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ORIGINAL ARTICLE

Days alive and out of hospital after left ventricular assist device implantation

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Abstract

Aims Implantation of left ventricular assist devices (LVADs) as a bridge to transplant or as destination therapy is increasing. The selection of suitable patients and outcome assessment belong to the key challenges. Mortality has traditionally been a focus of research in this field, but literature on quality of life is very limited. This study aimed to identify perioperative factors influencing patients' life as measured by days alive and out of hospital (DAOH) in the first year after LVAD implantation.

Methods and results This retrospective single-centre cohort study screened 227 patients who underwent LVAD implantation at the University Hospital Duesseldorf, Germany, between 2010 and 2020. First, the influence of 10 prespecified variables on DAOH was investigated by univariate analysis. Second, multivariate quantile regression was conducted including all factors with significant influence on DAOH in the univariate model. Additionally, the impact of all variables on 1 year mortality was investigated using Kaplan–Meier curves to oppose DAOH and mortality. In total, 221 patients were included into analysis. As pre-operative factors, chronic kidney disease (CKD), pre-operative mechanical circulatory support (pMCS), and Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) stadium < 3 were associated with lower DAOH at 1 year [CKD: 280 (155–322) vs. 230 (0–219), $P = 0.0286$; pMCS: 294 (155–325) vs. 243 (0–293), $P = 0.0004$; INTERMACS 1: 218 (0–293) vs. INTERMACS 2: 264 (6–320) vs. INTERMACS 3: 299 (228–325) vs. INTERMACS 4: 313 (247–332), $P \leq 0.0001$]. Intra-operative additional implantation of a right ventricular assist device (RVAD) was also associated with lower DAOH [RVAD: 290 (160–325) vs. 174 (0–277), $P \leq 0.0001$]. As post-operative values that were associated with lower DAOH, dialysis and tracheotomy could be identified [dialysis: 300 (252–326) vs. 186 (0–300), $P \leq 0.0001$; tracheotomy: 292 (139–325) vs. 168 (0–269), $P \leq 0.0001$]. Multivariate analysis revealed that all of these factors besides pMCS were independently associated with DAOH. According to Kaplan–Meier analysis, only post-operative dialysis was significantly associated with increased mortality at 1 year (survival: no dialysis 89.4% vs. dialysis 70.1%, hazard ratio: 0.56, 95% confidence interval: 0.33–0.94; $P = 0.031$).

Conclusions The results of this study indicate that there can be a clear discrepancy between hard endpoints such as mortality and more patient-centred outcomes reflecting life impact. DAOH may relevantly contribute to a more comprehensive selection process and outcome assessment in LVAD patients.

Keywords Heart failure; Cardiac surgery; Quality of life; Mechanical circulatory support; Patient-centred outcomes

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Introduction

Implantable left ventricular assist devices (LVADs) are increasingly used as a bridge to heart transplantation strategy or as destination therapy for patients with end-stage heart failure.[1–3] Although outcomes have continuously improved in recent years, the selection of patients who really profit from LVAD implantation remains one of todays' key challenges and there is good evidence that appropriate selection is critical for improved outcomes.[4–7] Numerous studies tried to identify perioperative factors influencing patient outcome; for example, an Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) analysis in 2019 revealed that age is a significant predictor of mortality.[8] Further factors such as post-operative acute kidney injury requiring dialysis or intra-operative right ventricular failure have also been shown to be associated with reduced survival rates.[9–13] While mortality has been traditionally in the focus of research in this field, literature on factors influencing patients' life is very limited, although this knowledge might be of utmost importance to decide whether a patient could really profit from LVAD implantation or not. Days alive and out of hospital (DAOH) is a potentially useful quality measure in this context that has been suggested to quantify life impact.[14–16] It combines several clinically important outcomes including death, length of hospital stay, hospital readmissions, and (indirectly) health care costs. Further advantages of DAOH include its patient-centredness, its easy collection (including dispensability of adjudication), and statistical efficiency.[16]

Against this background, the aim of this study was to identify perioperative factors with impact on patients' life as measured by DAOH within the first year after surgery. Our primary hypothesis was that there is a discrepancy between mortality and DAOH for several variables.

Methods

Study design

The present study is a retrospective, single-centre cohort study that was conducted in accordance with the guidelines for good clinical practice (GCP) and the Declaration of Helsinki. The study was approved by the ethical review board of the Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany (reference number 2020-1058). All patients gave written informed consent in the past to be registered in a dedicated prospective local database. This manuscript follows the STROBE reporting guidelines for retrospective cohort studies.

Participants

Consecutive patients aged ≥18 years who received LVAD implantation due to ischaemic heart disease or dilated cardiomyopathy at the University Hospital Duesseldorf, Germany, between 2010 and 2020 were included. Patients with missing data or incomplete medical records regarding the primary endpoint were excluded. Patients with other underlying diseases than ischaemic heart disease or dilated cardiomyopathy leading to chronic heart failure were also excluded to ensure a more homogenous cohort.

Outcome assessment

The primary endpoint of this study was DAOH 1 year after LVAD implantation. As performed previously,[15] DAOH were calculated by summing up the days of all hospitalizations in the first year after LVAD surgery and subtracting them from 365 days. In case the patient died within the first year, the difference between survived days and 365 days was added to days of hospitalizations before subtracting them from 365 days. This method is based on the validation study of DAOH in heart failure patients.[15] As LVAD patients are very closely connected to our centre, it is unlikely that these patients are hospitalized elsewhere so that retrospective calculation of DAOH can be regarded as reliable. The main secondary endpoint was mortality 1 year after LVAD implantation to oppose DAOH and mortality.

Data collection

Patient characteristics, comorbidities, comedication, and survived days at 1 year were extracted from electronic medical records and the local electronic LVAD database. This prospective database is continuously updated and consists of patients' perioperative values, which were directly extracted from patients' charts at the intensive care unit and electronic medical records.

Identification of candidate variables

The choice of variables that were included in the analysis was primarily based on two large network studies using a Bayesian model to predict survival after LVAD implantation.[17,18] In addition, literature research was performed to find further perioperative variables that have been shown to be associated with increased mortality after LVAD implantation. Accordingly, we predefined the following 10 variables: age (≥65 vs. <65 years), type of underlying disease (ischaemic heart disease vs. dilated cardiomyopathy), INTERMACS profile, intra-operative right ventricular assist device (RVAD) implantation, surgical approach (minimally invasive surgery vs. sternotomy), pre-existing chronic kidney disease (CKD) according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria, pre-operative mechanical circulatory support (pMCS), pre-operative levosimendan therapy,

post-operative dialysis, and post-operative tracheotomy. As the nature of this study was only exploratory, the choice of these variables does not claim to be complete and there are obviously numerous other variables that may influence DAOH and mortality after LVAD implantation.

Statistical approach and analysis

We conducted a complete case analysis. We first performed univariate analysis using each of the 10 candidate variables. We then included all factors showing significant univariate association with DAOH using step-wise forced entry into the multivariate model (level of significance = $P \leq 0.05$). Additionally, the influence of each variable on 1 year mortality was investigated to oppose DAOH and mortality.

For statistical analysis, GraphPad Prism© Version 8.02 (La Jolla, California, USA) and IBM SPSS© software Version 25.0 (Armonk, NY, USA) were used. Continuous data are presented as mean ± standard deviation (SD) or as median and interquartile ranges (25–75%), as appropriate. Categorical data are presented as counts (*n*) with corresponding percentages (%). DAOH were compared by Mann–Whitney *U*-test given that these data were supposed to be skewed. Multivariate quantile regression was conducted. In this analysis, DAOH was set as a dependent variable. Survival analysis was performed using Kaplan–Meier diagrams as well as univariate and multivariate Cox regression. For INTERMACS profile, Kruskal–Wallis test and Jonckheere–Terpstra test were performed. To compare survival rates, log-rank (Mantel–Cox) test was performed and results are presented as a percentage of survival (%) with hazard ratio (HR) and 95% confidence interval (CI). As this was a retrospective and exploratory data analysis, a formal sample size calculation was not implemented.

Results

In total, 227 patients were included in the institutional database. Six patients (2.6%) had to be excluded due to incomplete medical records or other underlying diseases than ischaemic heart disease or dilated cardiomyopathy. Thus, 221 patients remained for statistical analysis (*Figure 1*). Data on the primary endpoint and all other co-variables were complete. Median DAOH in the whole cohort was 273 (interquartile range 67–321). Overall 1 year mortality was 24.9%. Detailed patient characteristics are presented in *Table 1*.

Univariate analysis of days alive and out of hospital

After univariate analysis of the prespecified variables, six variables showed significant association with DAOH. As pre-operative factors, CKD, pMCS, and INTERMACS < 3 were associated with lower DAOH [CKD: 280 (155–322) vs. 230 (0–219), $P = 0.0286$; pMCS: 294 (155–325) vs. 243 (0–293), $P = 0.0004$; INTERMACS 1: 218 (0–293) vs. INTERMACS 2: 264 (6–320) vs. INTERMACS 3: 299 (228–325) vs. INTERMACS 4: 313 (247–332), $P \leq 0.0001$]. Intra-operative additional implantation of RVAD was also associated with lower DAOH [RVAD: 290 (160–325) vs. 174 (0–277), $P \leq 0.0001$]. As post-operative values that were associated with lower DAOH, dialysis and tracheotomy could be identified [dialysis: 300

Figure 1 Study flow chart. DCM, dilated cardiomyopathy; ICM, ischaemic cardiomyopathy; LVAD, left ventricular assist device.

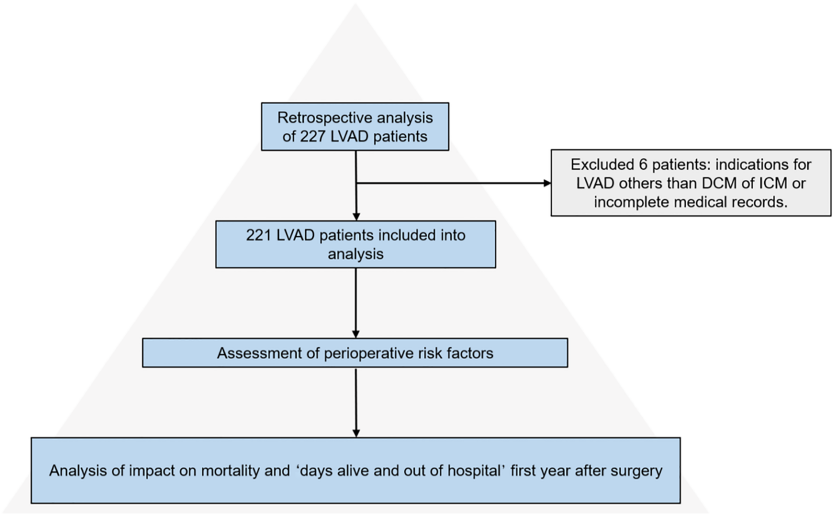


Table 1 Baseline patient characteristics

	LVAD patients (N = 221)	Survivors (N = 166)	Non-survivors (N = 55)	DAOH ≥ 273 days (N = 111)	DAOH < 273 days (N = 110)
Baseline characteristics, mean ± SD or no. (%)					
Male sex, no. (%)	191 (86.4)	144 (86.7)	47 (85.5)	100 (90.1)	91 (82.7)
Age (years)	58 ± 11	57 ± 11	59 ± 12	57 ± 12	58 ± 11
BMI (kg/m^2)	27 ± 5	27 ± 5	27 ± 6	27 ± 5	28 ± 6
LVEF (%)	18 ± 7	18 ± 7	18 ± 8	18 ± 7	17 ± 7
INTERMACS 1	84 (38)	60 (36.1)	24 (43.6)	28 (25.2)	56 (50.9)
INTERMACS 2	40 (18.1)	30 (18.1)	10 (18.2)	19 (17.1)	21 (19.1)
INTERMACS 3	41 (18.6)	32 (19.3)	9 (16.4)	29 (26.1)	12 (10.9)
INTERMACS 4	56 (25.3)	44 (26.5)	12 (21.8)	35 (31.5)	21 (19.1)
Pre-operative conditions, no. (%)					
Pre-operative mechanical circulatory support	89 (40.3)	65 (39.2)	24 (43.6)	34 (30.6)	55 (50.0)
Ischaemic heart disease	137 (62)	101 (60.8)	36 (65.5)	66 (59.5)	71 (64.5)
Dilated cardiomyopathy	84 (38)	65 (39.2)	19 (34.5)	45 (40.5)	39 (35.5)
CKD	80 (36.2)	59 (35.5)	21 (38.2)	33 (29.7)	47 (42.7)
CKD requiring dialysis	44 (19.9)	30 (18.1)	14 (25.5)	11 (9.9)	33 (30)
Levosimendan	134 (60.6)	103 (62.0)	31 (56.4)	67 (60.4)	67 (60.9)
Laboratory parameters before surgery, mean ± SD					
Creatinine (mg/dL)	1.4 ± 0.7	1.4 ± 0.8	1.5 ± 0.6	1.4 ± 0.8	1.5 ± 0.7
Bilirubin (mg/dL)	1.8 ± 2	1.7 ± 2	3.7 ± 13	1.3 ± 1	3.3 ± 9
Intra-operative conditions, no. (%)					
Minimally invasive cardiac surgery	70 (31.7)	53 (31.9)	17 (30.9)	37 (33.3)	33 (30.0)
Sternotomy	151 (68.3)	113 (68.1)	38 (69.1)	74 (66.7)	77 (70.0)
Additional RVAD implantation	51 (23.1)	39 (23.5)	12 (21.8)	13 (11.7)	38 (34.5)
Post-operative conditions, no. (%)					
Dialysis	117 (52.9)	82 (49.4)	35 (63.6)	39 (35.1)	78 (70.9)
Sepsis	37 (16.7)	28 (16.9)	9 (16.4)	10 (9.0)	27 (24.5)
Stroke	25 (11.3)	16 (9.6)	9 (16.4)	3 (2.7)	22 (20.0)
ARDS	24 (10.9)	17 (10.2)	7 (12.7)	5 (4.5)	19 (17.3)
Tracheotomy	48 (21.7)	34 (20.5)	14 (25.5)	11 (9.9)	37 (33.6)
Outcomes, median days (IQR) or no. (%)					
Days on ICU	18 (8–35)	17 (7–32)	25 (9–48)	12 (6–24)	29 (13–56)
DAOH	273 (67–321)	284 (172–321)	158 (1–293)	321 (298–333)	67 (0–232)
1 year mortality, no. (%)	55 (24.9)	0 (0)	55 (100)	18 (16.2)	37 (33.6)

ARDS, acute respiratory distress syndrome; BMI, body mass index; CKD, chronic kidney disease; DAOH, days alive and out of hospital; ICU, intensive care unit; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; IQR, interquartile range; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; RVAD, right ventricular assist device; SD, standard deviation.
Data are presented as mean ± standard deviation or as absolute values with percentages, as appropriate.

(252–326) vs. 186 (0–300), $P \leq 0.0001$; tracheotomy: 292 (139–325) vs. 168 (0–269), $P \leq 0.0001$] (*Figure 2*).

Multivariate analysis of days alive and out of hospital

Multivariate analysis using quantile regression model was performed using DAOH as dependent variable and CKD, pMCS, INTERMACS profile, intra-operative RVAD implantation, post-operative dialysis, and post-operative tracheotomy as independent variables. In this model, all factors besides pMCS showed an independent association with DAOH over different quantiles (*Figure 3*).

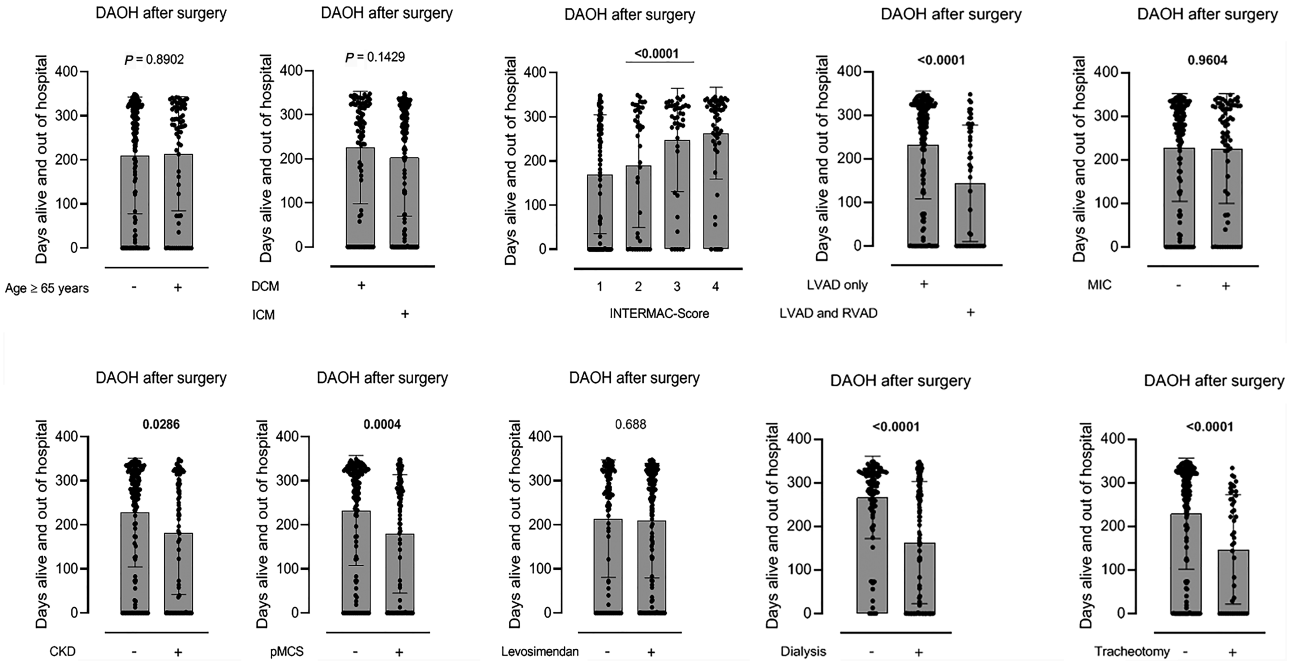
Survival analysis

According to Kaplan–Meier analysis, only post-operative dialysis was associated with significantly lower survival rates at 1 year after surgery (survival: no dialysis 89.4% vs. dialysis 70.1%, HR: 0.56, 95% CI: 0.33–0.94; P = 0.031). Univariate Cox regression confirmed these results (see Supporting Information, *Table S1*). Multivariate Cox regression revealed that none of the prespecified variables had a significant influence on 1 year mortality in this patient cohort (see Supporting Information, *Table S2*). Detailed results from Kaplan–Meier analysis are presented in *Table 2*. Kaplan–Meier curves for all 10 variables are presented in Supporting Information, *Figure S1*.

Discussion

This study investigated DAOH after LVAD implantation. The INTERMACS stadium, pre-existing CKD, RVAD, post-operative dialysis, and post-operative tracheotomy could be identified as independent factors associated with reduced DAOH. Pre-operative MCS showed a significant association

Figure 2 Univariate analysis: impact of 10 predefined variables on days alive and out of hospital after LVAD implantation. CKD, chronic kidney disease; DAOH, days alive and out of hospital; DCM, dilated cardiomyopathy; ICM, ischaemic cardiomyopathy; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; MIC, minimally invasive chest surgery; pMCS, pre-operative mechanical circulatory support; RVAD, right ventricular assist device.



with reduced DAOH only in the univariate model. Age ≥ 65 years, underlying disease, surgical approach, and pre-operative levosimendan therapy seem to have no significant impact on DAOH according to our data. Only post-operative dialysis was significantly associated with increased mortality according to Kaplan–Meier and Cox regression analysis. These results indicate discrepancies between DAOH and mortality, which is supposed to be discussed in the following (*Figure 4*).

Existing literature

To begin with a short review, there is extensive literature investigating outcomes after LVAD implantation. A huge amount of the existing studies focused on survival. A large number of patient-related and procedure-related factors associated with reduced survival could already be identified. Regarding the impact on quality of life of LVAD itself, the literature is clear: LVADs significantly improve quality of life in patients living with end-stage heart failure. But which factors do have an impact on that? As explicit data on DAOH after LVAD are scarce, we will also discuss data on other quality of life measures such as questionnaires or functional capacity.

Pavol and co-authors found out in a recently published retrospective cohort study including 59 patients that pre-operative cognitive status is suitable to predict DAOH after LVAD implantation.[19] The authors conclude that information about pre-LVAD cognition may be useful to optimize the selection of LVAD patients. Unfortunately, this study did not investigate other perioperative factors next to cognition. In a prospective comparison study, Kiernan and co-authors also tried to identify characteristics that are associated with quality of life and functional capacity response after LVAD implantation. This study included patients that were enrolled in the Heartmate II clinical trials[20] that were still alive at 6 months after LVAD implantation. Quality of life was quantified based on the Minnesota Living With Heart Failure Questionnaire or the Kansas City Cardiomyopathy Questionnaire (KCCQ). The authors concluded that several pre-operative comorbidities such as diabetes mellitus, right heart failure, and increased pulmonary artery pressure may limit quality of life. Therefore, these factors should be considered during the shared decision-making process pre-LVAD.[21] In another study by Cowger and co-authors, the European Quality of Life (EQ-5D-5L) and the KCCQ were obtained at baseline and 6 months after HeartMate 3 (n = 151) or HeartMate II (n = 138) implant as part of the MOMENTUM 3 randomized clinical trial.[22,23] This study revealed that younger age, higher pre-operative

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Figure 3 Multivariate analysis: quantile regression graphs. Due to the highly skewed nature of the primary endpoint 'days alive and out of hospital' (DAOH), a quantile regression model was performed. In contrast to linear regression, quantile regression modelling estimates how specified quantiles of the distribution of the primary outcome variable (= DAOH) vary dependent on patient-related or procedure-related characteristics. On the *x*-axis, the five quantiles are displayed. The *y*-axis displays the change of DAOH in days. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; RVAD, right ventricular assist device.

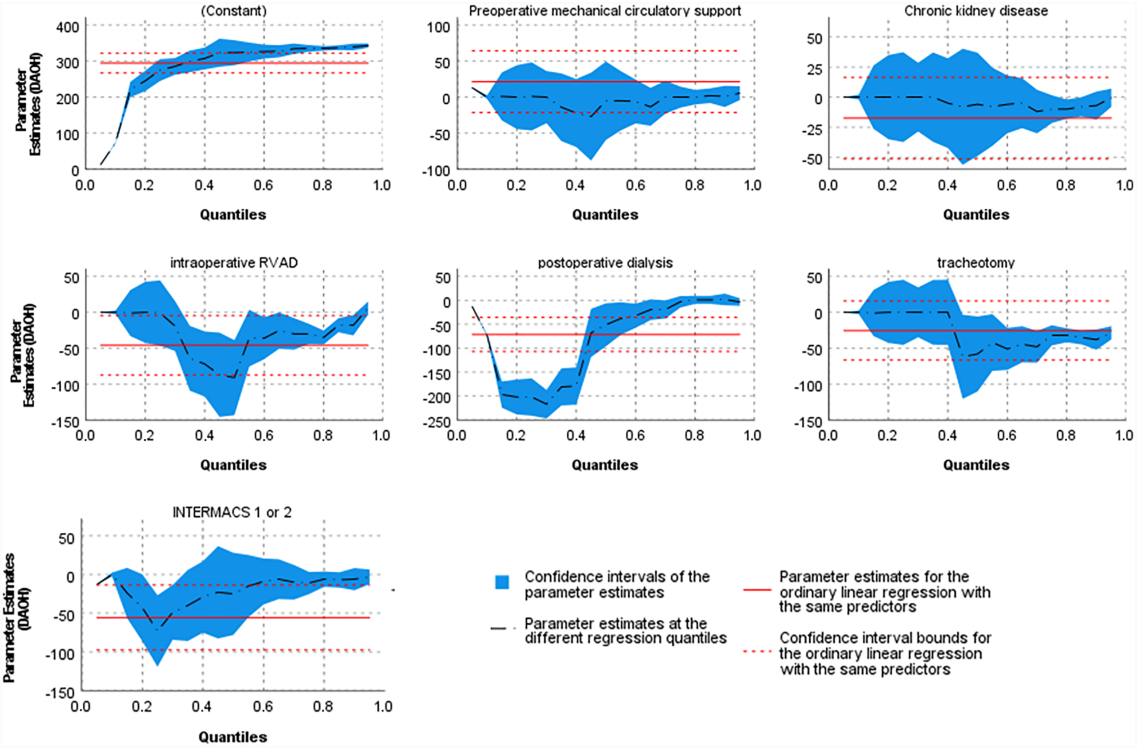
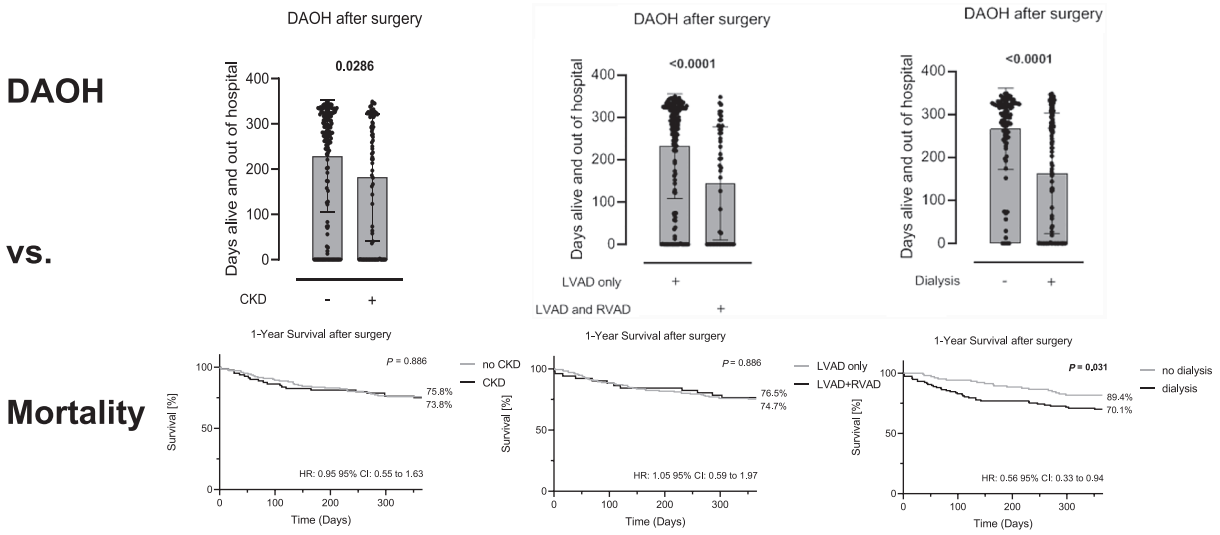


Table 2 Survival analysis

Variable	Classification	1 year survival (%)	HR	95% CI	*P* value
Age	≥65 years	74.7	1.02	0.57–1.80	0.936
	<65 years	75.3			
Underlying disease	ICM	73.7	0.93	0.54–1.61	0.813
	DCM	76.2			
INTERMACS	1	71.4	n/a	n/a	0.647
	2	75.0			
	3	78.6			
	4	78.0			
RVAD	Yes	76.5	1.05	0.59–1.97	0.886
	No	74.7			
Surgical approach	MIC	75.7	1.16	0.66–2.02	0.609
	Sternotomy	74.8			
Chronic kidney disease	Yes	73.8	0.95	0.55–1.63	0.886
	No	75.8			
Pre-op MCS	Yes	73.0	0.79	0.46–1.35	0.374
	No	76.5			
Pre-op levosimendan	Yes	76.9	1.29	0.75–2.23	0.341
	No	72.4			
Post-op dialysis	Yes	70.1	0.56	0.33–0.94	**0.031**
	No	89.4			
Post-op tracheotomy	Yes	70.8	0.77	0.40–1.46	0.385
	No	76.3			

CI, confidence interval; DCM, dilated cardiomyopathy; HR, hazard ratio; ICM, ischaemic cardiomyopathy; MCS, mechanical circulatory support; MIC, minimally invasive chest surgery; Post-op, Post-operative; Pre-op, Pre-operative; RVAD, right ventricular assist device.
Significant *P* values are presented in bold.

Figure 4 Three examples to illustrate the discrepancies between days alive and out of hospital and mortality. CI, confidence interval; CKD, chronic kidney disease; DAOH, days alive and out of hospital; HR, hazard ratio; LVAD, left ventricular assist device; RVAD, right ventricular assist device.



haemoglobin, higher baseline quality of life score, and the ability to complete the 6 min walk test pre-operatively were pre-implantation predictors for higher quality of life.

Factors influencing days alive and out of hospital and mortality after left ventricular assist device implantation

Regarding the results of the present analysis, some relevant points need to be discussed. First, this study identified not only pre-operative but also perioperative factors that seem to have an impact on DAOH. While intra-operative and post-operative factors (RVAD, dialysis, and tracheotomy) might not be modifiable, pre-operative factors (e.g. INTERMACS and CKD) might be used to optimize the selection process pre-LVAD. Our data show clearly that despite similar survival rates, lower INTERMACS profiles and pre-existing CKD are independently associated with reduced DAOH at 1 year. In addition, the information on perioperative factors without life impact might be of equal importance. For example, it is an interesting finding that age $\geq$ 65 years is not associated with reduced DAOH according to univariate analysis with age as dichotomized variable and by quartiles (*Figure 2* and Supporting Information, *Figure S2*). This might underline that higher age is not a contraindication for LVAD implantation and is strengthened by further analyses including linear regression that revealed the same results.

Second, this study shows clearly that survival rates may not always be an adequate endpoint from a patient-centred perspective. Our data reveal some interesting findings in this context: for example, temporary RVAD implantation is not associated with increased mortality but leads to a relevant reduction of DAOH. The same phenomenon could be found for INTERMACS profile, CKD, and post-operative tracheotomy. This is important knowledge from an epidemiologic perspective, but also to streamline patients and families' expectation management. From a patient point of view, it seems to be of utmost importance to know that an LVAD may be able to keep patients alive although the quality of life may be very limited under certain circumstances. DAOH is very easy to explain and to understand. This may help to improve shared decision-making.

Third, the choice of candidate variables in this study was based on two large network analyses. Both studies had a much larger sample size and analysis contained up to 10 000 LVAD patients with follow-up periods reaching from 30 days up to 2 years.[17,18] Against this background, the sample size and the follow-up period of the present study seem rather limited. While DAOH is statistically very efficient, the results of Kaplan–Meier analysis may have been influenced by that. Possibly, at least some of the included variables might get significant when increasing the sample size or length of follow-up. Nevertheless, our data should be sufficient to clarify the key message that only 'surviving the procedure' may not always be enough and to present DAOH as a sensitive marker for patients' outcome. Thus, this study might serve as 'hypothesis-generating'. In addition, we provide first epidemiologic data on DAOH after LVAD implantation in the so far largest cohort of LVAD patients. These data might be used for sample size calculations in further trials using DAOH as a primary endpoint.

Strengths and limitations

A strength of this study includes its 365 day follow-up period to calculate DAOH, which represents a more patient-centred outcome compared with mortality. Unfortunately, we cannot provide follow-up data exceeding 1 year. Further notable limitations of the study include its single-centre, retrospective nature and the limited sample size. Another relevant limitation is that only a limited number of perioperative factors influencing DAOH after LVAD implantation could be investigated. The reason for that mainly consists of the fact that other variables were not included in our database. To ensure an adequate choice of candidate variables, we based our decision on large registry data and performed a separate literature research. However, there might be additional relevant confounders that could not be included and should be investigated in future studies. Finally, a limitation is that we cannot guarantee that every hospitalization in the first year after surgery was reported as patients may have entered another hospital without our knowledge. In those cases, DAOH calculation might be incorrect. However, LVAD patients represent a cohort that is very closely connected to our centre and it is unlikely that these patients are hospitalized elsewhere without our knowledge.

Conclusions

The present study could identify a number of perioperative variables that are associated with reduced DAOH 1 year after LVAD implantation. Furthermore, this study found discrepancies between DAOH und mortality as most variables associated with reduced DAOH had no significant association with reduced survival rates. These findings indicate that only 'surviving the procedure' may not be enough and emphasize the relevance of more patient-centred outcomes reflecting life impact like DAOH. Although this is a retrospective cohort study, the results of this study may immediately be used by clinicians that are integrated into the challenging selection process of patients suitable for LVAD implantation. In addition, our data might contribute to a more comprehensive assessment of outcome in this cohort. In the future, further studies are warranted to replicate the results in a variety of larger cohorts and other settings.

Acknowledgements

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Conflict of interest

The authors have no conflict of interest to declare.

Supporting information

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

Figure S1. Kaplan–Meier graphs.
Figure S2. Univariate analysis for the association between age and „Days alive and out of hospital" (DAOH) presented by quartiles.
Table S1. Univariate Cox regression model.
Table S2. Multivariate Cox regression model.

References

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, Sisakian HS, Isayev E, Kurlianskaya A, Mullens W, Tokmakova M, Agathangelou P, Melenovsky V, Wiggers H, Hassanein M, van der Meer P. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J 2016*. 2016; **37**: 2129–2200m.
2. Miller L, Birks E, Guglin M, Lamba H, Frazier OH. Use of ventricular assist devices and heart transplantation for advanced heart failure. *Circ Res*. 2019; **124**: 1658–1678.
3. Briasoulis A, Inampudi C, Akintoye E, Adegbala O, Alvarez P, Bhama J. Trends in utilization, mortality, major complications, and cost after left ventricular assist device implantation in the United States (2009 to 2014). *Am J Cardiol* Elsevier Inc. 2018; **121**: 1214–1218.
4. Lietz K, Long JW, Kfoury AG, Slaughter MS, Silver MA, Milano CA, Rogers JG, Naka Y, Mancini D, Miller LW. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. *Circulation*. 2007; **116**: 497–505.
5. Atluri P, Goldstone AB, Kobrin DM, Cohen JE, Macarthur JW, Howard JL, Jessup ML, Rame JE, Acker MA, Woo YJ. Ventricular assist device implant in the elderly is associated with increased, but respectable risk: a multi-institutional study. *Ann Thorac Surg* Elsevier Inc. 2013; **96**: 141–147.
6. Miller LW, Guglin M. Patient selection for ventricular assist devices: a moving target. *J Am Coll Cardiol*. 2013; **61**: 1209–1221.
7. Aubin H, Petrov G, Dalyanoglu H, Saeed D, Akhyari P, Paprotny G, Richter M, Westenfeld R, Schelzig H, Kelm M, Kindgen-Milles D, Lichtenberg A, Albert A. A suprainstitutional network for

remote extracorporeal life support: a retrospective cohort study. *JACC Hear Fail*. 2016; **4**: 698–708.
8. Caraballo C, DeFilippis EM, Nakagawa S, Ravindra NG, Miller PE, Mezzacappa C, McCullough M, Gruen J, Levin A, Reinhardt S, Mullan C, Ali A, Maurer MS, Desai NR, Ahmad T, Topkara VK. Clinical outcomes after left ventricular assist device implantation in older adults: an INTERMACS analysis. *JACC Hear Fail*. 2019; **7**: 1069–1078.
9. Argiriou M, Kolokotron SM, Sakellaridis T, Argiriou O, Charitos C, Zarogoulidis P, Katsikogiannis N, Kougioumtzi I, Machairiotis N, Tsiouda T, Tsakiridis K, Zarogoulidis K. Right heart failure post left ventricular assist device implantation. *J Thorac Dis*. 2014: 6.
10. Immohr MB, Boeken U, Mueller F, Prashovikj E, Morshuis M, Böttger C, Aubin H, Gummert J, Akhyari P, Lichtenberg A, Schramm R. Complications of left ventricular assist devices causing high urgency status on waiting list: impact on outcome after heart transplantation. *ESC Hear Fail*. 2021; **8**: 1253–1262.
11. Lazar JF, Swartz MF, Schiralli MP, Schneider M, Pisula B, Hallinan W, Hicks GL, Massey HT. Survival after left ventricular assist device with and without temporary right ventricular support. *Ann Thorac Surg* Elsevier Inc;. 2013; **96**: 2155–2159.
12. Muslem R, Caliskan K, Akin S, Yasar YE, Sharma K, Gilotra NA, Kardys I, Houston B, Whitman G, Tedford RJ, Hesselink DA, Bogers AJJC, Manintveld OC, Russell SD. Effect of age and renal function on survival after left ventricular assist device implantation. *Am J Cardiol* Elsevier Inc. 2017; **120**: 2221–2225.
13. Mehdiani A, Immohr MB, Boettger C, Dalyanoglu H, Scheiber D, Westenfeld R, Aubin H, Akhyari P, Saeed D, Lichtenberg A, Boeken U. Extracorporeal membrane oxygenation after heart transplantation: impact of type of cannulation. *Thorac Cardiovasc Surg*. 2020; **69**: 263–270.
14. Moonesinghe SR, Jackson AIR, Boney O, Stevenson N, Chan MTV, Cook TM, Lane-Fall M, Kalkman C, Neuman MD, Nilsson U, Shulman M, Myles PS. Systematic review and consensus definitions for the standardised endpoints in perioperative medicine initiative: patient-centred outcomes. *Br J Anaesth Elsevier Ltd*. 2019; **123**: 664–670.
15. Ariti CA, Cleland JGF, Pocock SJ, Pfeffer MA, Swedberg K, Granger CB, McMurray JJV, Michelson EL, Östergren J, Yusuf S. Days alive and out of hospital and the patient journey in patients with heart failure: insights from the candesartan in heart failure: assessment of reduction in mortality and morbidity (CHARM) program. *Am Heart J* Mosby, Inc. 2011; **162**: 900–906.
16. Jerath A, Austin PC, Wijeysundera DN. Days alive and out of hospital: validation of a patient-centered outcome for perioperative medicine. *Anesthesiology*. 2019; **131**: 84–93.
17. Loghmanpour NA, Kanwar MK, Druzdzel MJ, Benza RL, Murali S, Antaki JF. A new Bayesian network-based risk stratification model for prediction of short-term and long-term LVAD mortality. *ASAIO J*. 2015; **61**: 313–323.
18. Kanwar MK, Lohmueller LC, Kormos RL, Teuteberg JJ, Rogers JG, Lindenfeld JA, Bailey SH, McIlvennan CK, Benza R, Murali S, Antaki J. A Bayesian model to predict survival after left ventricular assist device implantation. *JACC Hear Fail*. 2018; **6**: 771–779.
19. Pavol M, Boehme A, Yuzefpolskaya M, Maurer MS, Casida J, Festa J, Ibeh C, Willey J. Cognition predicts days-alive-out-of-hospital after LVAD implantation. *Int J Artif Organs*. 2021; **44**: 952–955.
20. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009; **361**: 2241–2251.
21. Kiernan M, Sundareswaran KS, Pham D, Kapur N, Pereira N, Strueber M, Farrar DJ, DeNofrio D, Rogers JG. Preoperative determinants of quality of life and functional capacity response to left ventricular assist device therapy. *J Card Fail*. 2016; **22**: 797–805.
22. Cowger J, Naka Y, Aaronson K, Horstmanshof D, Gulati S, Rinde-Hoffmann D, Pinney S, Adatya S, Farrar DJ, Jorde UP. Quality of life and functional capacity outcomes in the MOMENTUM 3 trial at 6 months: a call for new metrics for left ventricular assist device patients. *J Hear Lung Transplant*. 2018; **37**: 15–24.
23. Mehra MR, Uriel N, Naka Y, Cleveland JC, Yuzefpolskaya M, Salerno CT, Walsh MN, Milano CA, Patel CB, Hutchins SW, Ransom J, Ewald GA, Itoh A, Raval NY, Silvestry SC, Cogswell R, John R, Bhimaraj A, Bruckner BA, Lowes BD, Um JY, Jeevanandam V, Sayer G, Mangi AA, Molina EJ, Sheikh F, Aaronson K, Pagani FD, Cotts WG, Tatooles AJ, Babu A, Chomsky D, Katz JN, Tessmann PB, Dean D, Krishnamoorthy A, Chuang J, Topuria I, Sood P, Goldstein DJ. A fully magnetically levitated left ventricular assist device—final report. *N Engl J Med*. 2019; **380**: 1618–1627.