | 1.2 ± 0.2 | 1.2 ± 0.1          |
| LVEDD, cm                   |                      | 5.2 ± 0.4         | 4.7 ± 0.3 | 4.7 ± 0.2 | 4.5 ± 0.2***       |
| LVEDS, cm                   |                      | 4.1 ± 0.3         | 3.4 ± 0.2 | 3.1 ± 0.3 | 2.6 ± 0.2***       |
| LVEDV, ml                   |                      | 131 ± 33          | 104 ± 12* | 102 ± 10* | 93 ± 6***          |
| LVESV, ml                   |                      | 85 ± 29           | 48 ± 11*  | 36 ± 8*   | 27 ± 5*            |
| SV, mL                      |                      | 46 ± 12           | 57 ± 12*  | 66 ± 4*   | 66 ± 2*            |
| LVEF, %                     |                      | 35 ± 4            | 55 ± 7*   | 65 ± 5*   | 71 ± 3***          |
| Mitral valve regurgitation  |                      | 1.6 ± 0.5         | 1.1 ± 0.6* | 1.2 ± 0.6* | 1.2 ± 0.5*         |
| degree                      |                      |                   |         |         |                   |
| Tricuspid valve regurgitation| degree              | 1.3 ± 0.4         | 2.2 ± 0.8* | 2.1 ± 0.6* | 1.9 ± 0.8*         |

Note: Variables are presented as means ± SD or number of patients and percentages. Abbreviations: IVS, interventricular septum; LVEDD, left ventricle end-diastolic diameter; LVEDV, left ventricle end-diastolic volume; LVEF, left ventricle ejection fraction; LVESD, left ventricle end-systolic diameter; LVESV, left ventricle end-systolic volume; PW, posterior wall; RV, right ventricle; SV, stroke volume.

*P < .05 compared to pre-harvesting.; **P < .05 compared to 1st day after heart transplantation.
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How to cite this article: Poptsov V, Khututszy V, Skokova A, et al. Heart transplantation from donors with left ventricular ejection fraction under forty percent. Clin Transplant. 2021;35:e14341. https://doi.org/10.1111/ctr.14341