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# HEART TRANSPLANTATION IN PATIENTS UNDERGOING EXTRACORPOREAL CARDIOPULMONARY RESUSCITATION IN IN-HOSPITAL CARDIAC ARREST

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**Objective:** to analyze heart transplant (HT) outcomes in patients who suffered cardiac arrest requiring extracorporeal cardiopulmonary resuscitation (ECPR) by peripheral veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Materials and methods. The study included 41 patients (14 (34.1%) women and 27 (65.9%) men, aged  $42.6 \pm 16.8$  (40.0 [30.5; 54.0]) years with in-hospital cardiac arrest. The causes of cardiac arrest were acute decompensated heart failure (n = 19; 46.3%), irreversible graft dysfunction (n = 9; 22.0%), postcardiotomy acute heart failure (n = 5; 12.2%), acute myocardial infarction (n = 4; 9.8%), and acute graft rejection (n = 4; 9.8%). Results. Twenty-seven (65.9%) patients had cardiac arrest in the intensive care unit (ICU) and 14 (34.1%) outside ICU. The interval between femoral artery puncture and ECPR initiation was 4-17 ( $9 \pm 5$ ) minutes, while that between cardiopulmonary resuscitation (CPR) initiation and peripheral VA-ECMO was  $26 \pm 9$  minutes. Atonic seizure developed in 11 (26.8%) of 41 patients while receiving VA-ECMO. Of the 41 patients, 30 (73.2%) had irreversible brain damage. Four (9.8%) patients were discharged from the hospital without neurological or multiple organ dysfunction. In 26 (63.4%) patients (10 (38.5%) women and 16 (61.5%) men) aged 14 to 63 ( $40.7 \pm 15.8$ ) years, ECPR and subsequent treatment resulted in survival to HT while receiving VA-ECMO (duration 1-11 (4.0 [1.5; 5.0]) days). The age of the heart donor (6 (23.1%) women and 20 (76.9%) men) was 44.0 ± 9.9 years, the cumulative Eurotransplant Heart Donor Score was  $16.9 \pm 2.7$ , the Donor Risk Index was  $6.3 \pm 1.5$ , and the estimated incidence of severe primary graft dysfunction (RADIAL scale) was  $15.4 \pm 3.7\%$ . Graft ischemia lasted for  $188 \pm 72$  (170.0 [141.25; 185.0]) minutes. Five (19.2%) recipients developed severe dysfunction, which required continuation of peripheral VA-ECMO in the postperfusion period. The cause of death (n = 4; 15.3%) in the early post-HT period was irreversible multiple organ dysfunction. Conclusion. In-hospital survival after emergency HT in recipients who underwent ECPR before transplantation is 84.7%.

*Keywords: cardiac arrest, peripheral veno-arterial extracorporeal membrane oxygenation, heart transplantation.* 

### INTRODUCTION

Patients waiting for a heart transplant (HT) are at higher risk of cardiac arrest (CA), both inside and outside of hospitals, because of the advanced stages of heart failure and the underlying irreversible heart disease they have [1]. Extracorporeal cardiopulmonary resuscitation (ECPR), which uses veno-arterial extracorporeal membrane oxygenation (VA-ECMO) after conventional cardiopulmonary resuscitation (CPR) fails, using manual or mechanical chest compressions, is a growing life-saving intervention for both out-of-hospital and in-hospital CA (IHCA) [2, 3]. ECPR has demonstrated better survival rates in patients who have suffered CA compared to standard CPR [4].

The **objective** of this study was to evaluate HT outcomes in patients who experienced CA necessitating an ECPR.

### MATERIALS AND METHODS

The study included 41 patients (14 women [34.1%] and 27 men [65.9%]) with a mean age of  $42.6 \pm 16.8$  years (median 40.0 [IQR: 30.5-54.0] years), who had IHCA requiring ECPR between 2011 and 2023. ECPR was initiated due to no spontaneous recovery of heart rhythm and effective hemodynamics despite conventional CPR. These cases represented 3.4% (n = 41/1217) of all VA-ECMO initiations at our institution during the study period.

Sudden CA occurred in the context of decompensated chronic heart failure (CHF) in 19 patients (46.3%), irreversible cardiac allograft dysfunction in 9 (22.0%), postcardiotomy cardiogenic shock in 5 (12.2%), acute HF due to myocardial infarction in 4 (9.8%), and acute cardiac graft rejection in 4 patients (9.8%).

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Among the 41 patients included in the study, the underlying cardiac pathology was dilated cardiomyopathy (DCM) in 18 cases (43.9%), coronary heart disease (CHD) in 10 (24.4%), irreversible cardiac graft dysfunction in 9 (22.0%), and heart graft rejection in 4 patients (9.8%). Fourteen patients (34.1%) were on the heart transplant waiting list (HTWL) and had been admitted for pre-transplant management. An additional 9 patients (22.0%) were hospitalized for assessment within the potential HT candidate program.

All patients initially underwent conventional CPR in accordance with established clinical protocols, using either manual or mechanical chest compressions [5, 6]. ECPR was initiated after 20 minutes of unsuccessful conventional CPR, defined by failure to restore electrical cardiac activity, adequate myocardial contraction, or systemic hemodynamics. The decision to proceed with ECPR was made in line with current international guidelines and protocols [7].

During continued manual or mechanical chest compressions, percutaneous puncture and catheterization of the common femoral artery and vein (on one or both sides) were performed using 14–16 G single-lumen intravascular catheters. In 21 patients with pre-existing femoral artery catheterization for invasive blood pressure monitoring, this access was used to expedite placement of the femoral arterial ECMO cannula. Femoral access was guided either by anatomical landmarks or ultrasound using a portable device.

Following successful vascular access, 5,000 units of unfractionated heparin were administered intravenously for systemic anticoagulation. An Amplatz Super Stiff J-Tip guidewire (0.89 mm in diameter, 260 cm in length), or its equivalent, was introduced through the intravascular catheter placed in the femoral vein. After stepwise dilation of the percutaneous track, the femoral venous ECMO cannula was inserted to a depth of 35–45 cm, depending on the patient's anthropometric characteristics. The arterial cannula was inserted using the same technique. Both cannulas were then connected to the ECMO circuit, and VA-ECMO was initiated with the following initial settings: volumetric blood flow rate of 2.5–4.0 L/ min, gas flow rate of 4.0–8.0 L/min, and FiO<sub>2</sub> of 1.0.

Immediately after ECMO initiation, targeted temperature management was implemented for neuroprotection and prevention of irreversible cerebral injury. This included cooling the patient to 35.0–35.5 °C via the ECMO heat exchanger [8], elevating the head of the resuscitation bed to 35–45°, applying ice packs to the head, and administering intravenous mannitol and hypertonic sodium solution. These measures aimed to achieve serum osmolarity of 310 mOsm/L and serum sodium concentration of 145–155 mmol/L [9].

Hearts from brain-dead donors were used for HT. The presence and number of expanded criteria donation factors were documented according to widely accepted definitions for standard and expanded heart donation. Donor heart marginality was quantitatively assessed using the Eurotransplant Heart Donor Score, the Donor Risk Index, and the RADIAL score. The probability of developing severe primary graft dysfunction was estimated using the RADIAL score.

Quantitative data are presented as mean  $\pm$  standard deviation (M  $\pm \sigma$ ) and as median with interquartile range (Me [Q1; Q3]).

### RESULTS

In all cases, CA occurred in the presence of witnesses (medical staff or other patients). Specifically, 27 patients (65.9%) experienced CA in the intensive care unit (ICU), 12 (29.3%) in the ward, and 2 (4.9%) in the X-ray surgical operating room. The time of CA occurrence was distributed as follows: 9:00 AM to 6:00 PM in 22 patients (53.7%), 6:00 PM to 12:00 AM in 11 patients (26.8%), and 12:00 AM to 9:00 AM in 8 patients (19.5%).

The initial cardiac rhythm recorded upon connection to the ECG monitor was ventricular fibrillation in 26 patients (63.4%), ventricular flutter in 4 (9.8%), and bradyarrhythmia or asystole in 11 (26.8%).

In all cases, ECPR was preceded by comprehensive CPR, which included manual chest compressions in 31 patients (75.6%) and/or automatic mechanical compressions in 10 patients (24.4%). In 8 patients (38.1%) with asystole or severe bradycardia, endocardial pacing electrodes were placed.

In 32 patients (78.0%), CPR was initiated or continued in the ICU, where subsequent VA-ECMO preparation and connection were also carried out. Among the 12 patients who experienced CA in the ward, 7 were transferred to the cardiac surgical operating room for ongoing CPR. In 8 cases from this group, to avoid interruption of CPR and minimize time to VA-ECMO initiation, femoral artery puncture and cannulation were performed directly on the transport trolley wheelchair.

The interval between CPR onset and the initiation of femoral artery puncture for subsequent cannulation ranged from 14 to 35 minutes (mean  $23 \pm 8$  minutes) in patients (n = 27) who experienced CA in the ward, and from 4 to 20 minutes (mean  $11 \pm 7$  minutes) in patients (n = 14) who experienced CA in the ICU or X-ray surgical operating room.

In all cases, peripheral VA-ECMO was initiated via cannulation of the femoral vessels, either unilaterally (n = 34; 82.9%) or bilaterally (n = 7; 17.1%). Cannula sizes used for arterial access ranged from 15 F to 19 F, while venous cannulation utilized 21 F to 28 F cannulas.

Initial VA-ECMO settings included a pump speed of 7167  $\pm$  320 rpm, an extracorporeal blood flow rate of 3.91  $\pm$  0.27 L/min (or 2.14  $\pm$  0.19 L/min/m<sup>2</sup>), gas flow of 5.7  $\pm$  0.9 L/min, and a fraction of inspired oxygen (FiO<sub>2</sub>) of 1.0.

The mean time from CPR onset to VA-ECMO initiation was  $26 \pm 9$  minutes. The time from the start of femoral vascular puncture to the beginning of ECPR ranged from 4 to 17 minutes, with a mean of  $9 \pm 5$  minutes.

The interval between CPR initiation and VA-ECMO connection was significantly shorter in patients who experienced CA in the ICU compared to those in the ward  $(22 \pm 8 \text{ minutes } vs. 38 \pm 13 \text{ minutes, respectively; p} = 0.001).$ 

In 100% of cases, restoration of cardiac rhythm and mechanical heart activity – confirmed by the appearance of an arterial pressure waveform and visible ventricular contractions on transthoracic or transesophageal echocardiography – was achieved within 3 to 20 minutes after VA-ECMO initiation. Ten patients (24.4%) had a spontaneous return of rhythm, while the remaining 30 patients (75.6%) required repeated antiarrhythmic therapy or electrical defibrillation. Indirect cardiac massage was maintained until both rhythm restoration and mechanical ventricular activity were confirmed, ensuring continued upper body perfusion and decompression of the cardiac chambers.

Following successful peripheral VA-ECMO initiation and cessation of active resuscitation, the superficial femoral artery was catheterized in all patients to prevent lower limb ischemia from . This was achieved via percutaneous puncture in 33 cases (80.5%) and open surgical access in 8 cases (19.5%).

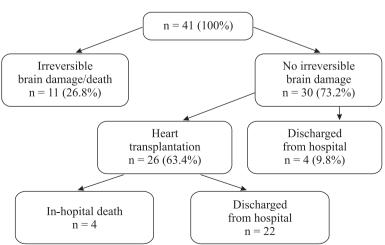
In 6 patients (14.6%), progressive deterioration of left ventricular systolic function and clinical/radiological signs of pulmonary edema necessitated percutaneous left atrial drainage. This was performed to relieve volume overload in the left heart chambers using an additional venous drainage cannula (18–21 F), inserted through the interatrial septum via transfemoral venous access.

Eleven (26.8%) out of 41 patients receiving VA-EC-MO had irreversible brain damage with the development of atonic coma and subsequent death (Fig.). The other 30 patients (73.2%) did not exhibit signs of irreversible neurological injury. In 4 patients (9.8%) - 3 with cardiac graft rejection and 1 with postcardiotomy acute heart failure – VA-ECMO was successfully discontinued on days 3 to 6. These patients were discharged from the hospital without clinically significant neurological deficits or manifestations of multiple organ dysfunction.

In 26 patients (63.4%) – including 16 males (61.5%) and 10 females (38.5%), aged 14 to 63 years (mean age 40.7  $\pm$  15.8 years) – ECPR followed by intensive care resulted in survival to HT while on VA-ECMO support. The underlying pathology in this subgroup (n = 26) included DCM (n = 12; 46.2%), CHD (n = 7; 26.9%), and irreversible cardiac graft dysfunction (n = 7; 26.9%).

All patients were successfully weaned to spontaneous breathing while continuing VA-ECMO support, with a maintained extracorporeal blood flow of  $3.1 \pm 0.5$  L/min (or  $1.78 \pm 0.46$  L/min/m<sup>2</sup>). In addition to extracorporeal circulatory support, all patients (n = 26) received sympathomimetic cardiotonic or vasopressor agents to support systemic hemodynamics and residual left ventricular function. Specifically, dopamine was administered in 23 patients (88.5%) at a mean dose of  $5.7 \pm 2.1$  µg/kg/min (median 6.0 [4.0; 7.0] µg/kg/min), adrenaline in 10 patients (38.5%) at 22.0 ± 12.9 ng/kg/min (median 17.5 [10.0; 37.75] ng/kg/min), dobutamine in 5 patients (19.2%) at 4.0 ± 2.7 µg/kg/min (median 3.0 [2.5; 4.0] µg/kg/min), and noradrenaline in 2 patients at 50 and 80 ng/kg/min, respectively.

The absence of impaired consciousness, severe organ dysfunction, electrolyte or metabolic impairments, and high pulmonary hypertension at the time of donor heart availability served as key criteria for proceeding with HT (Table 1). The duration of VA-ECMO support prior to HT in these patients ranged from 1 to 11 days, with a mean of  $4.1 \pm 2.9$  days and a median of 4.0 [1.5; 5.0] days.



#### Extracorporeal cardiopulmonary resuscitation

Fig. Study flow diagram

Table 1

#### Data (M $\pm \sigma$ and Me [Q1; Q3]) from preoperative examination of heart recipients who underwent extracorporeal cardiopulmonary resuscitation at the pre-transplant stage (n = 26)

Parameter	Value	
Age, sex and anthropometric indicators		
Age, years	$40.7 \pm 15.8 \; (39.0 \; [30.0; 53.0])$	
Female, n/%	10 (38.5%)	
Height, cm	$171.6 \pm 10.7 \ (170.0 \ [166.6; 176.0])$	
Weight, kg	73.3 ± 15.9 (77.5 [63.5; 84.25])	
Body surface area, $m^2$	1.87 ± 0.24 (1.90 [1.70; 2.04])	
BMI, kg/m <sup>2</sup>	24.6 ± 4.0 (24.80 [22.87; 27.04])	
Invasive central hemodynamic and echocardiographic study		
mAP, mmHg	$66.8 \pm 12.8 (74.5 [66.5; 80.75])$	
HR per min	$107.7 \pm 25.6 (107.5 [86.5; 130.25])$	
RAP, mmHg	1000000000000000000000000000000000000	
mPAP, mmHg	$28.5 \pm 10.3 (26.0 (20.0; 27.75))$	
PCWP, mmHg	$20.8 \pm 9.9 (20.0 [12.5; 27.75])$	
$CI, 1/min/m^2$	$\frac{26.8 \pm 9.9 (20.6 [12.3, 27.75])}{1.57 \pm 0.53 (1.50 [1.30; 1.70])}$	
TPG, mmHg	$\frac{1.37 \pm 0.33(1.30[1.30, 1.70])}{7.7 \pm 3.0(8.0[5.0; 10.0])}$	
PAP, Woods units $2.99 \pm 1.94$ (2.70 [1.70; 3.30])		
Laboratory examination		
Hb, g/L	$102.6 \pm 19.1 \ (95.0 \ [90.5; \ 118.5])$	
Red blood cell, 10 <sup>9</sup> /L	3.6 ± 0.7 (3.4 [3.18; 3.76])	
Platelets, 10 <sup>9</sup> /L	$139.4 \pm 103.0 \ (102.0 \ [79.25; 191.25])$	
White blood cells, 10 <sup>9</sup> /L	11.7 ± 6.1 (10.1 [7.08; 15.68])	
Albumin, g/L	36.1 ± 6.8 (35.0 [32.5; 40.0])	
Total protein, g/L	$62.4 \pm 10.7 (35.0 [32.5; 40.0])$	
Urea, mmol/L	$11.4 \pm 5.8 \ (10.1 \ [7.43; 14.4])$	
Creatinine, µmol/L	$111.1 \pm 49.1 \ (110.0 \ [85.58; 131.80])$	
Total bilirubin,	507 + 426 (224 [1749.9007])	
µmol/L	50.7 ± 43.6 (33.4 [17.48; 80.97])	
ALT, U/L	$66.9 \pm 122.4 \ (36.6 \ [26.0; 48.28])$	
AST, U/L	$82.0 \pm 123.8 \; (36.0 \; [33.0; 38.0])$	
INR	$1.47 \pm 0.17 (1.40 [1.34; 1.58])$	
pH <sub>B</sub>	$7.43 \pm 0.09$ (7.40 [7.40; 7.50])	
BE <sub>B</sub> , mmol/L	$1.6 \pm 3.7 (2.6 [-0.9; 3.4])$	
Р <sub>в</sub> О <sub>2</sub> , мм рт. ст.	33.6 ± 6.6 (33.8 [28.1; 37.5])	
$S_{B}O_{2}, \%$	$60.9 \pm 15.8 (58.7 [46.5; 71.5])$	
Blood lactate,		
mmol/L	$2.1 \pm 1.7 (1.4 [1.0; 2.4])$	
Blood Na <sup>+</sup> , mmol/L	138.3 ± 3.1 (138.0 [136.0; 141.0)]	

*Note:* BMI, body mass index; mAP, mean arterial pressure; HR, heart rate, RAP, right atrial pressure; mPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index; TPG, Transpulmonary pressure gradient; PAP, pulmonary artery pressure; ALT, alanine transaminase; AST, aspartate transaminase; INR, international normalized ratio. 45.0 [36.0; 52.0]) and a mean body weight of 86.8  $\pm$  14.9 kg (median 85.0 [75.0; 100.0] kg). The graft-to-recipient weight ratio was  $1.20 \pm 0.54$  (median 1.10 [0.90; 1.30]). Brain death resulted from traumatic brain injury in 9 cases (34.6%) and non-traumatic causes in 17 cases (65.4%). Two donors (7.7%) experienced cardiac arrest and underwent CPR lasting 6 and 11 minutes, respectively. Mechanical ventilation duration averaged  $2.4 \pm 1.7$  days (median 2.0 [1.0; 3.0] days).

During donor management, sympathomimetic support was required in 23 cases (88.5%) with norepinephrine administered at  $621 \pm 388$  ng/kg/min (median 550.0 [300.0; 900.0] ng/kg/min), and dopamine in 8 cases (30.8%). Echocardiographic and laboratory findings for heart donors (n = 26) are summarized in Table 2.

Expanded criteria for heart donation were identified in 16 donors (61.5%), with an average of  $1.4 \pm 0.4$  expanded criteria factors per donor. The mean Eurotransplant Heart Donor Score was  $16.9 \pm 2.7$  (median 16.5 [15.5; 18.0]), the Donor Risk Index was  $6.3 \pm 1.5$  (median 6.0 [5.5; 7.75]), and the predicted incidence of severe primary graft dysfunction based on the RADIAL score was  $15.4 \pm 3.7\%$  (median 16.25 [12.50; 18.50]%).

Table 2

#### Data (M $\pm \sigma$ and median with interquartile intervals) obtained from heart donor examination at transplantation to recipients who underwent ECPR at the pre-transplant stage (n = 26)

Parameter	Value	
Echocardiographic study parameters		
Aorta, cm	3.1 ± 0.4 (3.0 [2.8; 3.5])	
Left atrium, cm	$3.9 \pm 10.7 \ (170.0 \ [166.6; 176.0])$	
Right ventricle, cm	$2.5 \pm 0.2 \ (2.50 \ [2.40; 84.25])$	
IVS, cm	$1.15 \pm 0.16 \ (1.10 \ [1.00; \ 1.20])$	
LVEDV, ml	96.6 ± 32.1 (88.0 [80.0; 102.0])	
SV, ml	$60.5 \pm 20.2 \ (58.0 \ [63.0; \ 68.0])$	
LVEF, %	$64.4 \pm 7.0 \ (65.0 \ [63.0; 68.0])$	
Mitral valve	1.0 ± 0.3 (1.0 [1.0; 1.0])	
(regurgitation), degree		
Tricuspid valve	$0.94 \pm 0.17 (1.0 [1.0; 1.0])$	
(regurgitation), degree	· - · - ·	
Laboratory examination		
Hb, g/L	$102.6 \pm 19.1 \ (95.0 \ [90.5; \ 118.5])$	
White blood cells, 10 <sup>9</sup> /L	$12.4 \pm 3.2 \ (12.5 \ [11.0; \ 13.75])$	
Total protein, g/L	$65.6 \pm 7.5 \ (67.0 \ [60.0; 72.5])$	
Urea, mmol/L	$6.8 \pm 2.9 \ (5.20 \ [3.50; 7.40])$	
Creatinine, µmol/L	$97.8 \pm 23.9$ (87.5 [72.25; 98.5])	
Total bilirubin, µmol/L	$50.7 \pm 43.6 \ (33.4 \ [17.48; \ 80.97])$	
Blood glucose, mmol/L	$10.8 \pm 4.7 \ (8.9 \ [7.5; 11.5])$	
Troponin I, pg/mL	$0.19 \pm 0.08 \; (0.10 \; [0.02; \; 0.45])$	
pН <sub>в</sub>	$7.44 \pm 0.16$ (7.40 [7.30; 7.50])	
BE <sub>B</sub> , mmol/L	$2.2 \pm 1.5 \ (2.3 \ [0.55; 3.25])$	

*Note:* IVS, interventricular septum; LVEDV, left ventricular end-diastolic volume; VA, stroke volume; LVEF, left ventricular ejection fraction; Hb, hemoglobin.

The average duration of anesthesia was  $463 \pm 159$  minutes (median  $435.0 \ [407.5-482.5]$  minutes), and the surgical time averaged  $307 \pm 64$  minutes (median  $320.0 \ [262.5-358.5]$  minutes). Mean heart graft ischemia time was  $188 \pm 72$  minutes (median  $170.0 \ [141.25-185.0]$  minutes), while the duration of cardiopulmonary bypass averaged  $119 \pm 39$  minutes (median  $109.0 \ [96.25-125.0]$  minutes).

Maximum doses of sympathomimetic cardiotonic agents administered during surgery included dopamine hydrochloride in all patients (n = 26, 100%) at  $6.2 \pm 2.0 \text{ mcg/kg/min}$  (median 6.0 [6.0–7.5]), adrenaline hydrochloride in 25 patients (96.2%) at  $42.7 \pm 18.2$  (median 40.0 [40.0; 60.0]) ng/kg/min, and dobutamine hydrochloride in 5 patients (19.2%) at  $4.0 \pm 1.4 \text{ mcg/kg/min}$  (median 4.0 [4.0–4.0]).

In the preperfusion period, the VA-ECMO centrifuge pump speed was  $6778 \pm 358$  rpm (median 6600 [6600-6800]), and the extracorporeal blood flow rate was  $2.90 \pm 0.44$  L/min (median 2.80 [2.60-3.23] L/min). At the end of surgery, these parameters were  $5274 \pm 711$  rpm (median 4950 [4725-5975]) and  $1.65 \pm 0.75$  L/min (median 1.50 [1.13-2.23] L/min), respectively.

Early cardiac graft dysfunction with hemodynamic compromise was observed in 5 recipients (19.2%), necessitating continued VA-ECMO in the postperfusion period at blood flow rates exceeding 2.0 L/min (range 2.3-3.7 L/min; mean  $3.2 \pm 0.4$  L/min).

Perioperative blood loss averaged  $3499 \pm 3679$  mL (median 2000 [1550–4400] mL), requiring transfusion of red blood cell mass (1735.0 ± 1173.2 mL; median 1240.0 [1052.25–1798.25]), fresh frozen plasma (2413.2 ± 2012.9 mL; median 1820.0 [1066.25–2495.0]), and platelet mass (276.4 ± 135.9 mL; median 240.0 [157.5–397.5]).

Postoperative mechanical ventilation lasted for  $12.6 \pm 6.9$  hours (median 12.0 [9.5–16.5]). In patients without early cardiac graft dysfunction (n = 21), VA-ECMO support continued postoperatively for  $1.8 \pm 0.4$  days (median 1.8 [1.6–1.9]), while in patients with early graft dysfunction (n = 5), support lasted 4–7 days (mean 5.7  $\pm$  0.7 days).

Seven patients (26.9%) required postoperative renal replacement therapy via continuous veno-venous hemofiltration. Four recipients (15.3%) died in hospital due to multiple organ failure, which developed in two cases with and in two cases without early cardiac graft dysfunction.

#### DISCUSSION

In recent years, the number of patients on HTWL has increased significantly – by more than 25% – leading to longer waiting times and increased risk of severe adverse cardiovascular events. Both ambulatory and hospitalized patients awaiting HT face an elevated risk of sudden cardiac death due to life-threatening arrhythmias, such as ventricular tachycardia, ventricular fibrillation, and bradyarrhythmias, particularly in the absence of an implantable cardioverter-defibrillator (ICD) [10]. Notably, the underlying etiology – whether dilated or ischemic cardiomyopathy – does not significantly influence the incidence of sudden death in this population.

Sudden CA accounts for approximately 40–70% of all fatalities among patients awaiting HT [10]. Although ICD use can reduce mortality during the waiting period by 13% or more, the overall death rate from sudden CA in this group remains high [11]. One contributing factor is the limited indication for ICD implantation in patients with CHF classified as NYHA functional class IV, given the higher proportion of non-sudden cardiac deaths in this subset [12]. According to international guidelines, ICD implantation is recommended for potential HT recipients managed on an outpatient basis (class IIa, level of evidence C) [13].

ECPR enables not only the rapid restoration of systemic circulation and correction of blood gas abnormalities but also provides a critical window for identifying the underlying causes of sudden CA and implementing targeted therapeutic interventions [2]. The adoption of ECPR has been associated with improved early and long-term survival rates and better neurological outcomes compared to conventional CPR using manual or automated chest compressions [14].

However, the efficacy of ECPR varies considerably across studies, with reported rates of favorable neurological outcomes and survival ranging from 0.33% to 70.4% and 0.24% to 43.1%, respectively [3]. According to the International Extracorporeal Life Support Organization (ELSO) registry, a total of 28,007 ECPR cases involving adults, children, and neonates have been recorded, accounting for 12.6% of all documented extracorporeal life support cases (n = 222,383) [15]. Reported survival rates following ECPR were 30% in adults, 41% in children, and 42% in neonates. The majority of these CA cases occurred in the hospital [15].

Neurological outcomes and survival rates following ECPR for in-hospital cardiac arrest (IHCA) are generally superior to those for out-of-hospital cardiac arrest (OHCA), with reported survival ranging from 20% to 40% [16]. The success of ECPR in IHCA is strongly influenced by the duration and quality of resuscitative efforts [17]. A study by Bartos et al. (2020) demonstrated that ECPR initiated within 60 minutes of CA was associated with significantly better neurological and functional outcomes compared to conventional CPR alone [18]. Moreover, the study indicated that for every additional 10 minutes of CPR beyond the initial 30 minutes, patient survival decreased by approximately 25%.

The effectiveness of ECPR is further modulated by several factors, including the severity of initial metabolic disorders (e.g., blood pH, lactate levels), patient age, adherence to targeted temperature management protocols, and the timeliness of coronary angiography and subsequent interventions (e.g., angioplasty, stenting) in cases of coronary artery-related CA [2]. Advanced age and prolonged periods of hemodynamic instability prior to ECPR initiation are particularly detrimental, often leading to poorer outcomes during both resuscitation and subsequent intensive care management [19].

Given the multifactorial nature of ECPR outcomes in IHCA, the RESCUE-IHCA mortality prediction score was developed to assess prognosis. This score integrates 6 risk factors: (1) age; (2) presence of pre-existing renal failure; (3) patient type (cardiac vs. non-cardiac; medical vs. surgical); (4) timing of CA (daytime vs. nighttime); (5) initial heart rhythm; and (6) total duration of the CA event [21]. The scoring system ranges from -11 to +13 points. A score above 0 indicates a greater than 50% likelihood of mortality, while scores of 20 and 40 are associated with mortality risks exceeding 75% and 85%, respectively.

ELSO has also developed standardized ECPR protocols tailored to various patient age groups, which include recommendations for post-resuscitation management [7].

The annual institutional volume of ECMO procedures has been identified as a key determinant of ECPR program effectiveness. Centers performing more than 30 ECMO procedures annually report improved survival outcomes, likely attributable to greater cannulation proficiency and more experienced multidisciplinary patient management [22]. To enhance ECPR efficacy, it is recommended to establish specialized ECPR teams comprising an anesthesiologist-resuscitator, a physician trained in both percutaneous and surgical femoral vessel cannulation, and a cardiologist with expertise in acute cardiac care and heart failure management [23]. Integration with cardiogenic shock teams is also considered essential.

However, the widespread implementation of ECPR remains limited by its substantial cost, with treatment expenses ranging from  $\notin 12,000$  to  $\notin 156,000$  per patient. This high financial burden restricts access to ECPR in healthcare institutions with constrained budgetary resources [3].

Our study demonstrates the high efficacy of ECPR in both HT candidates and recipients who experience IHCA. At our center, the annual volume of VA-ECMO procedures – including those performed in the context of heart and lung transplantation, post-cardiac acute heart failure, and other emergent conditions – exceeds 80 cases. This extensive experience with percutaneous femoral cannulation for VA-ECMO, used as short-term mechanical circulatory support (MCS) prior to HT, has enabled the rapid initiation of extracorporeal support during ongoing manual or mechanical chest compressions as part of a comprehensive CPR protocol.

Irreversible brain injury and multi-organ dysfunction were both successfully prevented in 73.2% of patients,

creating the conditions necessary for urgent primary or repeat heart transplantation in 63.4% of cases. Despite the critical nature of the pre-transplant period, the use of temporary MCS, reliance on donor hearts with one or more expanded criteria in 61.5% of cases, and occurrence of early graft dysfunction in 19.2% of recipients, the inhospital survival rate following transplantation reached 84.7%. These outcomes are comparable to, and in some cases exceed, the survival rates reported by other leading transplant centers performing emergency HT supported by VA-ECMO [24–26].

# CONCLUSION

- 1. ECPR with peripheral VA-ECMO results in complete cardiac recovery in 100% of cases of IHCA.
- 2. The incidence of irreversible brain damage in patients who underwent ECPR following witnessed (by medical or nursing staff, patients) IHCA is 26.8%.
- 3. In 73.2% of patients who experienced witnessed IHCA followed by ECPR, the post-resuscitation period is marked by complete recovery of consciousness and the absence of severe multi-organ complications. This enabled subsequent HT (63.4%) or hospital discharge (9.8%).
- 4. In-hospital survival after emergency HT in recipients who underwent ECPR prior to transplantation was 84.7%.

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