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ORIGINAL ARTICLE

Life impact of VA-ECMO due to primary graft dysfunction in patients after orthotopic heart transplantation

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Abstract

Aims Primary graft dysfunction (PGD) is a feared complication after heart transplantation (HTX). HTX patients frequently receive veno-arterial extracorporeal membrane oxygenation (VA-ECMO) until graft recovery. Long-term mortality of patients weaned from VA-ECMO after HTX is comparable with non-ECMO patients. However, impact on quality of life is unknown. This study investigated days alive and out of hospital (DAOH) as patient-centred outcome in HTX patients at 1 year after surgery.

Methods and results This retrospective single-centre cohort study included patients who underwent HTX at the University Hospital Düsseldorf, Germany, from 2010 to 2020. Main exposure was VA-ECMO due to PGD. VA-ECMO and non-VA-ECMO patients were compared regarding the primary endpoint DAOH at 1 year after HTX. Subgroup analysis for patients weaned from VA-ECMO was performed. In total, 144 patients were included into analysis; 1 year mortality was significantly lower in non-ECMO patients [non-ECMO 14.3% (14/98) vs. VA-ECMO 34.8% (16/46), adjusted hazard ratio: 0.32, 95% confidence interval: 0.15–0.74; $P = 0.002$]. Mortality did not differ significantly between patients weaned from VA-ECMO and non-ECMO patients [non-ECMO 14.3% (14/98) vs. VA-ECMO (weaned) 18.9% (7/37), adjusted hazard ratio: 0.72, 95% confidence interval: 0.27–1.90; $P = 0.48$]. DAOH were significantly higher in non-ECMO patients compared with VA-ECMO patients and patients weaned from VA-ECMO [non-ECMO vs. VA-ECMO: median 310 (inter-quartile range 277–327) days vs. 243 (0–288) days; $P < 0.0001$; non-ECMO vs. VA-ECMO (weaned): 310 (277–327) days vs. 253 (208–299) days; $P < 0.0001$]. These results were still significant after multivariable adjustment with forced entry of predefined covariables.

Conclusions Despite similar survival rates, VA-ECMO due to PGD has a relevant life impact as defined by DAOH in the first year after HTX. As a more patient-centred endpoint, DAOH may contribute to a more comprehensive assessment of outcome in HTX patients.

Keywords VA-ECMO; ECLS; Quality of life; Days alive and out of hospital; Patient-centred outcomes; Cardiac surgery

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Introduction

Orthotopic heart transplantation (HTX) is the causal therapy for patients with end-stage heart failure.[1,2] After HTX, primary graft dysfunction (PGD) is a feared complication occurring in up to 30% and strongly affecting survival chances of patients.[3] Therefore, these patients frequently receive extracorporeal mechanical support by veno-arterial extracorpo-

real membrane oxygenation (VA-ECMO) devices.[4,5] VA-ECMO is the first-line therapy for severe PGD and helps to maintain circulation as well as to overcome cardiac failure until graft recovery.[6–9] Previous studies indicated that long-term survival of patients weaned from VA-ECMO after HTX was comparable with patients who did not experience PGD.[10–12] However, data on functionality in daily life and rehospitalization rates remain limited in these patients. Days alive and out of hospital (DAOH) has been recently introduced and evaluated as patient-centred outcome in different clinical settings.[13–15] It combines clinically important outcomes such as death, hospital length of stay, and rehospitalization rate. To date, impact of VA-ECMO on DAOH in patients after HTX is underexplored. Therefore, we aimed to investigate this topic and hypothesized that use of VA-ECMO due to PGD is associated with lower DAOH at 1 year after HTX.

Methods

The present study is a retrospective single-centre cohort study that has been conducted in accordance with the Declaration of Helsinki and the guidelines for Good Clinical Practice. The study was approved by the ethical review board of the Heinrich Heine University Düsseldorf, Germany (reference number: 4567). All patients gave written informed consent. This report follows the STROBE guidelines.

Study design and study population

This study included patients >18 years who underwent HTX between 2010 and 2020 at the University Hospital Düsseldorf, Germany. The main explanatory variable of this study was the early use of VA-ECMO therapy due to PGD (= initiation within the first 24 h after surgery according to consensus conference on PGD).[16] Patients were assigned to VA-ECMO group, if they had early VA-ECMO therapy due to PGD. Patients without PGD were assigned to non-VA-ECMO group. Afterwards, a subgroup of weaned VA-ECMO patients was set out of the VA-ECMO group. This group was defined as patients who had PGD and VA-ECMO therapy but were successfully weaned from VA-ECMO during the index hospital stay. Weaning was performed from peripheral and central cannulated ECMO while ventilated, according to local standards. Exclusion criteria were incomplete medical records, death during HTX, and the use of veno-venous ECMO. Central and peripheral VA-ECMO cannulation was included. Average caseload of VA-ECMO therapy in our centre is 60–80 patients per year, which was deemed appropriate in terms of experience and expertise in this field.

Outcome assessment

The primary endpoint was DAOH at 1 year after HTX. DAOH for the first year after HTX were calculated by individually summing up the days of all hospital stays per patient and subtracting them from 365 days. If the patient did not survive 365 days, the difference between survived days and 365 days was added to days of hospital stays before subtraction from 365 days. This method refers to the validation study of DAOH in heart failure patients.[15] According to the validation study of DAOH in major surgery, DAOH can also be calculated in another way: in a previously published approach, patients who died during the study period were assigned DAOH of 0 days. To test if the way to calculate DAOH influences our results, a sensitivity analysis using this additional definition of DAOH was performed. Secondary endpoints included mortality, duration of hospitalization, and reasons for hospitalization during the first year after HTX. Hospitalization was defined as every planned or unplanned readmission to the hospital of at least 1 day occurring within 1 year after HTX. Hospitalizations were divided into 10 categories: gastrointestinal disorders, pneumonia/respiratory infection, wound infection, kidney disorders including acute kidney injury, graft rejection reaction, bleeding complications, non-cardiac surgery, other infections than respiratory infections, endomyocardial biopsy, and HTX index hospitalization. All observed hospitalizations of our study cohort are included into these categories. HTX patients are very closely connected to our centre so that all information on hospitalizations could be assessed by screening local medical records.

Data collection

All data of patients were collected by screening electronic medical charts and the local electronic HTX database. Patient characteristics, co-morbidities, comedication, and survived days at 1 year were extracted from these sources.

Statistical analysis

Statistical analysis was conducted in GraphPad Prism© Version 8.02 (La Jolla, CA, USA) and IBM SPSS© software Version 22.0 (Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation or as median with inter-quartile ranges, as appropriate. Categorical variables are presented as absolute numbers (*n*) and percentage (%) in brackets. χ^2 test and Fisher's exact test were used for statistical comparison. Kaplan–Meier diagrams were used for graphical presentation of survival 1 year after HTX. Comparison of survival rates was performed using the log-rank (Mantel–Cox) test, and results are presented as percentage of survival (%) with hazard ratio (HR) and confidence interval

(CI) with confidence level of 95%. DAOH were compared by using Mann–Whitney *U* test given that these data were likely to be skewed. Normality testing was carried out by using Shapiro–Wilk test. Multivariate linear regression including ANOVA analysis was conducted as previously performed,[15] setting DAOH as dependent variable and VA-ECMO therapy, age, continuous veno-venous haemodialysis, duration of surgery, and neurological complications as predefined independent variables. Neurological complications were defined as a composite of ischaemic stroke or any intracranial bleeding with new onset of any documented neurological impairment. Transient ischaemic attack or neurological symptoms with duration $<$24 h were not included. No power analysis was conducted because of the retrospective nature of this study.

Results

Study population and patient characteristics

We investigated data of 154 HTX patients registered in the local HTX database of the University Hospital Düsseldorf, Germany; 10 patients (6.5%) were excluded from analysis due to incomplete medical records and impossibility to calculate DAOH [6 patients (3.9%)], death during surgery [3 patients (1.9%)], and veno-venous ECMO [1 patient (0.7%)]. Thus, we included 144 HTX patients into analysis (*Figure 1*). Overall mean age was 54 ± 12 years, and 114 patients (79.2%) were male. Mean age of donor hearts was 43 ± 13 years; 98 patients (68.1%) did not have VA-ECMO after surgery, and 46 patients (31.9%) had VA-ECMO due to PGD. Out of the VA-ECMO group, 30 (65.2%) patients suffered from biventricular failure while 16 (34.8%) patients had isolated right ventricular failure according to the International Society for Heart and Lung Transplantation PGD classification; 37/46 patients (80.4%) could be weaned successfully. There was no difference in successful weaning between biventricular and right ventricular failure group [biventricular 24 (80%) patients vs. right ventricular 13 patients (81.2%)]. Mean duration of VA-ECMO support was 8 ± 7 days. VA-ECMO patients were significantly older, and diabetes was more frequent than in patients without VA-ECMO (*Table 1*). Regarding laboratory parameters, VA-ECMO patients had higher levels of albumin compared with non-VA-ECMO patients. Intraoperative duration of surgery, cardiopulmonary bypass, and total ischaemia time were significantly longer in VA-ECMO group (*Table 1*). The use of continuous veno-venous haemodialysis, neurological complications, and resternotomy rates were higher in these patients compared with non-VA-ECMO patients (*Table 1*). In addition, reasons for hospital admissions and durations of hospital stays within the first year after HTX did not

Figure 1 Flow chart. HTX, heart transplantation; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VV-ECMO, veno-venous extracorporeal membrane oxygenation.

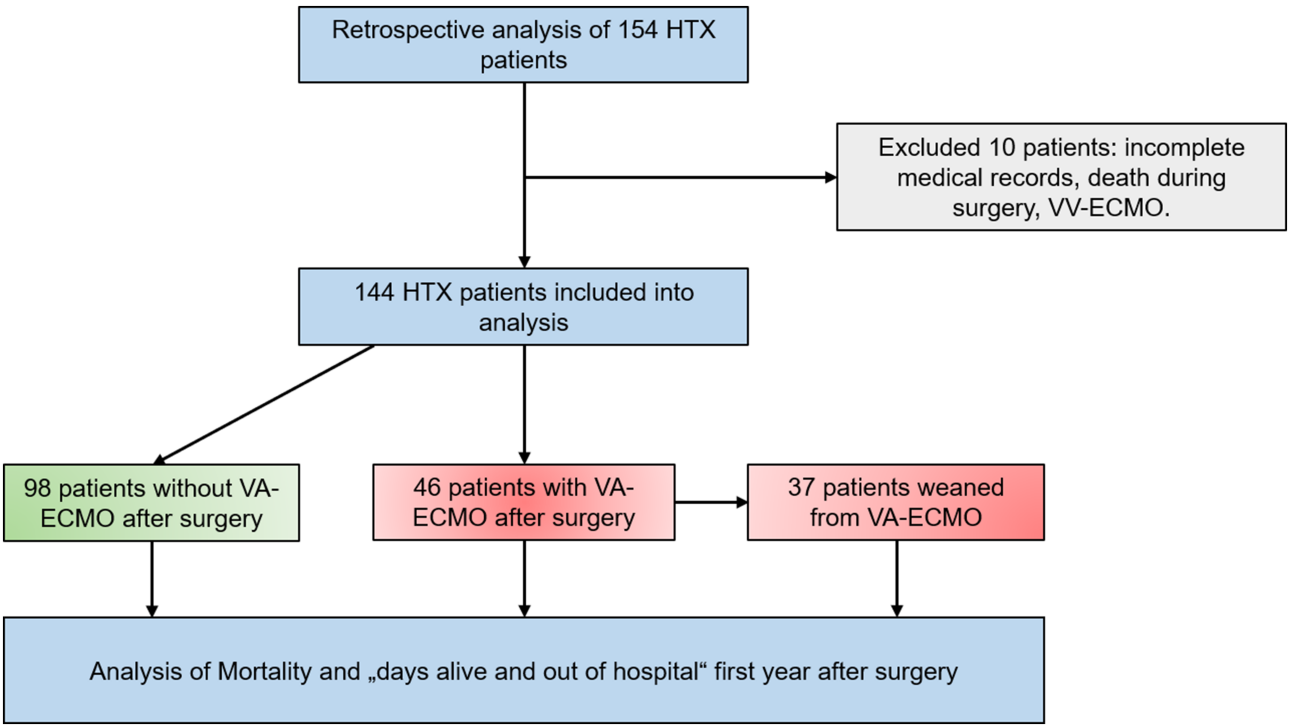

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Table 1 Baseline characteristics, co-morbidities, laboratory parameters, and intraoperative and post-operative parameters

	Non-ECMO patients (N = 98)	ECMO patients (N = 46)	P-value[a]
Baseline characteristics			
Male sex, no. (%)	77 (78.7%)	37 (80.4%)	0.999
Age (years)	54 ± 12	58 ± 9	**0.031**
BMI (kg/m^2)	25.3 ± 4.3	26.1 ± 5	0.360
MELD score	14.2 ± 6.6	14.8 ± 7.6	0.658
Co-morbidities, no. (%)			
Smokers	21 (21.4%)	11 (23.9%)	0.830
Diabetes	15 (15.3%)	14 (30.4%)	**0.045**
Hyperlipidaemia	32 (32.7%)	15 (32.6%)	0.999
Arterial hypertension	48 (49.0%)	30 (65.2%)	0.076
Pulmonary hypertension	9 (9.2%)	7 (15.2%)	0.393
COPD	10 (10.2%)	3 (6.5%)	0.551
CKD requiring dialysis	3 (3.1%)	4 (8.7%)	0.210
VAD	53 (54.1%)	29 (63.0%)	0.368
Laboratory parameters before surgery			
Creatinine (mg/dL)	1.40 ± 1.10	1.49 ± 0.64	0.580
GFR (mL/min)	62 ± 23	62 ± 29	0.983
Haemoglobin (g/dL)	11.8 ± 2.1	11.5 ± 3.2	0.538
Haematocrit (%)	36.4 ± 5.6	35.6 ± 9.6	0.610
aPTT (s)	37 ± 13	34 ± 9	0.110
Quick (%)	46 ± 29	46 ± 26	0.970
Bilirubin (mg/dL)	0.64 ± 0.75	0.69 ± 1.12	0.732
Albumin (g/L)	1.52 ± 1.98	2.36 ± 2.07	**0.020**
LDH (mg/dL)	290 ± 388	370 ± 343	0.232
Intraoperative parameters			
Duration of surgery (min)	417 ± 98	528 ± 100	<**0.0001**
Duration of CPB (min)	249 ± 64	317 ± 73	<**0.0001**
Total ischaemia time (min)	214 ± 43	239 ± 68	**0.011**
Post-operative parameters, no. (%)			
CVVHD	47 (48.0%)	36 (78.3%)	**0.001**
Neurological complications	11 (11.2%)	13 (28.3%)	**0.016**
Resternotomy	11 (11.2%)	31 (67.4%)	<**0.0001**

aPTT, activated partial thromboplastin time; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; CVVHD, continuous veno-venous haemodialysis; ECMO, extracorporeal membrane oxygenation; GFR, glomerular filtration rate; LDH, lactate dehydrogenase; MELD, model for end-stage liver disease; VAD, ventricular assist device.
Data are presented as mean ± standard deviation or as absolute values with percentages, as appropriate. Bolded values indicate significant differences between both groups.
[a]P value of χ^2 test or two-tailed unpaired t-test after Levene's test for equality of variances.

Table 2 Reasons for hospital admissions and durations of hospital stays within the first year after heart transplantation

Reason for hospital admission	Days of hospital stay Non-ECMO patients (N = 98)	Days of hospital stay ECMO patients (N = 46)	P-value[a]
HTX	40 ± 28	55 ± 41	**0.029**
Endomyocardial biopsy	7 ± 4	6 ± 3	0.162
Gastrointestinal disorders	19 ± 14	9 ± 3	0.173
Pneumonia/respiratory infections	16 ± 7	30 ± 17	0.071
Wound infection/impaired wound healing	18 ± 22	29 ± 35	0.512
AKI	11 ± 7	10 ± 2	0.875
Graft rejection reaction	17 ± 21	13 ± 9	0.717
Bleeding complications	21 ± 9	21 ± 16	0.953
Non-cardiac surgery	7 ± 2	19 ± 16	0.083
Other infections	24 ± 29	27 ± 18	0.839

AKI, acute kidney injury; ECMO, extracorporeal membrane oxygenation; HTX, orthotopic heart transplantation.
Data are presented as mean ± standard deviation. Bolded values indicate significant differences between both groups.
[a]P value of two-tailed unpaired t-test after Levene's test for equality of variances.

differ between groups. Patients with VA-ECMO had significantly longer initial hospital stay compared with non-VA-ECMO patients (non-VA-ECMO 40 ± 28 days vs. VA-ECMO 55 ± 41 days; P = 0.029; *Tables 1* and *2*).

Survival analysis

Overall mortality of the whole cohort was 20.8%. Patients without VA-ECMO therapy had significant lower rates of 1 year

mortality after HTX compared with patients who had VA-ECMO [non-ECMO 14.3% (14/98) vs. VA-ECMO 34.8% (16/46), HR: 0.32, 95% CI: 0.15–0.74; P = 0.002]. However, mortality did not differ significantly between weaned VA-ECMO patients and non-ECMO patients at 1 year after HTX [non-VA-ECMO 14.3% (14/98) vs. VA-ECMO (weaned) 18.9% (7/37), HR: 0.72, 95% CI: 0.27–1.90; P = 0.48] (*Figure 2*).

Days alive and out of hospital

Overall, median DAOH of the whole cohort were 293 (interquartile range 224–321). Data did not pass normality testing. DAOH were significantly higher in non-VA-ECMO patients compared with VA-ECMO patients [non-ECMO vs. VA-ECMO: 310 (277–327) days vs. 243 (0–288) days; $P < 0.0001$]. Non-VA-ECMO patients also had significantly higher rates of DAOH compared with patients weaned from VA-ECMO [non-ECMO vs. VA-ECMO (weaned): 310 (277–327) days vs. 253 (208–299) days; $P < 0.0001$] (*Figure 3*). In a sensitivity analysis using the alternative definition of DAOH from the non-cardiac surgery setting, results were comparable (Supporting Information, *Figure S1*).

Prediction of days alive and out of hospital in a linear regression model

We determined the influence of VA-ECMO and other covariates on DAOH in a multivariate linear regression model with DAOH as dependent variable. In addition to VA-ECMO therapy, we included age, duration of surgery, continuous veno-venous haemodialysis, and neurological complications as independent variables. The R^2 for the overall model was 0.258 (adjusted R^2 = 0.231) and therefore indicates a moderate goodness of fit. ANOVA analysis revealed that the included parameters could significantly predict DAOH with a significance level of <0.0001. In this multivariate linear regression model, VA-ECMO and neurological complications showed a significant impact on DAOH (VA-ECMO—unstandardized coefficients B: −54.10, standard error: 22.19, 95% CI −97.99 to −10.22, P = 0.016; neurological complications—unstandardized coefficients B: −91.14, standard error: 24.78, 95% CI −140.15 to −42.13, P = 0.0003) (*Table 3*). Of note, multivariable logistic and linear regression models showed no influence of continuous veno-venous haemodialysis, neurological complications, resternotomy, and ECMO cannulation type on DAOH, mortality, and successful weaning in a subgroup analysis of 46 VA-ECMO patients (Supporting Information, *Tables S1–S3*).

Post factum analysis

Based on review process, a *post factum* analysis of the yearly incidence of PGD and VA-ECMO after HTX revealed that there was a change over time. While in the first 5 years (2010–2014), PGD with VA-ECMO was present in 7/45 patients (= 15.6%), there were 39/99 (= 39.4%) HTX patients with PGD and VA-ECMO between 2015 and 2019. To address a potential centre bias, we performed a sensitivity analysis and compared the two observation periods, which did not change the results.

Discussion

The present study reveals two main findings: first, mortality at 1 year after HTX did not differ between weaned VA-ECMO

Figure 2 (A) Survival in non-extracorporeal membrane oxygenation (non-ECMO) patients is higher as compared with extracorporeal membrane oxygenation (ECMO) patients 1 year after heart transplantation (HTX). (B) Survival does not differ between non-ECMO patients and patients weaned from ECMO 1 year after HTX. CI, confidence interval; HR, hazard ratio.

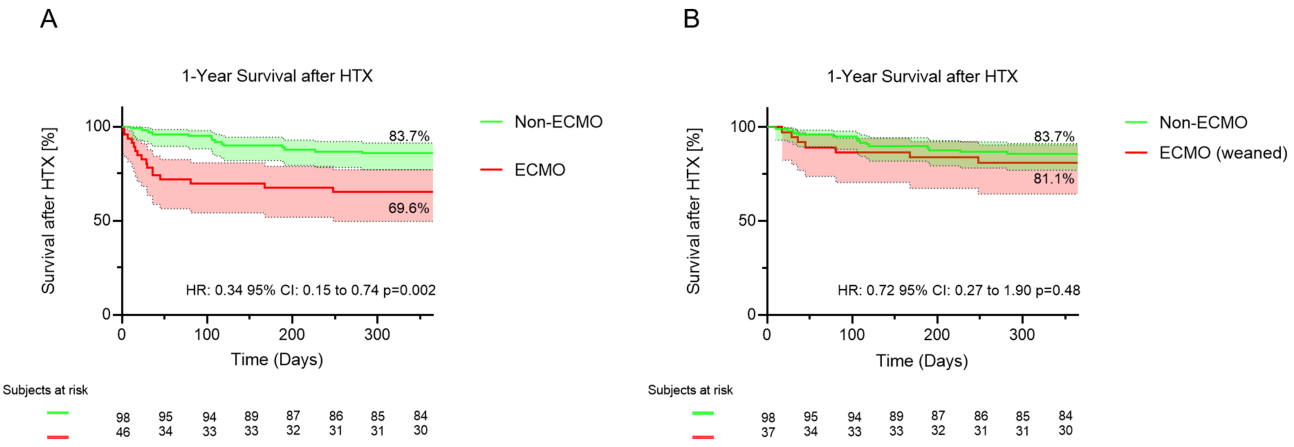

Figure 3 (A) Non-extracorporeal membrane oxygenation (non-ECMO) patients had significantly higher rates of 'days alive and out of hospital' (DAOH) as compared with extracorporeal membrane oxygenation (ECMO) patients 1 year after heart transplantation (HTX). (B) Non-ECMO patients had significantly higher rates of DAOH as compared with patients weaned from ECMO 1 year after HTX.

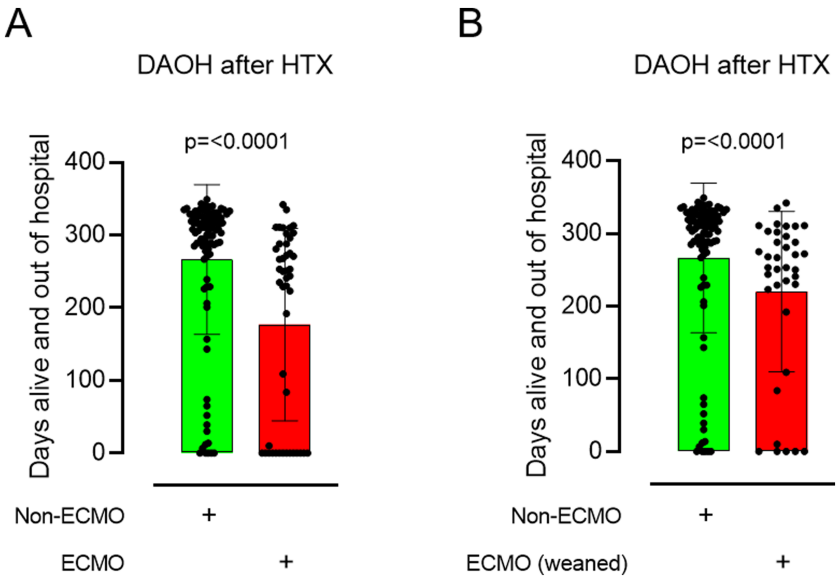

Table 3 Prediction of days alive out of hospital in a multivariate linear regression model

Model with DAOH as dependent variable	Unstandardized coefficients (*B*/standard error)	Standardized coefficients	95% CI of *B*	*P*-value[a]
Constant	376.83/59.26		259.65 to 494.01	<**0.0001**
VA-ECMO therapy	−54.10/22.19	−0.211	−97.99 to −10.22	**0.016**
Age	−1.29/0.81	−0.119	−2.85 to 0.15	0.112
Neurological complications	−91.14/24.78	−0.284	−140.15 to −42.13	**0.0003**
CVVHD	−37.10/19.15	−0.153	−74.97 to 0.77	0.055
Duration of surgery	−0.031/0.091	−0.029	−0.21 to 0.15	0.731

CI, confidence interval; CVVHD, continuous veno-venous haemodialysis; DAOH, days alive out of hospital; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.
Bolded values indicate significant differences between both groups.
[a]*P* value of multivariate linear regression.

patients receiving VA-ECMO therapy due to PGD and patients not receiving VA-ECMO therapy. This is remarkable as PGD is a relevant complication and VA-ECMO is a really invasive therapy. Second, weaned VA-ECMO patients had significantly lower DAOH compared with non-VA-ECMO patients at 1 year after HTX. Therefore, although survival is the same, VA-ECMO therapy due to PGD seems to have a relevant life impact in patients after HTX as these patients stay significantly longer in hospital during the first year after surgery.

Impact of veno-arterial extracorporeal membrane oxygenation on mortality

To date, there is limited evidence regarding the impact of VA-ECMO due to PGD in patients after HTX on outcome. According to our literature research, all existing studies had a retrospective design and no randomized trials exist so far. Focusing on short-term outcome, 45–80% of patients receiving VA-ECMO due to PGD survived until hospital discharge and the duration of VA-ECMO varied from 4 to 8 days.[3] Considering long-term outcome, current literature reports similar survival rates between patients weaned from VA-ECMO and non-VA-ECMO patients. D'Alessandro *et al*. retrospectively investigated the impact of temporary VA-ECMO due to early graft failure on mortality and 1 year survival in 394 HTX patients of whom 54 patients were treated with VA-ECMO. This study reported that VA-ECMO patients have the same survival rate compared with patients without PGD.[6] Another retrospective study by Marasco *et al*. also investigated 239 HTX patients with similar results: There was no difference in overall survival between non-VA-ECMO patients and weaned VA-ECMO patients with PGD.[17] Notably, this study defined weaned VA-ECMO patients as surviving the first 30 days and not only surviving VA-ECMO therapy as defined in the present study. In addition, there are also studies that

investigated VA-ECMO impact on survival at >1 year. Loforte *et al*. not only included patients treated with VA-ECMO but also intra-aortic balloon pump. The authors demonstrated in a retrospective analysis of 412 HTX patients that patients who survived and were treated with intra-aortic balloon pump or VA-ECMO due to PGD have the same long-term conditional survival rate at 5 years after surgery as patients who have not suffered from PGD.[11]

Definition of days alive and out of hospital

Regarding the current literature, two forms to calculate DAOH have been suggested. The difference consists in the evaluation of death within the study period. While the first definition by Ariti *et al*. counts every day patients were alive and not in hospital regardless of death within the observation period,[15] the second definition by Myles *et al*. assigns DAOH of 0 days if patients die.[18] In this study, we decided to choose the definition by Ariti *et al*. as this approach was employed in heart failure patients and thus in a cohort that is more comparable with HTX patients. Furthermore, 1 year mortality after HTX is reported to be ~15%[19] and is therefore higher than in perioperative non-cardiac surgery settings.[20] Overall mortality in our study was 20.8%. We decided to use the definition by Ariti *et al*. to calculate DAOH, as the definition by Myles *et al*. might underestimate DAOH after HTX. Nevertheless, we performed a sensitivity analysis using the definition by Myles *et al*., which revealed that the results were comparable (Supporting Information, *Figure S1*).

Impact of veno-arterial extracorporeal membrane oxygenation on days alive and out of hospital

The findings of our study regarding impact of VA-ECMO on mortality are in line with the mentioned literature and confirm that weaned VA-ECMO patients seem to have similar 1 year survival chances as non-VA-ECMO patients after HTX. However, in recent years, serious concerns have been raised if 'surviving the procedure' is the only meaningful measure of outcome. In this context, there might be other factors from a patient's point of view such as quality of life or functionality in daily life. Therefore, more patient-centred outcomes have been suggested recently. In the present study, DAOH was chosen as a measure of life impact. Data on DAOH after HTX do not exist yet so that the results of our study add new information to the current literature. First, we could show that DAOH are significantly lower in patients surviving VA-ECMO due to PGD compared with non-VA-ECMO patients after HTX. A multivariate linear regression revealed that after adjustment for age, neurological complications, renal replacement therapy, and duration of surgery, impact of VA-ECMO on DAOH was still significant. The only variable that also revealed a significant association with DAOH was 'neurological complications'. This clarifies that despite similar survival rates, VA-ECMO therapy has a relevant life impact in this cohort. Furthermore, we investigated not only the absolute number of DAOH at 1 year but also the duration of hospital stays for specific reasons. As presented in *Table 2*, a significant finding was that patients with VA-ECMO had a longer initial hospital stay compared with patients not treated with VA-ECMO. This suggests that impact of VA-ECMO therapy due to PGD after HTX on DAOH is mainly driven by prolonged initial hospital stay in these patients. The finding is supported by the fact that important variables such as age, duration of surgery, duration of cardiopulmonary bypass, and total ischaemia time of the donor heart were also significantly higher in patients who received VA-ECMO therapy afterwards. Most of these factors are associated with PGD. However, these findings were not associated with increased 1 year mortality in this study but with notable life impact, which seems surprising. This depicts the need for new concepts, especially in cases where long ischaemia or cardiopulmonary bypass times cannot be avoided and risk for PGD is high.

Referring to the existing literature, several studies came to similar conclusions. For example, Jalowiec *et al*. found in a retrospective study with 269 HTX patients that the length of the initial HTX hospital stay is the third strongest predictor for rehospitalizations during the first year after surgery.[21] Another large retrospective cohort study by Crawford *et al*. included 16 723 HTX patients and revealed that the risk for a prolonged hospital stay can already be determined at the time of HTX as it is mainly influenced by preoperative and intraoperative factors such as cold ischaemic time.[22] But despite the fact that prolonged HTX surgery (including the other intraoperative variables) could be a marker for adverse clinical outcomes, our linear regression model could not detect significant association with DAOH.

Finally, for the first time, this study provides epidemiological data on DAOH after HTX that might serve as a basis for future clinical trials investigating new methods in the prevention of PGD using DAOH as primary endpoint.

Limitations

This study has several limitations. First, this is a retrospective single-centre study. However, the majority of our data has been extracted from a prospectively conducted database. This ensures high data quality. Unfortunately, relevant parameters as SOFA score, SAVE score, or maximum lactate levels could not be assessed retrospectively as they were

not recorded in this database. Future studies should investigate the impact of VA-ECMO on outcome after HTX with a prospective design. Second, to assess the influence of covariates, multivariate linear regression was used. Nevertheless, other covariates that have not been included into analysis may have influenced our results. Third, we cannot guarantee that every hospitalization was reported as patients may have entered another hospital without our knowledge. However, HTX patients represent a cohort that is closely connected to our centre, and it is very unlikely that these patients are hospitalized elsewhere within the first year after HTX. Fourth, the sample size of 154 patients in a 10 year period is rather small, which raises concerns of a potential centre bias in regard of the overall experience with HTX patients. However, all our HTX patients are treated by the same specialized team so that expertise in this area may be regarded as good. Fifth, patients with other mechanical circulatory support devices such as combined VA-ECMO and Impella were not excluded in this study. Future studies should consider if the use of further devices might have an influence on DAOH.

Conclusions

Despite similar survival rates, VA-ECMO due to PGD after HTX has a relevant life impact as these patients spend significantly more time in hospital during the first year after surgery. Thus, DAOH may contribute to a more comprehensive assessment of outcome in this cohort.

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Conflict of interest

The authors report no conflict of interest or financial disclosures related to the current research project.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. DAOH analysis according to the alternative definition of DAOH.
Figure S2. Mortality analysis for the period 2010-2014.
Figure S3. DAOH analysis for the period 2010-2014.
Figure S4. Mortality analysis for the period 2015-2020.
Figure S5. DAOH analysis for the period 2015-2020.
Table S1. Multivariate logistic regression for association of selected variables with mortality in subgroup of VA-ECMO patients.
Table S2. Multivariate logistic regression for influence of selected variables on successful weaning in subgroup of VA-ECMO patients.
Table S3. Multivariate linear regression for influence of selected variables on DAOH in subgroup of VA-ECMO patients.

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