Extracorporeal Membrane Oxygenation after Heart Transplantation: Impact of Type of Cannulation

Arash Mehdiani[1,*] Moritz Benjamin Immohr[1,*] Charlotte Boettger[1] Hannan Dalyanoglu[1] Daniel Scheiber[2] Ralf Westenfeld[2] Hug Aubin[1] Payam Akhyari[1] Diyar Saeed[3] Artur Lichtenberg[1] Udo Boeken[1]

[1] Department of Cardiovascular Surgery, Heinrich-Heine-University Medical School, Duesseldorf, Germany
[2] Department of Cardiology, Pulmonology and Vascular Medicine, Heinrich-Heine-University Medical School, Duesseldorf, Germany
[3] Department of Cardiovascular Surgery, Leipzig Heart Center, Leipzig, Germany

Address for correspondence Payam Akhyari, PhD, Department of Cardiovascular Surgery, Heinrich Heine University, Medical Faculty, Moorenstrasse 5, 40225 Duesseldorf, Germany (e-mail: payam.akhyari@med.uni-duesseldorf.de).

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Abstract

Background Primary graft dysfunction (PGD) is a common cause of early death after heart transplantation (htx). The use of extracorporeal life support (ECLS) after htx has increased during the last years. It is still discussed controversially whether peripheral cannulation is favorable compared to central cannulation. We aimed to compare both cannulation techniques.

Methods Ninety patients underwent htx in our department between 2010 and 2017. Twenty-five patients were treated with ECLS due to PGD (10 central extracorporeal membrane oxygenator [cECMO] and 15 peripheral extracorporeal membrane oxygenator [pECMO] cannulation). Pre- and intraoperative parameters were comparable between both groups.

Results Thirty-day mortality was comparable between the ECLS-groups (cECMO: 30%; pECMO: 40%, $p = 0.691$). Survival at 1 year ($n = 18$) was 40 and 30.8% for cECMO and pECMO, respectively. The incidence of postoperative renal failure, stroke, limb ischemia, and infection was comparable between both groups. We also did not find significant differences in duration of mechanical ventilation, intensive care unit stay, or in-hospital stay. The incidence of bleeding complications was also similar (cECMO: 60%; pECMO: 67%). Potential differences in support duration in pECMO group (10.4 ± 9.3 vs. 5.7 ± 4.7 days, $p = 0.110$) did not reach statistical significance.

Conclusions In patients supported for PGD, peripheral and central cannulation strategies are safe and feasible for prolonged venoarterial ECMO support. There was no increase in bleeding after central implantation. With regard to the potential complications of a pECMO, we think that aortic cannulation with tunneling of the cannula and closure of the chest could be a good option in patients with PGD after htx.

Keywords
- transplantation
- heart
- extracorporeal membrane oxygenation
- ECMO

[*] Both authors contributed equally to the study.

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Introduction

Primary graft dysfunction (PGD) represents a common cause of early death after heart transplantation (htx). According to the International Society of Heart and Lung Transplantation (ISHLT) registry, PGD accounts for nearly 40% of early deaths within 30 days after htx.[1,2] However, previous studies show the incidence of PGD varied from 2.3 to 28%.[1,3,4] This lack of clarity stems not from the amount of research conducted on the topic of PGD but instead from the lack of standardization of diagnostic criteria.[3] To resolve this issue, a working group from the ISHLT recently published consensus statements about PGD in htx.[3] This statement has allowed clinicians to use unified criteria and share the management of PGD and was confirmed by an additional investigation by Sabatino et al.[5] In patients experiencing severe PGD or even primary graft failure (PGF) early after transplantation, mechanical circulatory support is required to maintain adequate end-organ perfusion.[1] The use of a venoarterial extracorporeal membrane oxygenator (va-ECMO) in PGD after htx is widely accepted.[4,6–12] Extracorporeal membrane oxygenator (ECMO) allows right-chamber unloading and sufficient circulatory support, though left ventricle (LV) distension can occur, resulting in LV stasis, thrombosis, and failure of the aortic valve to open.[6,13,14] In this clinical setting with peripheral ECMO (pECMO) cannulation, many surgical or percutaneous solutions have been described to relieve LV overload during ECMO support.[15,16] Additionally, upper body hypoxemia as well as a leg ischemia after femoral cannulation represent common complications in peripheral ECMO patients.[17]

Therefore, central cannulation is frequently used in post-cardiotomy patients.[15,16] Besides easily using the cardiopulmonary bypass (CPB) cannulas with the feasibility for greater cardiac decompression than in peripheral cannulation, oxygenated blood is returned to the ascending aorta, causing less concern for retrograde flow and upper body hypoxemia.[15] However, bleeding at the cannula site is reported to be more common after central cannulation, causing a higher incidence of chest reexploration due to bleeding.[18] In patients without open-chest management, the necessity of reopening the chest for discontinuation of ECMO represents another disadvantage of central cannulation, not only because of an increased incidence of mediastinitis.[15,19]

In patients with graft dysfunction early after htx, choice of ECMO cannulation as well as timing of implantation and device management often differ even within one transplantation center not to mention the variety between different centers.[1]

As a center with a high-volume usage of va-ECMO with more than 150 treated adult patients per year, we aimed to retrospectively investigate our htx patients with PGD. We particularly focused on the technique of ECMO implantation, analyzing the outcome depending on cannulation site.

Materials and Methods

Ethics Committee Approval

This study was approved by the ethics committee of the medical faculty of the Heinrich-Heine-University, complying with the principles outlined in the Declaration of Helsinki.

Study Design

We retrospectively analyzed our patients with orthotopic htx between October 2010 and October 2017. In this period 90 patients underwent htx in our department due to ischemic or dilated cardiomyopathy. Of these, 25 patients (27.8%) were treated with va-ECMO due to early graft dysfunction within 24 hours after transplantation, with 10 central ECMO (cECMO) and 15 pECMO cannulations. Both groups were comparable regarding pre- and intraoperative parameters.

Definition of Primary Graft Dysfunction

According to the consensus statement published by the ISHLT committee in 2014,[3] severe PGD is defined by a new grading system. A prerequisite is the dependence on left or biventricular mechanical support including ECMO, left ventricular assist device (LVAD), biventricular assist device (BiVAD), or percutaneous LVAD, excluding requirement for intra-aortic balloon pump (IABP). The diagnosis can be determined by intraoperative transesophageal echocardiogram (TEE), postoperative transthoracal echocardiogram (TTE), right heart catheter (including pulmonary and systemic resistance and cardiac output), central or mixed venous saturation, and lactate. Graft dysfunction can be classified into PGD or secondary graft dysfunction in case of a clear mechanism such as hyperacute rejection, pulmonary hypertension, or known surgical complications (e.g., uncontrolled bleeding). The diagnosis of PGD has to be made within 24 hours after completion of the cardiac transplantation, with two subtypes: primary graft dysfunction-left ventricle (PGD-LV) or primary graft dysfunction-right ventricle (PGD-RV).[3]

ECMO Implantation: Device and Cannulation Strategy, Anticoagulation

Our approach of managing severe PGD with regard to type of cannulation did not significantly change during the study period (►**Fig. 1**).

The ratio between pECMO and cECMO remained unchanged with an increasing total number of extracorporeal supports. A reduced threshold for ECMO use in PGD patients may have caused that during the course of our analysis.

The decision for pECMO or cECMO was mostly multifactorial, not least depending on the individual surgeon. Certainly, comorbidities, potential bleeding complications, importantly the urgency, and site and time of implantation displayed a relevant issue for ECMO type.

If central cannulation was performed, we usually anastomose a Dacron® graft to the ascending aorta. Tunneling the Dacron® graft from the aorta through the subxiphoid area allows the chest to be closed and subsequent ECMO weaning and discontinuation without reoperative sternotomy.[20] For arterial inflow we mostly use a Fem-Flex II arterial cannula (18–22 Fr) (Edwards Lifescience, Irvine, California, United States). For venous drainage we usually use an Edwards QuickDraw (22–25 Fr) or (25 Fr) Bio-Medicus Multi-Stage cannula (Medtronic, Inc., Minneapolis, Minnesota, United States) or reutilize the cannula used during CPB.

Peripheral cannulation was achieved in the majority of patients percutaneously using the Seldinger technique, if

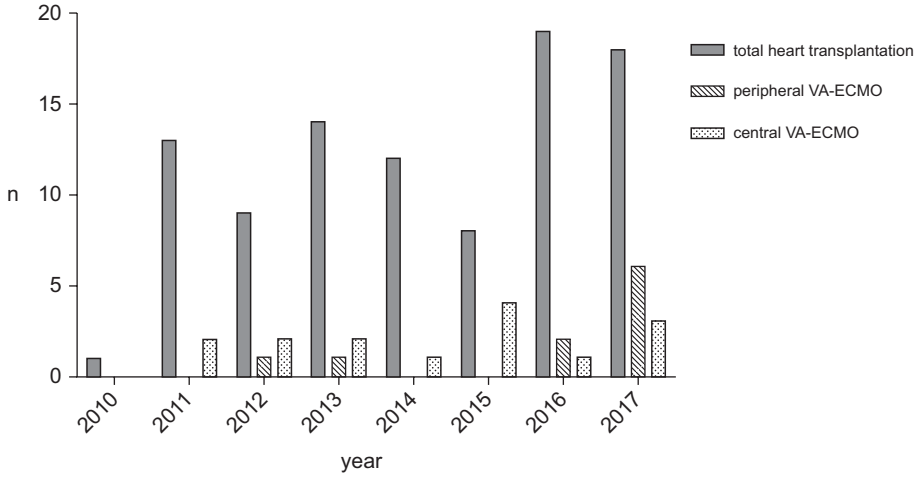

Fig. 1 Number of heart transplantations and implanted temporary extracorporeal membrane oxygenator (ECMO) systems during the study period per year. va-ECMO, venoarterial extracorporeal membrane oxygenator.

possible also reutilizing CPB cannulas. A distal leg perfusion catheter (7–8 Fr) was placed in all patients either percutaneously or through direct cut down of the corresponding femoral artery. An Edwards QuickDraw (22–25 Fr) or (25 Fr) Bio-Medicus Multi-Stage cannula (Medtronic, Inc., Minneapolis, Minnesota, United States) was used as venous cannula. A Fem-Flex II cannula (18–22 Fr) was used for arterial cannulation. In some cases, pECMO cannulation was performed by cut down of the femoral vessels. No vascular prosthesis was used in any of these patients with pECMO.

In the vast majority of patients, we used the same ECMO system (Sorin Lifebox, Sorin Group, Munich, Germany).

ECMO flow was initiated at 1.5 to 2.0 L/min and gradually increased and adjusted as necessary to meet the hemodynamic (mean arterial pressure >60 mm Hg) and oxygen requirements of the patient. Unloading of the heart was confirmed by echocardiography. If feasible, patients had an IABP placed to facilitate later weaning, afterload reduction, and provide pulsatility.

Anticoagulation was started right after ECMO implantation using heparin with target activated clotting time of 160 to 180 seconds. In stable patients, activated partial thromboplastin time (aPTT) was used to titrate heparin doses (target aPTT = 40–60 seconds). In patients with active bleeding, heparin was immediately discontinued.

Weaning

ECMO weaning was taken into account as soon as the patient was obviously improving (echocardiographic graft function recovery, end-organ recovery, reduction of inotropes, etc.). Clinical conditions are evaluated under echocardiographic and hemodynamic monitoring.[1] Our institutional weaning protocol is almost identical to the approach described by Santise et al.[6]

Follow-Up

We included patients with va-ECMO support of ≥24 hours. Various pre-, intra-, and postimplantation variables were investigated, including intraoperative parameters like ischemic time, CPB time, and blood product use at the time of transplantation. Following ECMO implantation, hemodynamic-, ECMO-, oxygenation/ventilation parameters, as well as renal and liver function tests were analyzed. Outcomes of patients receiving pECMO were compared with those who received cECMO.

Statistical Analysis

Statistical analyses were performed using Prism 7 (Version 7.0a, GraphPad Software, Inc., La Jolla, San Diego, California) and SPSS (Version 24.0.0.2, International Business Machines Corporation, Armonk, New York, United States). Data are expressed as frequencies and percentages for categorical variables. Unless otherwise stated, continuous variables are expressed as mean ± standard deviation. Dichotomous variables were compared with the chi-squared or Fisher's exact test where appropriate, and continuous variables were compared using the Student's *t*-test.

Kaplan–Meier curves were performed to represent survival and were compared using a log-rank test. A *p*-value of <0.05 was considered statistically significant.

Results

Baseline Parameters

Baseline data and statistical comparisons between pECMO and cECMO cannulation for va-ECMO are shown in ►**Table 1**. In our analysis all determined variables were comparable between the two groups. We did neither find significant differences for recipients nor for donor groups. Epidemiologic and biometric parameters were comparable as well as comorbidities and donor–gender matching with regard to blood group and gender.

Perioperative Parameters

►**Table 2** summarizes perioperative results. We did not find significant differences for the vast majority of the measured parameters as for example CPB time, duration of total ischemic time, and total time of surgery. Aortic cross-clamping was not

Table 1 Baseline parameters

Characteristic	Central ($n = 10$)	Peripheral ($n = 15$)	*p*-Value
Age, y	54.9 ± 14.1	54.1 ± 10.9	0.892
Size, cm	168.8 ± 17.1	173.1 ± 8.7	0.48
Weight, kg	70.0 ± 18.1	78.4 ± 20.8	0.296
Body mass index, kg/m^2	24.3 ± 4.1	25.9 ± 5.2	0.395
Male gender	7 (70)	11 (73)	0.856
Primary disease	6 (60)	11 (73)	0.667
Hypertension	5 (50)	7 (47)	0.87
Pulmonary hypertension	1 (10)	1 (7)	
Smoker	0 (0)	2 (13)	0.5
Diabetes mellitus	4 (40)	5 (33)	1
Hyperlipidemia	4 (40)	5 (33)	0
Preoperative mechanical circulatory support (VAD)	6 (60)	14 (93)	0.121
Duration of preoperative mechanical circulatory support (VAD), d	409.5 ± 355.8	463.9 ± 281.0	0.750
Preoperative infection	3 (30)	3 (20)	0.653
Preoperative dialysis	1 (20)	1 (8)	0.490
Preoperative ventilator support	2 (20)	3 (20)	1
Preoperative sternotomy	6 (24)	10 (40)	0.734
Prior cardiac surgery	7 (70)	14 (93)	0.267
Creatinine, mg/dL	1.6 ± 0.6	1.3 ± 0.8	0.206
Total bilirubin, mg/dL	1.6 ± 1.7	0.9 ± 0.5	0.216
PTT, s	35.5 ± 8.0	34.0 ± 4.3	0.649
INR	1.9 ± 0.6	2.3 ± 0.7	0.311
Hemoglobin, g/dL	11.7 ± 2.7	10.7 ± 2.6	0.358
Hematocrit, %	35.2 ± 7.8	33.5 ± 7.5	0.599
Aspartate transaminase, U/L	38.9 ± 24.4	36.8 ± 18.3	0.821
Alanine transaminase, U/L	21.8 ± 10.2	21.5 ± 14.9	0.965
Lactate dehydrogenase, U/L	356.7 ± 204.0	417.2 ± 400.1	0.665
Albumin, g/dL	4.0 ± 0.8	3.8 ± 0.7	0.610
Sodium, mmol/L	137.3 ± 3.6	134.4 ± 5.2	0.191
Potassium, mmol/L	4.6 ± 0.24	4.3 ± 0.5	0.188
HU status	6 (60)	11 (73)	0.667
Blood group			
A	5 (50)	11 (73)	
B	1 (10)	0 (0)	
AB	1 (10)	1 (7)	
O	3 (30)	3 (20)	0.217
Donor age, y	42.8 ± 9.2	46.5 ± 11.6	0.381
Size, cm	173.4 ± 8.2	176.4 ± 8.6	0.389
Weight, kg	78.0 ± 14.5	77.7 ± 13.0	0.963
Donor body mass index, kg/m^2	25.8 ± 4.3	24.7 ± 2.8	0.497
Donor male gender	5 (50)	8 (53)	0.87
Donor LVEF, %	64 ± 5.6	63 ± 4.7	0.943
Cardiopulmonary resuscitation	2 (20)	1 (7)	0.543
Duration of cardiopulmonary resuscitation, h	0.75 ± 2.1	1.1 ± 4.0	0.808
Donor peak creatine kinase, U/L	818.3 ± 1317.7	448.5 ± 759.6	0.486

Table 1 (*Continued*)

Characteristic	Central ($n = 10$)	Peripheral ($n = 15$)	*p*-Value
Donor lowest hemoglobin, g/dL	10.24 ± 3.2	10.5 ± 2.4	0.791
Donor lowest sodium, mmol/L	259.3 ± 378.4	140.9 ± 6.0	0.348
Donor lowest potassium, mmol/L	3.9 ± 1.1	3.7 ± 0.4	0.527
Donor peak lactate dehydrogenase, U/L	383.7 ± 226.5	296.1 ± 109.3	0.28
Donor peak C-reactive protein, mg/dL	146.2 ± 113.3	172.5 ± 107.1	0.567
Donor peak white blood cells count, x1.000/mL	18.5 ± 6.3	23.7 ± 10.7	0.138
Donor blood group			
A	5 (50)	10 (66)	
B	1 (10)	1 (7)	
AB	1 (10)	0	
O	3 (30)	4 (27)	0.597
Gender mismatch	2 (20)	5 (33)	0.659
Body weight-ratio	1.09 ± 0.2	0.97 ± 0.20	0.226
Blood type identical	9 (90)	14 (93)	1

Abbreviations: INR, international normalized ratio; LVEF, left ventricular ejection fraction; PTT, partial thromboplastin time; VAD, ventricular assist device.
Note: Medical records and laboratory parameters of the patients with central extracorporeal membrane oxygenator and peripheral extracorporeal membrane oxygenator implantations as well as donor data. Data are shown as mean ± standard deviation or as frequencies and percentages for categorical variables.

Table 2 Perioperative parameters

Variable	Central ($n = 10$)	Peripheral ($n = 15$)	*p*-Value
Warm ischemic time, min	68.5 ± 14.2	66.5 ± 14.9	0.734
Cold ischemic time, min	187.1 ± 44.5	170.3 ± 105.3	0.588
Cardiopulmonary bypass time, min	330 ± 78	339 ± 112	0.809
Reperfusion time, min	174 ± 37	174 ± 81	0.996
Cross-clamp time, min	112 ± 61	140 ± 68	0.302
Transfusion during surgery			
Packed red blood cells, mL	8775.0 ± 4737.7	5751.0 ± 3541.1	0.211
Fresh frozen plasma, mL	3166.7 ± 3231.4	2325.0 ± 2141.0	0.586
Platelets, mL	2493.3 ± 1083.7	1738.0 ± 997.2	0.195
Open chest	2 (20)	5 (33.3)	0.653
Timing of device implantation			
Intraoperative implantation	10 (100)	8 (53)	0.02
Support duration, d	5.70 ± 4.7	10.4 ± 9.3	0.110
Transfusion on ICU			
Packed red blood cells, mL	5580 ± 2815	9842 ± 7108	0.101
Fresh frozen plasma, mL	8000 ± 6017	12363 ± 9516	0.267
Platelets, mL	1833 ± 865	4660 ± 4958	0.093
Duration on ICU, d	23.5 ± 13.2	26.7 ± 25.3	0.681
Ventilation time, h	301.9 ± 268.9	298.5 ± 255.2	0.979
Total hospital time, d	43.3 ± 28.4	43.9 ± 34.4	0.965

Abbreviation: ICU, Intensive care unit.
Note: Operative and device support parameters of the patients with central extracorporeal membrane oxygenator and peripheral extracorporeal membrane oxygenator implantations. Data are shown as mean ± standard deviation or as frequencies and percentages for categorical variables.

only slightly longer in the pECMO group (cECMO: 112 ± 61 min; pECMO: 140 ± 68 min) but also did not reach statistical significance ($p = 0.302$). Duration on intensive care unit, mechanical ventilation time, as well as total hospital stay did not significantly differ between the two groups. Furthermore, no significant differences were found in the intra- and postoperative administered amount of packed red blood cells, fresh frozen plasma, and platelets. The thorax was closed

adequately after the operation in 80% ($n = 8$) of the cECMO patients as well as 64% ($n = 10$) of the pECMO group ($p = 0.653$).

ECMO Details: Indication, Timing, and Type of Cannulation

In 60% of the patients of both groups (cECMO and pECMO), severe biventricular failure was the reason for mechanical postoperative support. In almost all other patients we observed isolated right ventricular dysfunction or failure as underlying pathology causing the necessity for ECMO support. One patient in each group suffered from hemodynamic impairment caused by asystolia with prolonged unreliable pacemaker stimulation.

cECMO support was immediately initiated in the operating room in all 10 of the group's patients (100%). In contrast, in 47% ($n = 7$) patients of the pECMO group, extracorporeal life support (ECLS) was implanted within the first 24 hours after the primary operation ($p = 0.02$; ►**Table 2**). Support duration of the pECMO group appeared to be prolonged compared with the cECMO patients (cECMO: 5.7 ± 4.7 days; pECMO: 10.4 ± 9.3 days) but did not reach statistical significance ($p = 0.110$).

Early Postoperative Outcomes and One-Year Survival

Early clinical outcomes were comparable between both groups and are presented in ►**Table 3**. Successful weaning from the ECMO system was achieved in 70% ($n = 7$) of the cECMO and 47% ($n = 7$) of the pECMO patients ($p = 0.414$). One patient (10%) of the cECMO group as well as six patients (40%) with pECMO received additional IABP support ($p = 0.179$). Major bleeding (cEMCO: 60%; pECMO: 67%) as well as renal failure with need of hemodialysis (60% respectively 60%) were the most common morbidities during mechanical support in both groups. Although not statistically significant, presence of infective constellations as well as compartment syndrome and limb ischemia was slightly increased in the pECMO group compared with the cECMO patients. Nonetheless, 30-day mortality did not show any difference between the two groups (cECMO: 30%; pECMO: 40%, $p = 0.691$).

►**Fig. 2** shows the Kaplan–Meier curve of the long-term follow-up. One-year follow-up was achieved in 18 patients (cEMCO: $n = 5$; pECMO: $n = 13$). The remaining 7 patients (cECMO: $n = 5$; pECMO: $n = 2$) did not finished the 1-year follow-up period by now and were therefore censored. All of these patients were still alive at the time they were censored. Two patients with need of mechanical circulatory support and central cannulation survived the first year after htx (40%). In the pEMCO group, $n = 4$ patients survived (30.8%), which was quite similar at this time.

Table 3 Early outcomes

Outcome	Central ($n = 10$)	Peripheral ($n = 15$)	*p*-Value
Successful weaning from ECLS	7 (70)	7 (47)	0.414
Additional IABP support	1 (10)	6 (40)	0.179
Major morbidity during support			
Stroke	1 (10)	3 (20)	0.626
Sepsis/bacteremia/infection[a]	0 (0)	3 (20)	0.25
Major bleeding	6 (60)	10 (67)	1
Compartment or ischemia of lower limbs	1 (10)	3 (20)	0.626
Renal failure requiring dialysis	6 (60)	9 (60)	1
Mortality			
30-day	3 (30)	6 (40)	0.691

Abbreviations: ECLS, extracorporeal life support; IABP, intra-aortic balloon pump.
Note: Weaning, morbidity, and mortality of the patients with central extracorporeal membrane oxygenator and peripheral extracorporeal membrane oxygenator implantations. Data are shown as frequencies and percentages for categorical variables.
[a]Including wound infection.

Discussion

PGD is still a remaining major cause for early death after orthotopic htx. In the last few years, mechanical circulatory support by va-ECMO increasingly gained more and more importance in the handling of this disease. In our study, we compared the different cannulation techniques for va-ECMO, central aortic, and peripheral femoral artery to investigate potential benefits for one of these procedures in the case of PGD after htx.

We retrospectively reviewed all of our 90 transplantation patients between October 2010 and October 2017 and identified 25 patients with PGD and ECMO treatment within the first 24 hours after the primary operation. Ten patients with central ECMO implantation were included in our study as well as 15 patients with peripheral cannulation.

Preoperative data of included transplanted patients as well as donor specific values did not differ between the two groups; therefore, both groups were comparable without selection bias. Implantation techniques for both groups followed regular clinical practice as previously described by different groups.[15,18,20] Indication for ECMO implantation as described for PGD followed the current ISHLT consensus.[3] We could not find any significant differences in early outcome and 1-year survival between the central and peripheral cannulation techniques. Nonetheless, our data indicated a few trends that may influence future clinical practices. Whereas central cannulation was only performed in the primary operation, pECMO was also applied in early postoperative PGD patients. Tunneling of the cECMO prosthesis as described before,[20] allowed us to achieve a closed chest in 80% of all cECMO patients and was not inferior to the pECMO group (64%) to decrease the risk of mediastinitis as reported in the literature.[15,19] Bleeding, known as one of the major complications under ECMO support, did also not differ between both the groups in our study.[21] Furthermore, risk for severe postoperative infections (sepsis, bacteremia/wound infections) as well as compartment syndrome seemed to be reduced by cECMO

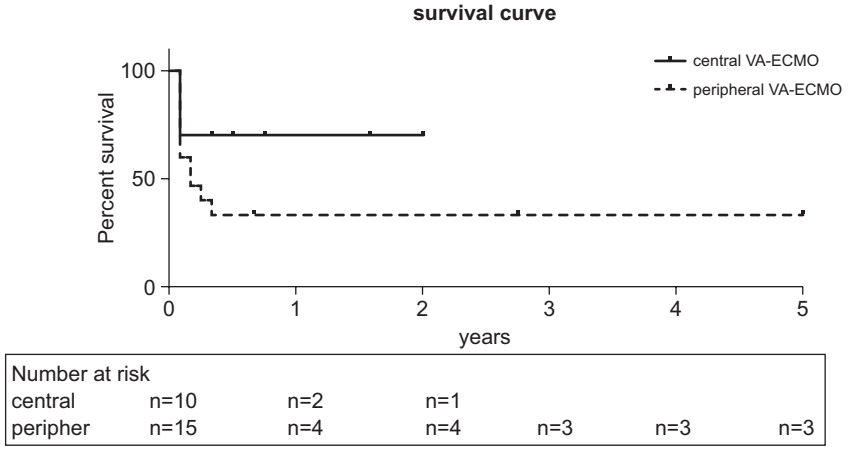

Fig. 2 Kaplan–Meier survival curve of the patients with cECMO (central extracorporeal membrane oxygenator) and pECMO (peripheral extracorporeal membrane oxygenator) implantations. va-ECMO, venoarterial extracorporeal membrane oxygenator.

indicating another potential beneficial effect. A recent large meta-analysis by Raffa et al[22] of central and peripheral ECMO implantations reported similar advantages with regard to limb complications for central cannulation but contrary results for bleeding and infective complications. This might be affected by the unknown incidences of open-chest situations in the cECMO group of this report.[22] Weaning from extracorporeal support was successful in 70% of cECMO as well as 47% of the pECMO patients, which was again not statistically significant. In addition, 30-day mortality was quite similar in both groups indicating that successful weaning alone did not guarantee successful treatment of PGD in the following period. Marasco et al[23] also reported similar results with comparable outcomes for both central and peripheral cannulation. Thirty-day mortality of 30% (cECMO), respectively, 40% (pECMO), in our study as well as 1-year survival was comparable to the results previously reported in the literature for mechanically supported early graft dysfunction.[24]

In 2017, Takeda et al[1] published a large study of 597 consecutive htx patients with 44 PGD cases with 17 patients receiving a temporary continuous-flow external VAD and 27 patients va-ECMO to compare these two common options for mechanical circulatory support. As successful weaning and survival increased as well as major complications decreased in the va-ECMO group. Takeda et al[1] reported advantage of va-ECMO for PGD. However, there was no differentiation between peripheral (85.2%) and central (14.8%) va-ECMO cannulation techniques.[1] Weaning was reported in 88.9% for overall ECMO implants and 58.8% for VAD support; major bleeding appeared in 29.6% (ECMO), respectively 76.5% (VAD), of all cases and 30-day mortality was 11.1% (ECMO), respectively 23.5% (VAD).[1] In comparison, only 56% (cECMO: 70%; pEMCO: 47%) of the patients in our study cohort were successfully weaned from the support device with major bleeding complications in 64% (cECMO: 60%; pEMCO: 67%) and 30-day mortality of 36% (cECMO: 30%; pEMCO: 40%). As the vast majority of the patients of Takeda et al[1] were cannulated peripherally, these differences appear to be even more distinct. Although ischemic as well as CPB time and support duration were comparable between the both studies, a much higher amount of blood transfusion was applied in our cohort.[1] This might be an indicator for a difference of the severity of the PGD as well as of course be caused by the higher incidence of bleeding complications in our cohort.

Limitations

This study is obviously limited by its small group sizes as well as its retrospective and single-center design. Although the donor and host data between both groups did not show any significant differences, larger group sizes are needed to confirm these early results. While central cannulation was always applied directly in the operating room, peripheral technique was also used directly on the intensive care unit for delayed onset of PGD. DeRoo et al[25] showed that early implantation of ECLS in patients with PGD may decrease the mortality, which may affect our study in a by now unknown way. Additionally, incidence of IABP implantation differed between the two groups, which was also caused by surgeons' preferences. Subsequently, standardized operation procedures should be implemented in the clinical setting to equally handle PGD after htx due to clinical data and regardless of personal surgeon differences. By this, evidence of our findings can be further strengthening in the future.

Conclusion

Mechanical circulatory support by va-ECMO is a reliable option for patients suffering from PGD after htx. Our study showed no statistically significant differences in the outcome between central and peripheral ECMO cannulation. Morbidity as well as mortality was comparable in both groups for early outcomes as well as 1-year follow-up period. Although larger study populations are needed, with regard to the earlier described complications of peripheral ECMO, we think central cannulation with tunneling of the cannula to receive a closed-chest situation could be a good option as there was no increase of bleeding complications in our study group.

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Conflicts of interest
None declared.

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All authors participated sufficiently in the work to take public responsibility for the content. In detail:

- Conception of the work: Moritz Benjamin Immohr, Arash Mehdiani, Udo Boeken
- Analysis and interpretation of data: Moritz Benjamin Immohr, Arash Mehdiani, Charlotte Boettger, Udo Boeken
- Drafting of the manuscript: Moritz Benjamin Immohr, Arash Mehdiani
- Critical revision of the manuscript for important intellectual content: Alexander Albert, Charlotte Boettger, Bozena Sowinski, Hannan Dalyanoglu, Daniel Scheiber, Ralf Westenfeld, Payam Akhyari, Diyar Saeed, Artur Lichtenberg, Udo Boeken
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- Supervision: Artur Lichtenberg, Udo Boeken, Payam Akhyari

The report was approved in its current form by the ethical committee of Heinrich-Heine-University Düsseldorf, Germany.

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