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REPORT

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The European Registry for Patients with Mechanical Circulatory Support of the European Association for Cardio-Thoracic Surgery: third report

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Abstract

OBJECTIVES: In the third report of the European Registry for Patients with Mechanical Circulatory Support of the European Association for Cardio-Thoracic Surgery, outcomes of patients receiving mechanical circulatory support are reviewed in relation to implant era.

METHODS: Procedures in adult patients (January 2011–June 2020) were included. Patients from centres with <60% follow-ups completed were excluded. Outcomes were stratified into 3 eras (2011–2013, 2014–2017 and 2018–2020). Adverse event rates (AERs) were calculated and stratified into early phase (<3 months) and late phase (>3 months). Risk factors for death were explored using univariable Cox regression with a stepwise time-varying hazard ratio (<3 vs >3 months).

RESULTS: In total, 4834 procedures in 4486 individual patients (72 hospitals) were included, with a median follow-up of 1.1 (interquartile range: 0.3–2.6) years. The annual number of implants (range: 346–600) did not significantly change ($P = 0.41$). Both Interagency Registry for Mechanically Assisted Circulatory Support class (classes 4–7: 23, 25 and 33%; $P < 0.001$) and in-hospital deaths (18.5, 17.2 and 11.2; $P < 0.001$) decreased significantly between eras. Overall, mortality, transplants and the probability of weaning were 55, 25 and 2% at 5 years after the implant, respectively. Major infections were mainly noted early after the implant occurred ($AER_{<3\ months}$: 1.44 vs $AER_{>3\ months}$: 0.45). Bilirubin and creatinine levels were significant risk factors in the early phase but not in the late phase after the implant.

CONCLUSIONS: In its 10 years of existence, EUROMACS has become a point of reference enabling benchmarking and outcome monitoring. Patient characteristics and outcomes changed between implant eras. In addition, both occurrence of outcomes and risk factor weights are time dependent.

Keywords: Mechanical circulatory support • Ventricular assist device • Registry • End-stage heart failure

ABBREVIATIONS

AERs	Adverse event rates
BiVAD	Biventricular assist device
CI	Confidence interval
CF-AF	Continuous flow with axial flow
CF-FML	Centrifugal flow with full magnetic levitation
CF-HL	Centrifugal flow with hybrid levitation
DT	Destination therapy
EUROMACS	European Registry for Patients with Mechanical Circulatory Support
ICUs	Intensive care units
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	Left ventricular assist device
MCS	Mechanical circulatory support

INTRODUCTION

As a registry of the European Association for Cardio-Thoracic Surgery, the European Registry for Patients with Mechanical Circulatory Support (EUROMACS) offers a robust repository of clinical data on long-term mechanical circulatory support (MCS) from a large international community. EUROMACS has enabled scientists to publish 24 papers using data from its registry, whereas another 7 studies are in progress and will be published in the course of 2021. Ultimately, providing these data on survival and morbidity for clinicians and industry representatives enables them to understand the factors that influence the results of MCS therapy in more detail.

In the third annual EUROMACS report, we focused on the changes in patient characteristics, treatment strategies and outcomes over time. In addition, we investigated the risk factors for death.

METHODS

Structure of the European Registry for Patients with Mechanical Circulatory Support

The EUROMACS registry is governed by the European Association for Cardio-Thoracic Surgery Council. The council is advised by the EUROMACS Committee with respect to its strategy and policy.

A paediatric subcommittee has been established from among the EUROMACS Committee members to carry out studies on the treatment of children with MCS.

A 'study proposals evaluation sub-committee' evaluates incoming proposals from those centres that have an agreement with and submit data to EUROMACS. If the proposal is accepted, the principal investigator receives a data set to execute the study. The selection criteria include originality, innovativeness, focus, methodology and feasibility. Of the 52 received proposals, 24 were approved, 23 were withdrawn or rejected and 5 are in process at different centres.

Data selection

Data of 6192 implants in 5735 patients who gave permission to the participating hospitals to share their data with EUROMACS were selected for this report. A flow chart of included patients is shown in Fig. 1. Procedures before 2011 and children were excluded. This EUROMACS report analysed 3 time periods: 2011–2013, 2014–2017 and 2018–2020.

Completeness and data quality

Completeness of follow-up is estimated by dividing the total observed follow-ups by the total theoretical follow-ups. This method is known as Clark C [1]. The end date used was 1 June

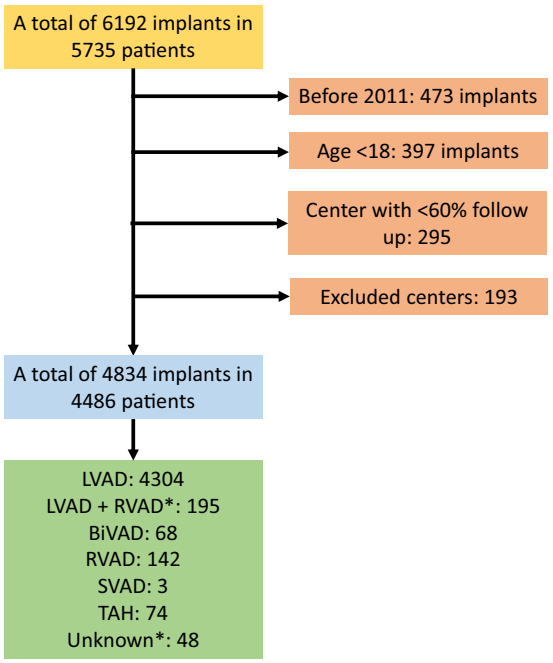

Figure 1: Flow chart of included patients. BiVAD: biventricular assist device; LVAD: left ventricular assist device; RVAD: right ventricular assist device; SVAD: subcutaneous vascular access device; TAH: total artificial heart.

2020. Completeness per centre is presented in Supplementary Material, Table S1. Data from 193 implants in 6 centres and 1 collective that ceased to provide data were excluded, and centres that had <60% completeness of data were additionally excluded in the data extraction and analyses. The EUROMACS database includes 570 baseline variables, 26 of which are included in this report. The percentage of missing values per variable is presented in Supplementary Material, Table S2. For the purpose of this analysis, only complete cases are used. Patients without any follow-up information ($n = 194$) were censored at day 1 after the index implant. If patients received a transplant and died on the same day ($n = 59$), the patient was assumed to have died during left ventricular assist device (LVAD) therapy.

End points

The primary end point of this report was death. Secondary end points included unexpected readmission, neurological events, major bleeding, major infection and pump thrombosis. End points were defined according to the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) definitions [2].

Statistical analyses

Continuous data are presented as mean (standard deviation) (Gaussian distribution) or median [interquartile range] (non-Gaussian distribution). Categorical data are presented as frequencies (percentage). Comparisons among continuous variables were made with the one-way analysis of variance or the Kruskal–Wallis test. Comparisons of categorical variables were made with the χ^2 test or with the Fisher's exact test.

Mortality on LVAD is a competing risk with weaning and a transplant; hence, Kaplan–Meier estimates overestimate the rate of an event [3]. A cumulative incidence function was computed to provide less biased estimates using Fine–Gray models [4]. Gray tests were done to compare strata [5].

Factors associated with death were explored using univariable Cox proportional hazard regression with a stepwise time-varying hazard ratio for the first 3 months and beyond 3 months. Predictors were chosen based on clinical significance. In addition, factors associated with death were explored using a constant hazard ratio. Complete case analyses were used for analyses. As a sensitivity analysis, missing baseline variables were imputed using multiple imputation. In total, 5 data sets were created using 15 iterations. Analyses were pooled according to Rubin's rules [6]. A sensitivity analysis was performed comparing patients from centres with complete follow-up (≥95%) to centres with less complete follow-up (<95%). To limit confounding, a propensity score matching approach was applied. A detailed explanation and covariate balance are provided in Supplementary Material, Text 1 and Supplementary Material, Fig. S1.

The rate of adverse events was calculated using adverse event rate (AER), calculated by dividing the total number of events by the total person-years. In addition, linearized incidence rates (%/month) were computed. The incidence rate is calculated by dividing the number of new events by total person-years. Both were stratified to early (<3 months) and late (>3 months) phases after the LVAD was implanted.

Most adverse events, such as unexpected readmission for LVAD-related morbidity, bleeding, neurological dysfunction and infection, can recur multiple times in 1 patient, affecting the mean occurrence rates. To give a comprehensive overview, considering multiple recurrent events, the cumulative mean number of events over time was calculated using a non-parametric mean cumulative function and presented in a plot [7]. Variance was estimated using the Lawless and Nadeau method [8]. Statistical analyses were done in R (Version 4.0.3) (R Foundation for Statistical Computing, Institute for Statistics and Mathematics, Vienna, Austria).

RESULTS

In total, 4834 procedures (range 1–5) were performed in 4486 individual patients (Fig. 1). The median follow-up was 1.1 (interquartile range 0.26–2.6) years. Completeness of follow-up was 87% (Clark C).

Patient demographics and hospital outcome

The number of implants performed per year did not significantly change over time ($P = 0.41$, Supplementary Material, Fig. S2). The type of device implanted changed significantly over the eras ($P < 0.001$; Supplementary Material, Table S4). The device type shifted from predominantly continuous flow–axial flow (CF-AF) and continuous flow hybrid levitation (CF-HL) to predominantly continuous flow full magnetic levitation (CF-FML) devices ($P < 0.001$, Fig. 2).

The demographics of patients who received isolated LVAD therapy are presented in Table 1. Notably, a shift from preoperative INTERMACS class 1 and 2 towards class 4 and lower was observed over the years ($P < 0.001$), whereas the pre-LVAD use of extracorporeal membrane oxygenation was similar

Table 1: Perioperative characteristics of patients with an isolated left ventricular assist device implant

Era	[2011–2013]	(2014–2016]	(2017–020]	*P*-Value
N	1795	1617	1087	
Age, median [IQR]	57.00 [48.00, 63.00]	57.00 [48.00, 63.00]	58.00 [49.00, 64.00]	0.322
Male, *n* (%)	1488 (82.9)	1373 (84.9)	908 (83.5)	0.273
Non-ischaemic cardiomyopathy, *n* (%)	888 (60.1)	855 (64.2)	606 (69.8)	<0.001
INTERMACS profile				<0.001
1: Critical cardiogenic shock, *n* (%)	236 (14.7)	236 (15.8)	135 (13.5)	
2: Progressive decline, *n* (%)	552 (34.3)	459 (30.7)	255 (25.6)	
3: Stable but inotrope dependent, *n* (%)	449 (27.9)	424 (28.4)	277 (27.8)	
4–7: Resting symptoms—NYHA 3, *n* (%)	372 (23.1)	376 (25.2)	331 (33.2)	
ECLS, *n* (%)	158 (10.0)	184 (12.6)	112 (11.5)	0.081
IABP, *n* (%)	198 (13.5)	110 (8.2)	67 (7.9)	<0.001
Temporary RVAD, *n* (%)	76 (4.2)	60 (3.7)	59 (5.4)	0.096
Diabetes, *n* (%)	415 (25.9)	416 (27.7)	269 (26.8)	0.518
IV inotropes, *n* (%)	969 (68.2)	857 (68.8)	480 (61.7)	0.002
COPD, *n* (%)	166 (11.3)	151 (11.5)	85 (9.6)	0.339
Smoking, *n* (%)	148 (17.4)	157 (16.4)	77 (11.7)	0.021
BUN, median [IQR]	49.00 [32.00, 76.80]	52.40 [33.40, 83.00]	42.00 [26.23, 72.45]	<0.001
Bilirubin, median [IQR]	1.30 [0.80, 2.10]	1.30 [0.81, 2.18]	1.18 [0.72, 2.00]	0.012
Creatinine, median [IQR]	106.00 [82.00, 144.00]	113.00 [87.00, 150.00]	112.00 [88.00, 151.00]	0.001
Pulsatile device, *n* (%)	4 (0.2)	1 (0.3)	0 (0.0)	0.172
Device strategy				<0.001
Bridge to recovery, *n* (%)	22 (1.3)	46 (3.0)	11 (1.0)	
Bridge to transplant, *n* (%)	538 (32.7)	596 (38.9)	453 (43.2)	
Destination therapy, *n* (%)	298 (18.1)	315 (20.5)	224 (21.4)	
Others, *n* (%)	4 (0.2)	2 (0.1)	2 (0.2)	
Possible bridge to transplant, *n* (%)	685 (41.6)	514 (33.5)	313 (29.9)	
Rescue therapy, *n* (%)	100 (6.1)	60 (3.9)	45 (4.3)	
Rhythm				0.001
Atrial fibrillation, *n* (%)	196 (14.1)	199 (15.5)	113 (13.1)	
Atrial flutter, *n* (%)	17 (1.2)	18 (1.4)	14 (1.6)	
Other, *n* (%)	31 (2.2)	28 (2.2)	18 (2.1)	
Paced, *n* (%)	464 (33.4)	319 (24.9)	242 (28.1)	
Sinus, *n* (%)	680 (49.0)	718 (56.0)	473 (55.0)	
Hospital outcome				
Hospital deaths, *n* (%)	291 (18.5)	242 (17.2)	108 (11.1)	<0.001
ICU/CCU stay, days, median [IQR]	11.00 [5.00, 25.00]	10.00 [5.00, 24.00]	7.00 [4.00, 17.00]	<0.001

BUN: blood urea nitrogen; CCU: cardiac care unit; COPD: chronic obstructive pulmonary disease; ECLS: extracorporeal life support; IABP: intra-aortic balloon pump; ICU: intensive care unit; IQR: interquartile range; INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; IV: intravenous; NYHA: New York Heart Association; RVAD: right ventricular assist device.

($P = 0.081$). The demographics of patients undergoing biventricular assist device (BiVAD) and isolated right ventricular assist device (RVAD) implants are presented in Supplementary Material, Tables S3 and S5.

Hospital deaths and lengths of stay in intensive care units (ICUs) for patients receiving LVAD alone decreased significantly over the years (Table 1). In the case of BiVAD and RVAD, hospital deaths and ICU–cardiac care unit stays were comparable between eras (Supplementary Material, Tables S4 and S5).

Adverse events

Early and late AERs are presented in Table 2. Infection rates were higher in the early period (<3 months) compared to the late period (1.44 vs 0.45 events/person-year) in the overall cohort.

A patient can experience multiple adverse events before a terminal event (Supplementary Material, Fig. S3). These events include readmission, bleeding, neurological dysfunction, pump thrombosis and infection. Cumulative mean numbers of events over time are presented in Fig. 3. Of note, 86 patients presented with an infection and neurological dysfunction simultaneously. At 4 years after the index implant, a patient experienced on average ~0.42 [95% confidence interval (CI) 0.37–0.45] neurological events, 0.63 (95% CI 0.57–0.69) bleedings, 2.03 (95% CI 1.89–2.16) infections, 0.36 (95% CI 0.32–0.42) pump thrombosis and 2.4 (95% CI 2.25–2.57) readmissions. The early risk of neurological events seemed to decrease in later eras (Supplementary Material, Tables S6 and S7).

Table 2: Major adverse event rates

Event	Early rate (<3 months)		Late rate (>3 months)	
	Number events	Adverse event rate	Number events	Adverse event rate
Unexpected readmission	481	0.52	4328	0.62
Major bleeding	808	0.88	866	0.12
Pump thrombosis	81	0.09	627	0.09
Neurological dysfunction	305	0.33	696	0.11
Major infection	1315	1.44	3181	0.45

Unit: number of events per person-year.

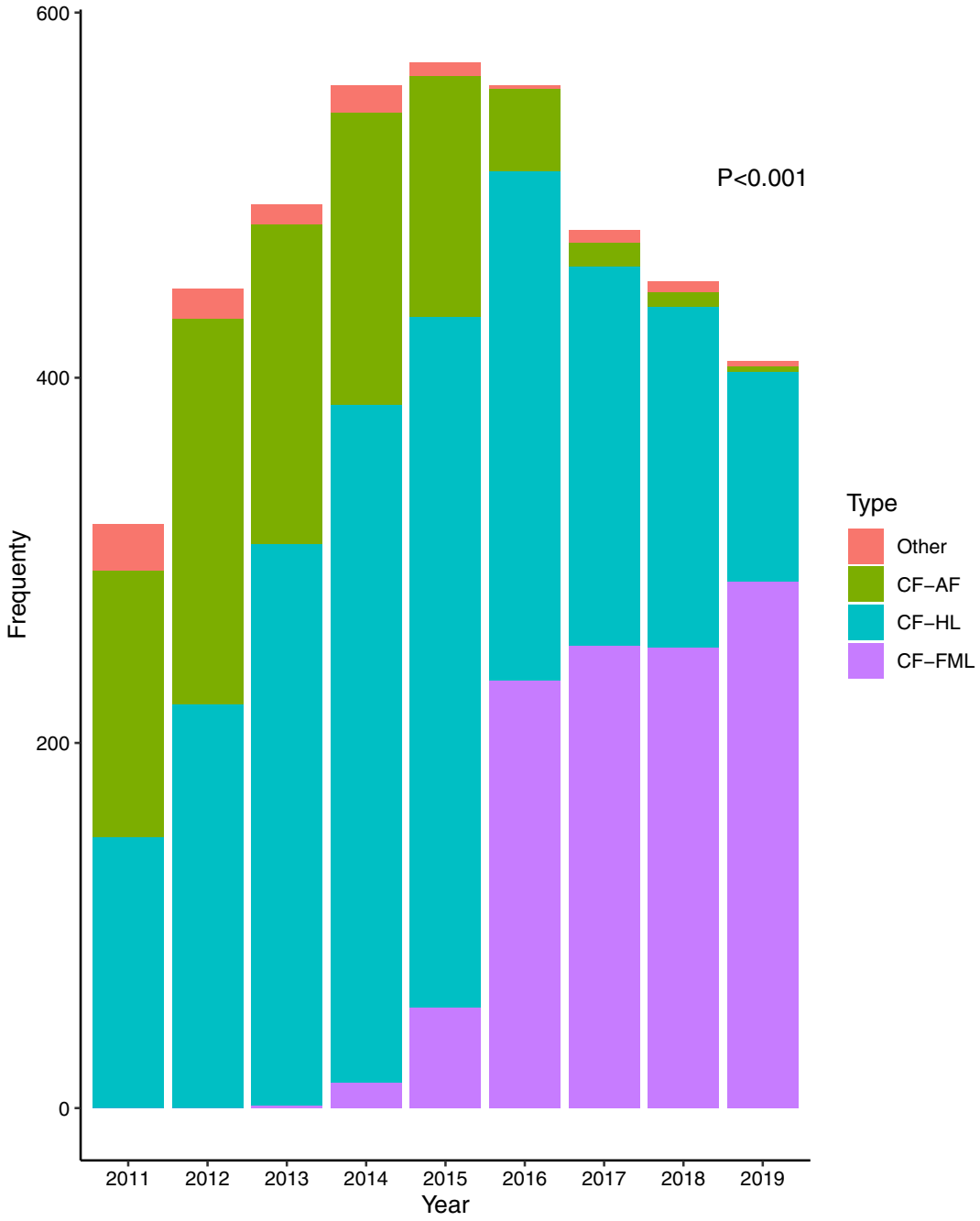

Figure 2: Temporal change in type of driver. CF-AF: continuous flow–axial flow; CF-HL: continuous flow–hybrid levitation; CF-FML: continuous flow–full magnetic levitation.

Mortality and transplantation

In total, 2036 patients died during the follow-up period, yielding an actual probability of mortality of 30.0%, 44.5% and 55.5% at 1, 3 and 5 years, respectively (Fig. 4).

Survival differed significantly among different INTERMACS classes, eras, devices and strategies (Fig. 5A–D). The cumulative mortality was higher for the CF-HL devices, especially early after they were implanted (Fig. 5B). Patients undergoing a CF-HL LVAD device implant presented in INTERMACS class 1 more frequently [19% vs 10.9% (CF-FML) and 9% (continuous flow–axial flow), $P < 0.001$] and were more often implanted in a BiVAD configuration (Supplementary Material, Table S8). However, excluding BiVAD implants yielded comparable observations (Supplementary Material, Fig. S4).

Three-month mortality in the overall cohort was found to be 17%, with a linearized incidence rate of 1.7%/month, thereafter meaning that on average 1.7% of patients will die each month (Supplementary Material, Tables S6 and S7).

In total, 864 patients were successfully given transplants, yielding an actual probability of having a transplant of 7.5%, 20.2% and 25.2% at 1, 3 and 5 years, respectively. In total, 11 patients originally listed as scheduled for destination therapy (DT) received a transplant and 3 were weaned.

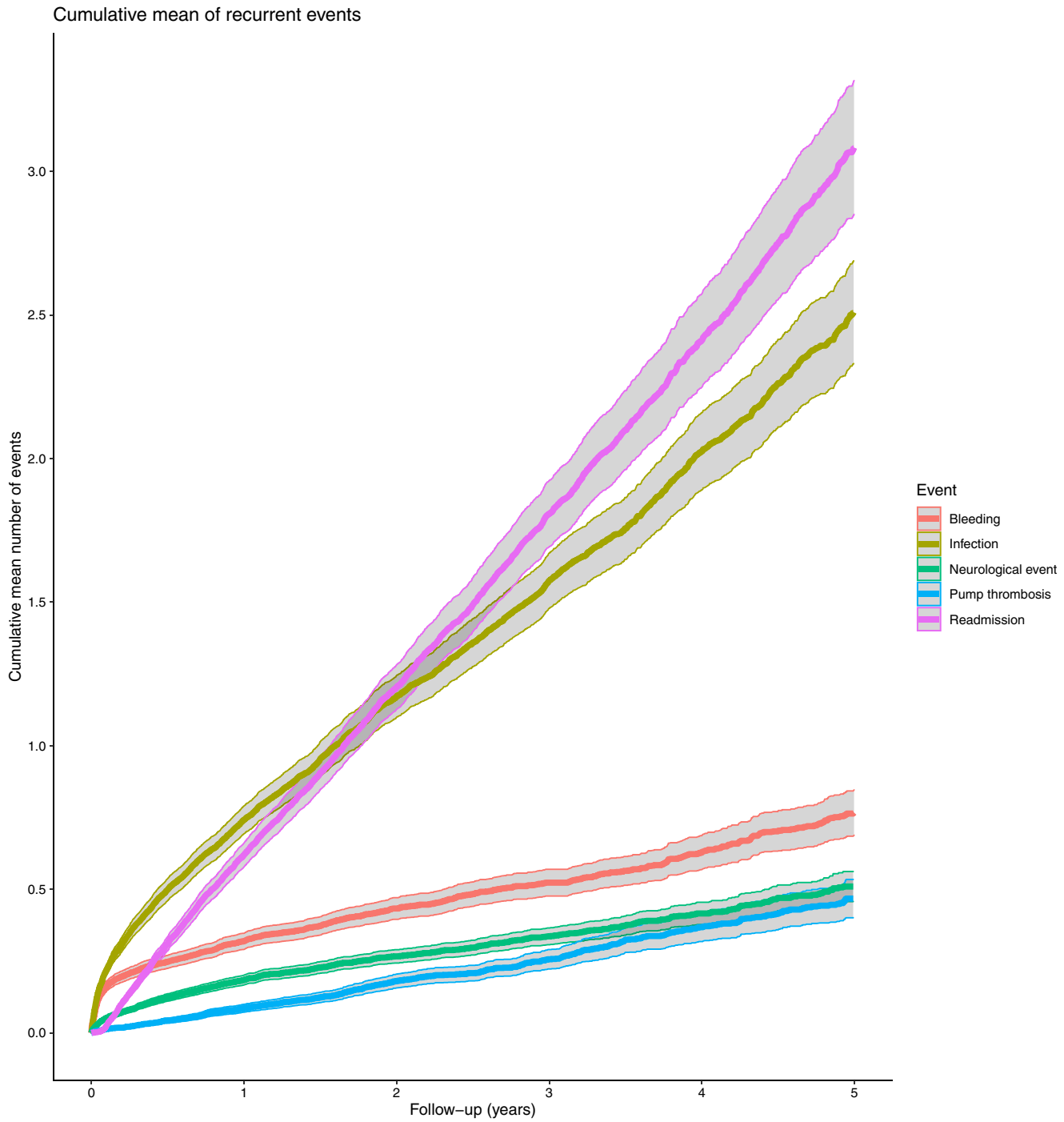

Figure 3: Cumulative mean of recurrent events.

Table 2 presents factors associated with mortality in patients having an isolated LVAD implant. Higher INTERMACS class and creatine levels were significant predictors for death in the early phase (<3 months), whereas female sex was associated with fewer deaths in the late phase (>3 months) (Table 3). This result indicates that the weights of the risk factors changed over time. A sensitivity analysis using multiple imputations for missing baseline variables revealed comparable hazard ratios and significance, except for bilirubin (Supplementary Material, Fig. S5). Missingness of bilirubin seems to depend upon other baseline variables (Supplementary Material, Table S9).

Patients from centres with <95% completeness of follow-up had survival levels comparable to those of patients from centres with less complete follow-up in a propensity score matched cohort, when centre heterogeneity was accounted for (HR: 1.31 95% CI 0.98–1.74, $P = 0.066$) (Supplementary Material, Fig. S5).

DISCUSSION

This third EUROMACS report shows a growth of participating hospitals from 52 to 72 since the second report, and the data

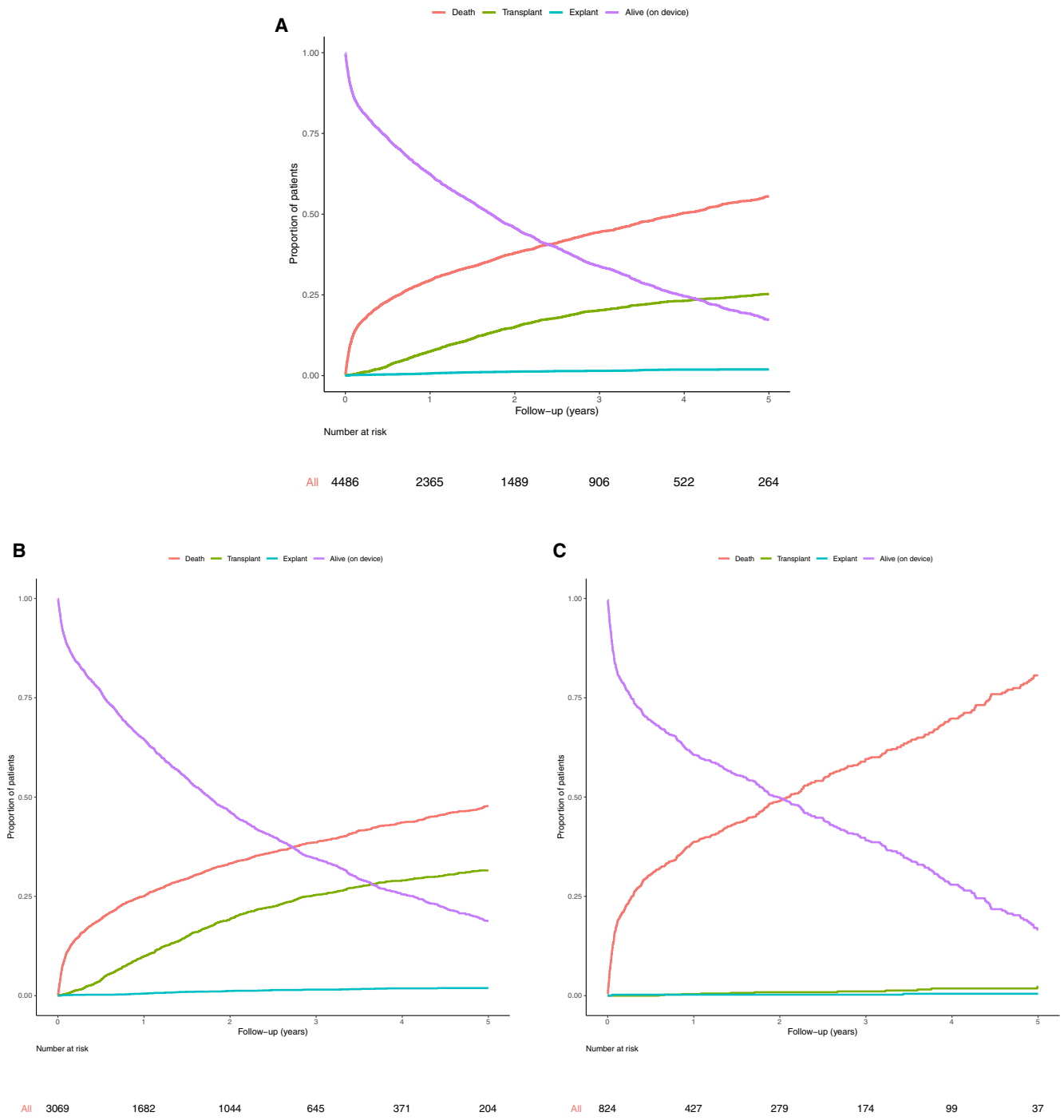

Figure 4: Competing risk plot for death, transplant, explant and ongoing therapy for the overall population (**A**), bridge to transplant (**B**) or destination therapy (**C**). Of note, some patients had the strategy bridge to recovery ($n = 82$), rescue therapy ($n = 223$) or other strategy ($n = 8$) and are not incorporated in (**B**) and (**C**).

from the registry were used in an increasing number of scientific studies [9]. In its 10 years of existence, the registry has become a point of reference enabling professionals to put MCS data as a source of scientific data into an international perspective [10–12].

The number of registered implants more than doubled from 2947 to 6192. Despite the growing incidence of chronic heart failure, the total number of implants in the participating hospitals seems to have stabilized at around 500 per annum (Supplementary Material, Fig. S1). Whether this situation reflects better medical treatment for chronic heart failure or a significant underuse of end-stage heart failure therapies due to other factors may be a subject for further studies. It must be determined if the stabilizing trend keeps in step with a similar observation in the USA [13].

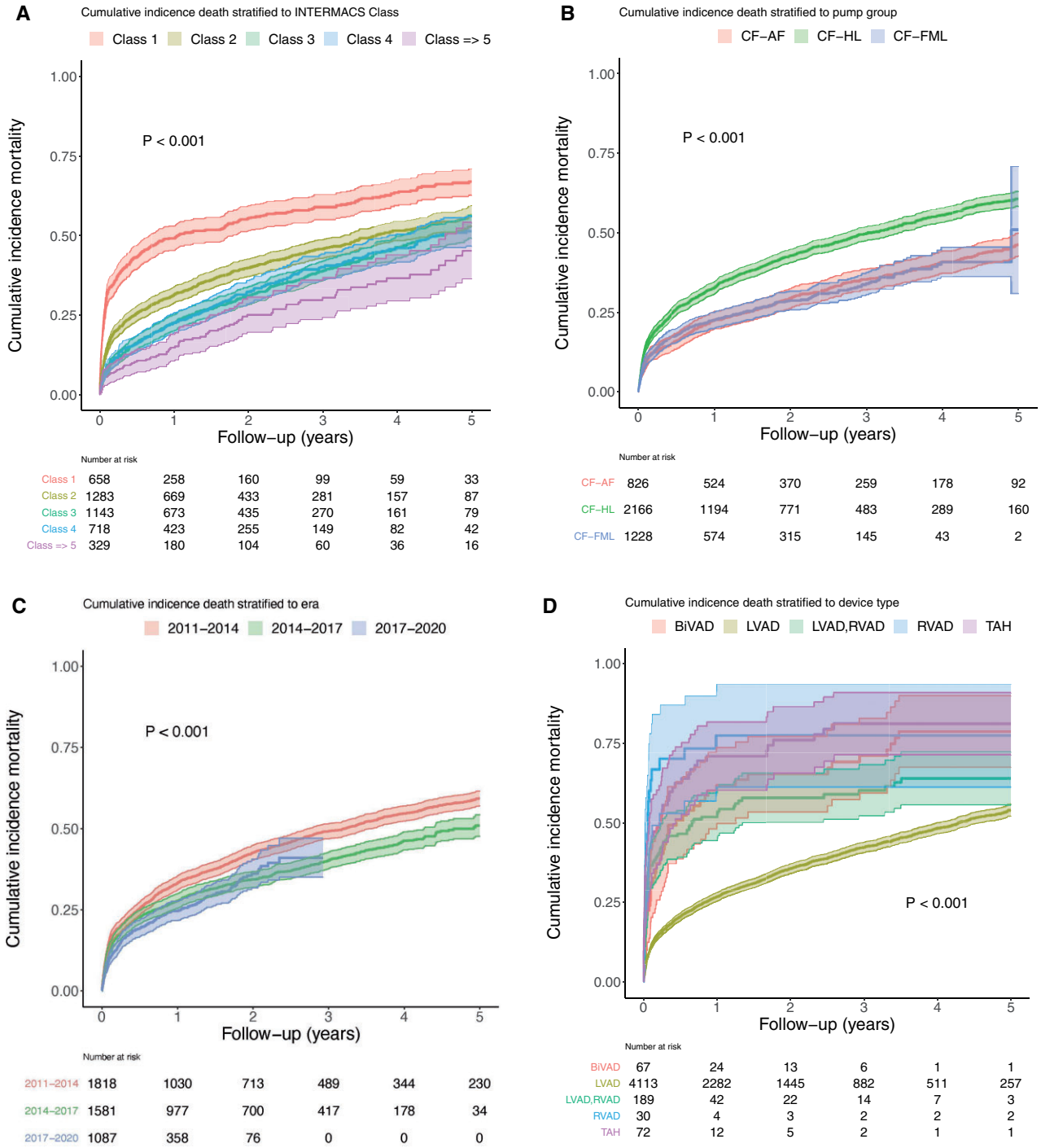

Figure 5: Cumulative incidence of death as estimated by the Fine-Gray model stratified to INTERMACS class (**A**), pump group (**B**), era (**C**) and device type (**D**). INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support.

Patient characteristics and device strategy

Compared to the situation in earlier eras, fewer patients in INTERMACS classes 1 and 2 were observed in the period 2017 to 2020. Several factors may play a role, including earlier referral of patients with heart failure and updated guidelines. These guidelines provide ground rules for weighing parameters and considerations to balance the risks and benefits and to find the right moment for an early LVAD implant. Specifically, in areas with extended waiting times for a heart transplant, optimal timing may be a leading factor in deciding for an early LVAD implant [14–16].

Another important aspect shown in the current report is a decrease of primary BiVAD use over time and a simultaneous increase of staged procedures. This change may partially be explained by patient selection. Nevertheless, 2 published studies with data from EUROMACS centres discuss this topic and the

Table 3: Early, late and constant hazard ratio for death in patients receiving a left ventricular assist device based upon univariable Cox proportional hazard models

Risk factor	Early HR (<3 months)		Late HR (>3 months)		Constant HR	
	HR (95% CI)	*P*-Value	HR (95% CI)	*P*-Value	HR (95% CI)	*P*-Value
Age	1.02 (1.02–1.03)	<0.001	1.03 (1.03–1.04)	<0.001	1.03 (1.02–1.03)	<0.001
Female	1.07 (1.3–0.87)	0.529	0.81 (0.96–0.69)	0.014	0.9 (0.79–1.02)	0.111
Smoking	1.19 (0.92–1.54)	0.192	1.03 (0.86–1.23)	0.784	1.07 (0.93–1.24)	0.341
Ischaemic aetiology	1.28 (1.5–1.09)	0.003	1.35 (1.53–1.2)	<0.001	1.33 (1.2–1.46)	<0.001
Sinus rhythm	0.71 (0.6–0.84)	<0.001	0.77 (0.68–0.88)	<0.001	0.75 (0.68–0.83)	<0.001
INTERMACS class 1[a]	3.76 (3–4.71)	<0.001	1.06 (0.87–1.3)	0.54	2.00 (1.72–2.32)	<0.001
INTERMACS class 2[a]	1.82 (1.45–2.26)	<0.001	0.99 (0.85–1.14)	0.864	1.32 (1.16–1.51)	<0.001
INTERMACS class 3[a]	0.91 (0.69–1.18)	0.467	0.92 (0.79–1.08)	0.319	1.1 (0.96–1.26)	0.169
Destination therapy	1.59 (1.89–1.34)	<0.001	1.73 (1.98–1.52)	<0.001	1.32 (1.18–1.48)	<0.001
IV inotropes	1.84 (2.25–1.51)	<0.001	1.11 (1.28–0.97)	0.122	1.68 (1.51–1.86)	<0.001
$\text{Bilirubin}_{\text{per 10}}$	1.05 (1.01–1.09)	0.008	0.94 (0.76–1.17)	0.602	1.04 (1.00–1.08)	0.038
$\text{Creatinine}_{\text{per 50}}$	1.02 (1.01–1.03)	0.004	1.00 (0.98–1.02)	0.851	1.01 (1.00–1.02)	0.04
$\text{BUN}_{\text{per 10}}$	1.05 (1.04–1.06)	<0.001	1.03 (1.02–1.04)	<0.001	1.04 (1.03–1.05)	<0.001

[a]Versus INTERMACS class 4–7.

BUN: blood urea nitrogen; CI: confidence interval; HR: hazard ratio; INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; IV: intravenous.

optimal approach [17, 18]. Because neither of the studies demonstrated impaired outcomes with a staged procedure (LVAD + temporary RVAD and re-evaluation during hospital stay) versus a primary BiVAD implant, it may be the case that this has become the preferred approach in most centres. This assumption can also explain the high mortality in the negatively selected BiVAD cohort with the advantage for those who end up (after prolonged inotropic or short-term RVAD support) with permanent support for the left ventricle only.

Patients who are entered in the EUROMACS database as DT rarely receive a heart transplant, which is in sharp contrast to patients in the INTERMACS database. In the USA, 15% of patients with DT as the treatment strategy eventually receive a transplant [13, 19]. The reasons may be related to reimbursement policies, which are restricted in some parts of Europe, and/or may be due to a change in device strategy that, in the absence of a specific data field, was not registered.

Adverse events

Contrary to the latest INTERMACS data, the early AER of unexpected readmissions is found to be relatively low in the EUROMACS database. Several explanations can underlie these observations. First, readmissions may be under-reported as a result of incompleteness of data, as mentioned in the 'Methods' section of this study, and may also be due to treatment in peripheral hospitals not participating in EUROMACS. Second, hospital stay and step-down care stay after an LVAD implant may be longer in EUROMACS, leading to fewer readmissions because the patient is not yet discharged.

Mortality and transplants

A striking difference between outcomes in the USA and those observed in EUROMACS is the treatment strategy. From 2014 to 2019 in the USA, the number of patients receiving an assist device as a bridge to transplant decreased dramatically from 29.2% in 2014 to 8.9% in 2019; the corresponding data in EUROMACS showed an increase from 38.9% to 43.2% during the same period. This difference may be attributed to the new United Network for Organ Sharing allocation system [20, 21]. Evidently, the rate of heart transplants is low in most countries whose hospitals are contributing to the EUROMACS registry: on average, 4.3 per 10^6 inhabitants [22]. This number is in sharp contrast to the 10.9 per 10^6 cardiac transplants in the USA [23]. Therefore, waiting times are much longer in the EUROMACS area; hence, the need for bridging with a durable device is higher. The Society of Thoracic Surgeons INTERMACS Report 2020 details, respectively, 1-, 3- and 5-year heart transplant rates of 14.3%, 28.3% and 32.2% [19], whereas these data for EUROMACS are 7.5% 20.2% and 25.3%. Not surprisingly, the number of deaths of patients on LVADs is higher in the EUROMACS database; the 1-, 3- and 5-year mortality in EUROMACS is 29.6%, 44.4% and 55.5%, whereas INTERMACS reports 16.9%, 30.0% and 39.2% [19].

Risk factors for deaths

Hospital deaths decreased in each sequential era. The lower prevalence of risk factors such as INTERMACS 1 and 2 may have led to the observed decrease in in-hospital deaths, although the evolution of devices and the increased perioperative experience of the centres most certainly have played a role in reducing in-hospital mortality and decreased ICU/cardiac care unit stays.

Comparable to other large registry data [19], CF-HL devices are associated with higher mortality, especially early after an LVAD implant (Fig. 5C). Different patient profiles (more INTERMACS 1–2) and various further confounders may underlie these observations. So far, no direct head-to-head comparison between contemporary CF-HL and CF-FML devices has been performed. Nevertheless, factors intrinsic to the pump itself may play a role, because Medtronic recently announced that they will cease new implants of the HVAD device (a CF-HL pump) due to a growing body of observational data indicating a higher frequency of neurological events and deaths with the HVAD pump compared to other pumps [24].

In this report, we performed a weighted risk analysis to display the early (<3 months) and late (>3 months) hazard ratios of different preoperative factors on mortality. Overarching demographics, similar age and aetiology of heart failure have a general impact on short- and long-term outcomes, whereas markers for acute organ dysfunction [INTERMACS level, inotropic support, end-organ failure (creatinine, bilirubin levels)] have a more pronounced impact on short-term survival. This result is in line with findings from the INTERMACS 2018 report [25]. Along with markers for acute organ dysfunction, short-term MCS use prior to a permanent ventricular assist device implant was evident in about 20% of all patients. The impact of preoperative MCS on outcome was studied in different cohorts with different devices [26, 27]. Derived from the current EUROMACS data, the use of a preoperatively implanted short-term MCS had a negative impact on short-term as well as long-term outcomes, but close interaction with the INTERMACS level was seen. No conclusion regarding different devices can be drawn from this cohort.

Markers for acute organ dysfunction may improve over time after an LVAD is implanted (e.g. kidney function), and preoperative levels may be of less importance later in the follow-up period. Creatinine and bilirubin levels especially can also be interpreted as right ventricular impairment prior to implanting an LVAD, displaying another important risk factor for impaired postoperative outcome [11, 28]. On the contrary, stable/underlying risk factors, such as the aetiology of heart failure and comorbidities, are equally important in early and late follow-up. Interestingly, female sex was associated with lower mortality beyond 3 months of follow-up, whereas the results of other studies suggest otherwise [29, 30]. These phenomena should be further addressed in future research to accurately predict long-term adverse outcome after having an LVAD implant. Specifically, researchers should investigate potential changes of risk factor weights over time.

Limitations

Contrary to registries in other parts of the world, participation in EUROMACS is not mandatory. Therefore, surveillance and improvement of data quality are ongoing efforts. We were faced, as are other multicentre international registries, with missing data and incomplete follow-up. Both may introduce bias, and especially missing follow-up data may cause bias in survival estimates [1]. Patients from centres with complete follow-up had survival rates comparable with those of centres with less complete follow-up when rigorously controlled for confounding, but the non-significance may also be driven by added variance due to multiple layers of statistical analyses. Various measures were taken to safeguard the completeness and correctness of the data submitted by the participating centres to improve data quality. These methods include data input control, statistical analyses and on-site audits (due to COVID-19 these could not be done in 2020). Another limitation is the observational origin of the data, so unaddressed confounding may influence outcomes.

CONCLUSIONS

This third EUROMACS report reflects the close cooperation of many clinicians who have voluntarily collected data from hundreds of implants with MCS devices. To maintain a high level of data quality, data with overdue follow-up were eliminated in the outcomes we present.

Although a shift to a lower INTERMACS level, resulting in fewer deaths, can be observed, time and focused research will show whether this happens under the influence of publications and guidelines. The long wait for a transplant in many centres makes patients more dependent on MCS, resulting in high morbidity and mortality for those on the device.

This report comes at a time when only 1 mainstream device remains on the market, a device mainly implanted in new-borns and children continues to be applied and a new total artificial heart has been launched. These developments show that the structural collection, analysis and publication of European data remain of great importance to maintain insight into the development of factors that contribute to the results of MCS therapy.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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