Extracorporeal life support for primary graft dysfunction after heart transplantation

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ABSTRACT

Objectives. Survival after heart transplantation (HTx) is steadily improving but primary graft dysfunction (PGD) is still a leading cause of death. Medical management seems useful in mild or moderate PGD while extracorporeal life support (ECLS) could be suggested for severe PGD refractory to conventional treatment. Our aim is to present the results of ECLS for PGD after HTx at a single-centre experience.

Methods. We performed an observational analysis of our local database. According to the International Society for Heart and Lung Transplantation classification, patients were divided into a left and biventricular failure (PGD-LV) or isolated right ventricular failure (PGD-RV) group. The primary end-point was survival to hospital discharge.

Results. Between January 2010 and December 2016, 38 patients presented PGD (PGD-LV n=22, 58%; PGD-RV n=16, 42%) requiring ECLS support. The mean age was 50.8 ± 12.4 years with 79% of males. Baseline characteristics were comparable between the two groups. PGD-LV patients displayed a significantly higher mortality rate on ECLS support as opposed to PGD-RV patients (46% vs. 13%, p=0.033). The complications' rate during ECLS support was comparable between the two groups. Twenty-three (61%) patients were successfully weaned from ECLS (PGD-LV=50% vs. PGD-RV=75%, p=0.111) after a mean support of 9.0 ± 6.4 days. Seventeen (45%) patients survived to hospital discharge (PGD-LV=41% vs. PGD-RV=50%, p=0.410).

Conclusions. In case of severe PGD with various manifestations of ventricular failure refractory to conventional treatment, ECLS can be considered as a feasible option with a satisfactory survival in this critically ill population.

Keywords: heart transplantation, primary graft dysfunction, left-sided heart failure, right-sided heart failure, extracorporeal membrane oxygenation.

INTRODUCTION

Although overall survival after heart transplantation (HTx) has continued to improve in the last three decades, primary graft dysfunction (PGD) is still a leading cause of death in the early post-transplant period [1]. The relevant literature of PGD shows heterogeneous results and conclusions owing to inconsistent definitions of PGD used by different authors [2]. This lack of standardization of the definition, diagnostic criteria and treatment strategies led the International Society for Heart and Lung Transplantation (ISHLT) to develop a consensus document in 2014 [3].

PGD is now clearly differentiated by secondary graft dysfunction where a specific cause - i.e. hyperacute rejection, pulmonary hypertension or surgical complications - could be recognized. Moreover the diagnosis of PGD must be performed within 24 hours after the completion of HTx and should distinguish between left and biventricular failure (PGD-LV) or isolated right ventricular failure (PGD-RV). Finally the introduction of a grading system of PGD severity could guide the subsequent decision-making algorithm [3]. Medical management seems useful in mild or moderate PGD while extracorporeal life support (ECLS) could be suggested as a therapeutic option for those severe cases of PGD that are refractory to maximal conventional treatment including inotropes, vasodilators and nitric oxide [4-15].

We aimed to report the results of ECLS for PGD after HTx according to the ISHLT classification.

MATERIALS AND METHODS

Study design

We undertook an observational analysis of our local database of ECLS implantation for PGD after HTx. Authorization from an ethics committee and written informed consent from participants were not required owing to national regulations on “non-interventional clinical research” (articles L.1121-1 and R.1121-2 of the French Public Health Code).

Patient population

Adult patients who received an ECLS for PGD after HTx at our institution from January 2010 to

December 2016 were included. We excluded patients: 1) undergoing HTx and aged <18 years (n=29); 2) requiring ECLS for graft dysfunction secondary to isolated pulmonary hypertension (n=2); 3) receiving ECLS more than 24 hours after HTx completion (n=4). PGD was defined according to the ISHLT criteria [3]. In particular, severe PGD-LV was defined as the need of left or biventricular mechanical circulatory support. Conversely, there were no grades for the severity of PGD-RV because isolated right ventricular failure can often be more difficult to quantify.

Surgical technique

ECLS was implanted in the event of: 1) inability to wean the patient from cardiopulmonary bypass despite inotropic support, 2) refractory cardiogenic shock in the postoperative period within 24 hours after completion of HTx. Failure of weaning from cardiopulmonary bypass was assessed by intraoperative transesophageal echocardiography (left ventricular ejection fraction ≤40% and/or evidence of right ventricular dysfunction) coupled to right heart catheterization (cardiac index <2 L/min/m2). Cardiogenic shock was defined as hypotension (systolic blood pressure <90 mmHg) despite adequate filling status with signs of hypoperfusion [16]. The implantation of ECLS could be performed in a peripheral or intrathoracic configuration and the choice was left to the surgeon's discretion. Peripheral ECLS was implanted surgically. Venous and arterial cannulae were placed using a modified Seldinger technique after surgical exposure of the femoral vessels at the groin. As per institutional policy, an arterial catheter was systematically placed distally to the entry site of the arterial cannula to prevent lower limb ischemia. In the intrathoracic or central ECLS, the venous drainage was obtained using either a direct cannulation of the right atrium or a percutaneous femoral venous cannula. The arterial reinjection was placed in the ascending aorta. Left ventricular unloading, if necessary, was accomplished after cannulation of the right superior pulmonary vein or left ventricular apex. The cannulae were tunnelled in the subxyphoid or subcostal region and the sternum was completely closed. The ECLS circuit consisted also of venous and arterial heparin-bounded tubing, a membrane oxygenator (Quadrox Bioline, Jostra-Maquet, Orléans, France), a centrifugal pump (Rotaflow, Jostra-Maquet, Orléans, France) and an oxygen/air blender (Sechrist Industries, Anaheim, CA, USA).

ECLS management

As previously described [17], ECLS flow was initially set at the theoretical cardiac output owing to the patient's body surface area. However an inotropic support with dobutamine was used in order to maintain a left ventricular ejection with aortic valve opening. Moreover a vasopressor support with norepinephrine was usually added with a target mean blood pressure of 60-80 mmHg. After admission to our intensive care unit, the anticoagulation with unfractioned heparin was usually started 6 hours after the completion of HTx if the surgical bleeding from the chest drains was less than 50 ml/hour. Target unfractionated heparin anti-Xa factor activity was maintained between 0.30 and 0.35 IU/ml during ECLS support. Serial transoesophageal echocardiography was performed after progressive reduction of ECLS flow to assess the myocardial recovery. Patients stable during reduction trials and with left ventricular ejection fraction > 25% and time-velocity integral > 10 cm were weaned from ECLS [18]. Right ventricular function was considered recovered when: 1) systemic arterial pressure remained stable without the augmentation of central venous pressure; 2) major inotropic support or need for escalation of inotropic support were not required; 3) a transthoracic echocardiography showed satisfactory right ventricular systolic function without dilatation. Right-sided hemodynamic parameters were not considered, because their interpretation under ECLS support is complicated. If the weaning trial was hemodynamically tolerated and the echocardiographic criteria were fulfilled, the decannulation procedure was performed in a surgical manner with reopening of the operative field at the groin or chest depending on the ECLS configuration. Successful weaning was defined as ECLS decannulation without the need for ECLS reinsertion or mortality within 48 hours. In patients without complete myocardial recovery, cardiac retransplantation could be considered as a rescue therapeutic option. Conversely, ECLS support was considered futile and then stopped in the presence of multiple organ failure or brain death.

Outcome and statistical analysis

Preoperative, perioperative and postoperative data were retrieved from the computerized medical charts of our hospital. Moreover, heart donors' data were collected from the French regulatory agency of transplantation ("The Agence of Biomedecine"). Patients were divided into a left and biventricular

failure (PGD-LV) or isolated right ventricular failure (PGD-RV) group according to the echocardiographic and hemodynamic parameters defined in the ISHLT classification [3]. The secondary endpoints were complications rate during ECLS support, successful weaning rate from ECLS and short-term outcome. Neurological complications included seizure, cerebral infarction and intracerebral hemorrhage. Only infections occurring >24 hours after ECLS initiation and within 48 hours after ECLS discontinuation were defined as ECLS-associated [19].

Statistical analysis was performed with SPSS software, version 24.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as counts and percentages and compared by using the Pearson's chi-squared test or Fisher's exact test (>20% of expected counts with <5 counts). Continuous variables were presented as mean ± standard deviation and compared using Student's t-test or Mann–Whitney U-test depending on their normality, which was assessed by the Kolmogorov–Smirnov test. Survival was calculated with the use of Kaplan–Meier analysis and compared using the log-rank test. A level of 0.05 was used to test for significance.

RESULTS

Baseline characteristics

Of the 212 patients who had orthotopic HTx, 38 (18%) developed PGD (PGD-LV n=22, 58%; PGD-RV n=16, 42%) requiring ECLS support and met our selection criteria. The mean age was 50.8 ± 12.4 (range, 22-64) years with 79% of males. Table 1 shows the preoperative characteristics. Ischemic cardiomyopathy was the most frequent (48%) diagnosis leading to HTx and 14 (38%) patients were bridged to HTx with a temporary (n=6, 16%) or long-term (n=8, 21%) mechanical circulatory support. Baseline characteristics were comparable between both groups. The mean age of heart donors was 41.3 ± 12.6 (range, 21-63) years with 68% of males. Table 2 summarises the characteristics of heart donors. The heart donors' characteristics were comparable between both groups. In particular, there was no difference in term of sex mismatch (donor female to recipient male). Table 3 displays the baseline biological and hemodynamic evaluation of our patient population. The biological profile was typical of end-stage heart failure patients. PGD-LV patients showed numerically higher total bilirubin levels

compared to PGD-RV patients but the difference did not reach statistical significance (28.4 vs. 16.9 μmol/L, p=0.069).

Short-term outcomes

Table 4 shows the operative and postoperative outcomes of our study population. ECLS was implanted directly at the operatory theatre when weaning from cardiopulmonary bypass was not possible in 30 (79%) patients (PGD-LV=86% vs. PGD-RV=69%, p=0.189). No patients underwent ECLS implantation during cardiopulmonary resuscitation. Peripheral ECLS was used in 25 (66%) patients (PGD-LV=64% vs. PGD-RV=69%, p=0.743). PGD-LV patients displayed a significantly higher mortality rate on ECLS support compared to those with PGD-RV (46 vs. 13%, p=0.033). The rate of complications during ECLS support was comparable between both groups. Twenty-three (61%) patients were successfully weaned from ECLS (PGD-LV=50% vs. PGD-RV=75%, p=0.111) after a mean support of 9.0 ± 6.4 (range, 3-32) days (PGD-LV=7.5 days vs. PGD-RV=9.3 days, p=0.429). One (3%) patient died in the first 24 hours after ECLS weaning for multi-organ failure while two (5%) were bridged to cardiac retransplantation owing to the absence of myocardial recovery. Seventeen (45%) patients survived to hospital discharge (PGD-LV=41% vs. PGD-RV=50%, p=0.410). Figure 1 depicts the outcome of our study population. Overall survival was 43% (95%CI 27.2 - 59.4%; 13 remaining observations) at 1 year. The log-rank test showed no significant difference on overall survival between the two groups (median overall survival in the PGD-LV group=11 days, 95%CI 0-39; median overall survival in the PGD-RV group=201 days, 95%CI 0-796; p=0.315; Figure 2).

DISCUSSION

PGD is a life-threatening complication after HTx that negatively affects short- and long-term outcome. It accounts for approximately 40% of deaths within 30 days of cardiac transplantation [20]. Moreover overall late survival is significantly lower in patients experiencing PGD [7,8,10,11,14,21]. The pathophysiology is multifactorial and several risk factors involving the donor, recipient and surgical procedure have been identified over time [3,14,21].

The incidence of severe PGD requiring ECLS was quite high (18%) in our experience. Although the

definitions of PGD were heterogeneous making comparisons difficult to carry out, this incidence was consistent with previous reports. In papers providing detailed information the incidence of PGD supported with ECLS ranged between 7% and 23% [5,7-15,21]. Interestingly, D'Alessandro et al. found a temporal trend of PGD after HTx. The raising of incidence in more recent years was explained by an evolving profile of recipients and donors, with more critically ill patients transplanted with marginal donors [7]. This increasing rate of PGD after HTx reflects a more general effort of every transplant team to overcome the shortage of heart's donors. This effort is also witnessed by our prolonged total ischemic time. Allograft ischemic time affects predominantly early outcomes and ischemic time <4 hours is associated with considerably higher survival [22]. The high incidence of severe PGD requiring ECLS in our series could be partially explained by the presence of several well-known risk factors like older donor age [22], longer total ischemic time and high rate of preoperative short- and long-term mechanical circulatory support, previous sternotomy and emergency transplant [3].

Our analysis showed that ECLS provided a survival to hospital discharge of 45%. These results compare favourably with other previous series that reported survivals to hospital discharge between 44% and 81% [5,7,8,10-15,21]. In only one small study (11 patients) this outcome improved to 91% [6] while other investigators reached a survival to hospital discharge of 82% adopting a systematic ECLS implantation in the setting of known preceding donor cardiac dysfunction [9]. This extreme variability in survival across studies could be partially explained by the complex and multifactorial physiopathology of PGD after HTx, as opposed to other conditions with a high potential of myocardial recovery and more reproducible ECLS results such as drug intoxication and myocarditis.

ECLS was most frequently implanted directly at the operatory theatre and in a peripheral configuration. Our institutional policy is to be as aggressive as possible in the implantation of ECLS before the onset of end-organ dysfunction. Interestingly, of the 8 patients who were not implanted directly at the operatory theatre, 6 (75%) did not survive to hospital discharge. Prompt ECLS implantation could reduce the dose of inotropic support, which increases myocardial oxygen consumption and limits the chances of myocardial recovery. Moreover, we prefer a femoro-femoral rather than a central ECLS as its decannulation does not need a sternal re-entry, which has a potentially increased risk of bleeding and infection. However, any previous attempt to compare central and peripheral ECLS failed to find any

significant difference in outcomes with the only exception of an increased rate of lower limb ischemia in the femoral group [7,21]. Lower limb ischemia was encountered in 12% of our peripheral ECLS subgroup and this complication rate is comparable to that reported in the literature [23-25] and in previous reports of ECLS for PGD after HTx [7,8].

We observed a disproportionate rate (approximately 50%) of surgical re-exploration for bleeding. This complication rate was experienced in 26-38% of patients in previous analyses [7,8,14]. A possible explanation for this bleeding complications could be the higher proportion (21%) of patients bridged to HTx with a long-term mechanical circulatory support.

In our study population left and biventricular failure was the leading (58%) manifestation of PGD after HTx. Despite a comparable preoperative profile between both groups, PGD-LV patients displayed a significantly higher mortality rate on ECLS support as opposed to PGD-RV patients. The main cause of death (6 out of 10 patients) in the PGD-LV group was multi-organ failure. However, there was no difference on overall survival between both groups at hospital discharge and short-term follow-up. In fact four patients in the PGD-RV group were weaned from ECLS support but did not survive to hospital discharge. Conversely in a recent paper by Loforte et al. evaluating early graft failure (primary and secondary according to the ISHLT consensus document) after HTx, the ECLS group was characterized mainly by biventricular dysfunction (93%) and, rarely, by isolated right ventricular failure (7%) [14].

Based on our results and those from previous reports [4-15], ECLS can be considered as a feasible option in the setting of PGD after HTx as: 1) the implantation – especially in the peripheral configuration – is easy and quick, 2) it allows a rapid hemodynamic stabilization with progressive end-organ function improvement and 3) it represents a reasonable solution in term of cost-effectiveness in such a critically ill population. Cardiac retransplantation could no more be considered an acceptable option because of the shortage of donors entailing ethical considerations and the dismal survival. In our study two patients were addressed to cardiac retransplantation in the absence of myocardial recovery during ECLS support and died. Recently Takeda et al. conducted a comparative analysis between ECLS (n=27) and temporary ventricular assist devices (n=17) in patients with severe PGD [15]: ECLS was associated with fewer postoperative complications, higher graft recovery rate and lower in-hospital mortality compared to ventricular assist devices. Taghavi et al. analysed retrospectively their experience

with either right ventricular assist device (n=15) or ECLS (n=13) to treat acute right ventricular failure after HTx [26]. Although no difference in survival to hospital discharge was observed between the two groups, the weaning rate and graft survival were significantly better in the ECLS group. In fact right ventricular assist devices could not allow a successful recovery of graft function and most patients either died during mechanical support (47%) or underwent urgent heart retransplantation (40%).

Study limitations

The present study displays several limitations. The small sample size represents a limiting factor that could undermine the statistical power of our analysis. Our conclusions are gathered from a single-centre observational experience and thus may not be generalizable to other settings. The ISHLT criteria for the definition and classification of PGD were applied retrospectively to our local database, with obvious intrinsic limitations. We did not consider as a comparison group patients with PGD not requiring ECLS or supported with other types of mechanical circulatory support. From a statistical standpoint the survival estimates have been evaluated from a very limited sample size of patients, which leads to wide 95% confidence intervals around the estimates overlapping between both groups. The absence of statistical difference using the log-rank test translates the lack of power of our study. With regards to survival analysis, our results can be considered as inconclusive.

CONCLUSION

PGD is still a serious complication in the immediate postoperative period of cardiac transplantation. In case of severe PGD refractory to conventional treatment ECLS can be considered as a feasible option with an acceptable complications' rate and a satisfactory survival in this critically ill population. Further studies with larger study populations are however mandatory in order to best define the prognostic role of the ISHLT classification.

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CONFLICTS OF INTEREST

None declared.

FIGURE LEGENDS

Figure 1. Flow diagram of the outcome of the study population. ECLS = extracorporeal life support, PGD = primary graft dysfunction, HTx = heart transplantation, PGD-LV = left and biventricular primary graft dysfunction, PGD-RV = isolated right ventricular primary graft dysfunction.

Figure 2. Survival of ECLS for PGD after HTx. A) Group analysis, B) Total population. ECLS = extracorporeal life support, PGD = primary graft dysfunction, HTx = heart transplantation, PGD-LV = left and biventricular primary graft dysfunction, PGD-RV = isolated right ventricular primary graft dysfunction.

292 **Table 1.** Preoperative characteristics.

Variable	**Overall n=38**	**PGD-LV n=22**	**PGD-RV n=16**	***p-value***
Age, years	50.8 ± 12.4	50.4 ± 10.5	51.4 ± 14.9	0.814
Male sex, n (%)	30 (79)	18 (82)	12 (75)	0.453^
BSA, m^2	1.8 ± 0.2	1.8 ± 0.2	1.7 ± 0.2	0.265
BMI, Kg/m^2	24.7 ± 3.8	25.4 ± 3.5	23.7 ± 4.1	0.196
CV risk factors, n (%)				
Hypertension	10 (26)	6 (27)	4 (25)	0.589^
Diabetes	8 (21)	6 (27)	2 (13)	0.245^
Dyslipidaemia	11 (29)	6 (27)	5 (31)	0.790#
History of smoking	20 (53)	11 (50)	9 (56)	0.480#
Obesity[a]	4 (11)	3 (14)	1 (6)	0.433^
Previous cardiac surgery, n (%)	17 (45)	9 (41)	8 (50)	0.578
ICD, n (%)	23 (61)	12 (55)	11 (69)	0.376#
CRT, n (%)	10 (26)	6 (27)	4 (25)	0.589^
Diagnosis, n (%)				0.369^
ICM	18 (48)	11 (50)	7 (44)	
DCM	10 (26)	4 (18)	6 (38)	
Other	10 (26)	7 (32)	3 (19)	
Waiting list time, months	41.1 ± 207.2	5.5 ± 7.7	13.3 ± 24.2	0.228
High emergency waiting list, n (%)	25 (66)	14 (64)	11 (69)	0.743#
Clinical status, n (%)				

Inotropes	15 (39)	9 (41)	6 (38)	0.832[#]
Mechanical ventilation	5 (13)	4 (18)	1 (6)	0.286[^]
IABP	10 (26)	6 (27)	4 (25)	0.589[^]
ECLS	6 (16)	5 (23)	1 (6)	0.180[^]
Long-term MCS	8 (21)	6 (27)	2 (13)	0.245[^]

293 [a]Obesity was defined as BMI > 30 Kg/m^2.

294 For categorical variables, [#] denotes p-value obtained with the chi-square test while [^] with the Fisher's
295 exact test.

296 PGD-LV = left and biventricular primary graft dysfunction, PGD-RV = isolated right ventricular
297 primary graft dysfunction, BSA = body surface area, BMI = body mass index, CV = cardiovascular,
298 CVA = cerebrovascular accident, ICD = implantable cardioverter defibrillator, CRT = cardiac
299 resynchronization therapy, ICM = ischemic cardiomyopathy, DCM = dilated cardiomyopathy, IABP =
300 intra-aortic balloon pump, ECLS = extracorporeal life support, MCS = mechanical circulatory support.

301

Table 2. Characteristics of heart donors.

Variable	**Overall n=38**	**PGD-LV n=22**	**PGD-RV n=16**	***p-value***
Age, years	41.3 ± 12.6	41.7 ± 12.8	40.9 ± 12.8	0.841
Male sex, n (%)	26 (68)	15 (68)	11 (69)	0.970[#]
BSA, m^2	1.9 ± 0.2	1.9 ± 0.2	1.8 ± 0.2	0.450
BMI, Kg/m^2	25.3 ± 4.8	25.2 ± 4.1	25.5 ± 5.7	0.838
Vasopressor support, n (%)	34 (90)	20 (91)	14 (88)	0.567[^]
LVEF, %	62.1 ± 6.2	61.3 ± 5.5	63.0 ± 7.2	0.424
Sex mismatch (recipient M, donor F), n (%)	9 (24)	5 (23)	4 (25)	0.584[^]
Cause of death, n (%)				0.447[^]
Trauma	15 (39)	10 (45)	5 (31)	
CVA	11 (29)	7 (32)	4 (25)	
Other	12 (32)	5 (23)	7 (44)	

For categorical variables, [#] denotes p-value obtained with the chi-square test while [^] with the Fisher's exact test.

PGD-LV = left and biventricular primary graft dysfunction, PGD-RV = isolated right ventricular primary graft dysfunction, BSA = body surface area, BMI = body mass index, LVEF = left ventricular ejection fraction, M = male, F = female, CVA = cerebrovascular accident.

309 **Table 3**. Baseline biological and hemodynamic evaluation.

Variable	**Overall** **n=38**	**PGD-LV** **n=22**	**PGD-RV** **n=16**	***p-value***
Hemoglobin, g/dL	11.5 ± 2.3	11.3 ± 2.5	11.7 ± 2.0	0.588
Platelets, 10^9/L	201.0 ± 90.2	202.0 ± 95.7	199.6 ± 85.2	0.937
WBC, 10^9/L	9.3 ± 4.2	9.2 ± 3.1	9.3 ± 5.4	0.990
INR	1.8 ± 1.0	1.9 ± 1.0	1.8 ± 0.9	0.605
BUN, mmol/L	12.5 ± 9.0	11.9 ± 8.1	13.4 ± 10.3	0.611
Creatinine, µmol/L	116.6 ± 15.5	110.4 ± 40.3	124.5 ± 61.9	0.430
Total bilirubin, µmol/L	23.6 ± 21.6	28.4 ± 26.9	16.9 ± 7.7	0.069
ASAT, U/L	83.0 ± 137.0	79.2 ± 130.9	88.1 ± 149.1	0.847
ALAT, U/L	81.5 ± 169.2	95.0 ± 209.6	63.1 ± 92.1	0.573
sPAP, mmHg	46.3 ± 16.7	44.7 ± 18.5	48.6 ± 13.8	0.552
mPAP, mmHg	30.3 ± 11.4	29.8 ± 12.4	31.0 ± 10.5	0.798
TPG, mmHg	11.6 ± 6.7	11.4 ± 8.3	11.8 ± 3.1	0.929
PVR, Wood units	2.5 ± 1.5	2.3 ± 1.4	2.9 ± 1.7	0.337

310 PGD-LV = left and biventricular primary graft dysfunction, PGD-RV = isolated right ventricular
311 primary graft dysfunction, WBC = white blood cells, INR = international normalized ratio, BUN =
312 blood urea nitrogen, ASAT = aspartate aminotransferase, ALAT = alanine aminotransferase, sPAP =
313 systolic pulmonary artery pressure, mPAP = mean pulmonary artery pressure, TPG = transpulmonary
314 gradient, PVR = pulmonary vascular resistance.

315

316 **Table 4.** Operative and postoperative outcomes.

Variable	**Overall n=38**	**PGD-LV n=22**	**PGD-RV n=16**	***p-value***
Total ischemic time, min	273.6 ± 57.8	280.9 ± 66.4	263.6 ± 43.2	0.369
Mortality on ECLS, n (%)	12 (32)	10 (45)	2 (13)	**0.033**
Complications on ECLS, n (%)				
Lower limb ischemia	3 (8)	2 (9)	1 (6)	0.621
Neurological	5 (13)	3 (14)	2 (13)	0.654
Renal replacement therapy	25 (66)	14 (64)	11 (69)	0.743
Surgical re-exploration	20 (53)	12 (55)	8 (50)	0.520
Infection	14 (37)	7 (32)	7 (44)	0.452
Successful weaning rate, n (%)	23 (61)	11 (50)	12 (75)	0.111
Survival to hospital discharge, n (%)	17 (45)	9 (41)	8 (50)	0.410

317 Bold indicates p value < 0.05.

318 PGD-LV = left and biventricular primary graft dysfunction, PGD-RV = isolated right ventricular
319 primary graft dysfunction, ECLS = extracorporeal life support.

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