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

Theo M.M.H. de By a,*†, Felix Schoenrath b,c,†, Kevin M. Veen d, Paul Mohacsi e, Julia Stein b,c,‡, Khalid M.M. Alkhamees f, Kyriakos Anastasiadis g, Alexander Berhnardt h, Friedhelm Beyersdorf i,j, Kadir Caliskan d, David Reineke k, Kevin Damman l, Arnt Fiane m, Angeliki Gkouziouta n, Can Gollmann-Tepeköylü o, Gustafsson Finn p, Michal Hulman q, Attilio Iacovoni r, Antonio Loforte s, Bela Merkely t, Francesco Musumeci u, Petr Nemec h, Ivan Netuka v, Mustafa Özbaran w, Evgenij Potapov b,c, Yuri Pya x, Gregorio Rábago y, Faiz Ramjankhan z, Hermann Reichenspurner a, Diyar Saeed ab, Elena Sandoval ac, Bernard Stockman ad, Marc Vanderheyden a, Laurens Tops ae, Thorsten Wahlers af, Michael Zembala ag, Daniel Zimpfer ah, Thierry Carrel ai, Jan Gummert aj and Bart Meyns ak

a EUROMACS, EACTS House, Windsor, UK
b Department of Cardiothoracic and Vascular Surgery, German Heart Center Berlin, Berlin, Germany
c DZHK (German Centre for Cardiovascular Research), Partner Site, Berlin, Germany
d Thorax Center, Department of Cardiology, Erasmus University Medical Center, Rotterdam, Netherlands
e HerzZentrum Hirslanden, Zürich, Switzerland
f Prince Sultan Cardiac Center Al Hassa, Saudi Arabia
g Cardiothoracic Dept, AHEPA University Hospital, Aristotle University, Thessaloniki, Greece
h Center for Cardiovascular Surgery and Transplantation Surgery Brno, Brno, Czech Republic
i Department of Cardiovascular Surgery, University Hospital Freiburg, Freiburg, Germany
j Medical Faculty of the Albert-Ludwigs-University, Freiburg, Germany
k University Hospital Bern, Bern, Switzerland
l Universitair Medisch Centrum Groningen, Groningen, Netherlands
m Rigshospitalet, Copenhagen, Denmark
n Klinika Kardiochirurgie NUSCH, Bratislava, Slovakia
o Ospedale Papa Giovanni XIII, Bergamo, Italy
p San Orosio Hospital, Bologna, Italy
q Heart Center of the Semmelweis University, Budapest, Hungary
r Azienda Ospedaliera San Camillo-Forlanini, Rome, Italy
s Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic
t Ege University Hospital, Izmir, Turkey
u National Research Cardiac Surgery Center, Astana, Kazakhstan
v Clinica Universidad de Navarra, Pamplona, Spain
w Utrecht University Medical Center, Utrecht, Netherlands
x Universitair Ziekenhuis Gent, Gent, Belgium
y České zemské inštitúcie, Bratislava, Slovakia
z Ospedale Papa Giovanni XIII, Bergamo, Italy
aa Onze Lieve Vrouwenziekenhuis, Aalst, Belgium
ab University Hospital Zürich, Zürich, Switzerland
ac ESAPAC, Sociedad Española de Cirugía Cardiovascular y Endovascular (SECCE), Madrid, Spain
ad Onze Lieve Vrouwenziekenhuis, Aalst, Belgium
ae Umeå University Medical Center, Umeå, Sweden
af Karolinska Institutet, Stockholm, Sweden
ag Medical University, Vienna, Austria
ah University Hospital Bern, Bern, Switzerland
ai University Hospital Zurich, Zurich, Switzerland
aj Herz- und Diabeteszentrum NRW, Bad Oeynhausen, Germany
ak Katholieke Universiteit Leuven, Leuven, Belgium

* Corresponding author. EUROMACS, EACTS House, Madeira Walk, Windsor Berks SL1 4EU, UK. Tel: +44-1753-832166; e-mail: theo.deby@eacts.co.uk (T.M.M.H. de By).

†The first two authors contributed equally to this report.

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Association for Cardio-Thoracic Surgery. All rights reserved.
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

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.
A total of 6192 implants in 5735 patients

Before 2011: 473 implants
Age <18: 397 implants
Center with <60% follow up: 295
Excluded centers: 193

A total of 4834 implants in 4486 patients

LVAD: 4304
LVAD + RVAD*: 195
BiVAD: 68
RVAD: 142
SVAD: 3
TAH: 74
Unknown*: 48

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.

The demographics of patients who received isolated LVAD therapy are presented in Table 1. Notably, a shift from pre-operative 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.
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 1: Perioperative characteristics of patients with an isolated left ventricular assist device implant

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1795</td>
<td>1617</td>
<td>1087</td>
<td></td>
</tr>
<tr>
<td>Age, median [IQR]</td>
<td>57.00 [48.00, 63.00]</td>
<td>57.00 [48.00, 63.00]</td>
<td>58.00 [49.00, 64.00]</td>
<td>0.322</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>1488 (82.9)</td>
<td>1373 (84.9)</td>
<td>908 (83.5)</td>
<td>0.273</td>
</tr>
<tr>
<td>Non-ischaemic cardiomyopathy, n (%)</td>
<td>888 (60.1)</td>
<td>855 (64.2)</td>
<td>606 (69.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 2: Major adverse event rates

<table>
<thead>
<tr>
<th>Event</th>
<th>Early rate (&lt;3 months)</th>
<th>Late rate (&gt;3 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number events</td>
<td>Adverse event rate</td>
<td>Number events</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Unexpected readmission</td>
<td>481</td>
<td>0.52</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>808</td>
<td>0.88</td>
</tr>
<tr>
<td>Pump thrombosis</td>
<td>81</td>
<td>0.09</td>
</tr>
<tr>
<td>Neurological dysfunction</td>
<td>305</td>
<td>0.33</td>
</tr>
<tr>
<td>Major infection</td>
<td>1315</td>
<td>1.44</td>
</tr>
</tbody>
</table>

Unit: number of events per person-year.

P (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).

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.
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.
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
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].
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. Nonetheless, 2 published studies with data from EUROMACS centres discuss this topic and the

---

### 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. Nonetheless, 2 published studies with data from EUROMACS centres discuss this topic and the

---

### 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.
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 patients in the INTERMACS database. In the USA, 15% of patients rarely receive a heart transplant, which is in sharp contrast to the latest INTERMACS data, the early AER of unexposed DT patients is 16.9%, 30.0% and 39.2% [19]. unexpectedly, the number of deaths of patients on LVADs is higher in the EUROMACS database; the 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 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%. 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 pump-related complications. 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 pump-related complications.

### 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 area; hence, the need for bridging with a durable device is higher.

### 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 periprocedural 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].

### 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

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Early HR (&lt;3 months)</th>
<th>Late HR (&lt;3 months)</th>
<th>Constant HR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P-Value</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>1.02 (1.02–1.03)</td>
<td>&lt;0.001</td>
<td>1.03 (1.03–1.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.03 (1.02–1.03)</td>
</tr>
<tr>
<td>Female</td>
<td>1.07 (1.3–0.87)</td>
<td>0.529</td>
<td>0.81 (0.96–0.69)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.9 (0.79–1.02)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.19 (0.92–1.54)</td>
<td>0.192</td>
<td>1.03 (0.86–1.23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.07 (0.93–1.24)</td>
</tr>
<tr>
<td>Ischaemic aetiology</td>
<td>1.28 (1.5–1.09)</td>
<td>0.003</td>
<td>1.35 (1.53–1.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.33 (1.2–1.46)</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>0.71 (0.66–0.84)</td>
<td>&lt;0.001</td>
<td>0.77 (0.68–0.88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.75 (0.68–0.83)</td>
</tr>
<tr>
<td>INTERMACS class 1*</td>
<td>3.76 (3–4.71)</td>
<td>&lt;0.001</td>
<td>1.06 (0.87–1.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.00 (1.72–2.32)</td>
</tr>
<tr>
<td>INTERMACS class 2*</td>
<td>1.82 (1.45–2.26)</td>
<td>&lt;0.001</td>
<td>0.99 (0.85–1.14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.32 (1.16–1.51)</td>
</tr>
<tr>
<td>INTERMACS class 3*</td>
<td>0.91 (0.69–1.18)</td>
<td>0.467</td>
<td>0.92 (0.79–1.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.1 (0.96–1.26)</td>
</tr>
<tr>
<td>Destination therapy</td>
<td>1.59 (1.89–1.34)</td>
<td>&lt;0.001</td>
<td>1.73 (1.98–1.52)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.32 (1.18–1.48)</td>
</tr>
<tr>
<td>IV inotropes</td>
<td>1.84 (2.25–1.51)</td>
<td>&lt;0.001</td>
<td>1.11 (1.28–0.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.68 (1.51–1.86)</td>
</tr>
<tr>
<td>Bilirubinper 10</td>
<td>1.05 (1.01–1.09)</td>
<td>0.008</td>
<td>0.94 (0.76–1.17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.04 (1.00–1.08)</td>
</tr>
<tr>
<td>Creatinineper 50</td>
<td>1.02 (1.01–1.03)</td>
<td>0.004</td>
<td>1.00 (0.98–1.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.01 (1.00–1.02)</td>
</tr>
<tr>
<td>BUNper 10</td>
<td>1.05 (1.04–1.06)</td>
<td>&lt;0.001</td>
<td>1.03 (1.02–1.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.04 (1.03–1.05)</td>
</tr>
</tbody>
</table>

*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.
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 a 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.

ACKNOWLEDGEMENTS

We express our special thanks to Rongbing Xie for her advice. We are grateful to those medical doctors, ventricular assist device coordinators and data managers who submitted the data from the participating hospitals: Irina Borschchevskiy, Ymkje Hendriksma, Vicky Hernandez, Christian Baier, Maks Mihalj, Gro Sørensen, Matej Ondrusek, Andrea Montalto, Balasz Sax, Vladimir Horvath, Aynur Yildiz, Boran Onung Gordes, Roman Solov, Maksat Sabitov, Leticia Jimeno San Martin, Susanne Rietbroek-Schneider, Julia Holtz, Bianca Weinert, Sandra Eifert, Elly Boel, Eva Janssen, Ilja Djordjevic, Justyna Barys, Johann Horvat, Ellen von Rössing and Marieke Roppe.

Funding

This work was funded and supported by European Association for Cardio-Thoracic Surgery (EACTS).

Conflict of interest: Ivan Netuka is a consultant and an advisory board member for Abbott. Laurens Tops is an advisory board member for Medtronic. The other authors have nothing to disclose.

Author contributions

Théo M.H. de By: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Writing – original draft; Writing – review & editing. Felix Schoenrath: Conceptualization; Formal analysis; Investigation; Methodology; Resources; Validation; Writing – original draft; Writing – review & editing. Kevin Mitchel Veen: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Validation; Writing – original draft; Writing – review & editing. Paul Mohacsi: Conceptualization; Writing – original draft; Writing – review & editing; Julia Stein: Formal analysis; Investigation; Methodology; Software. Kyriakos Anastasiadis: Writing – review & editing. Khalid Mohamed Menawer Alkhames: Writing – review & editing. Alexander M. Bernhardt: Writing – review & editing. Friedhelm Beyersdorf: Writing – review & editing; Kadir Caliskan: Writing – review & editing. David Reineke: Writing – review & editing. Kevin Dammann: Writing – review & editing. Arnt Elhedt: Fiane: Writing – review & editing. Angeliki Gkouziouta: Writing – review & editing. Can Gollmann-Tepeköl: Writing – review & editing.
Gustafsson Finn: Writing – review & editing. Michael Halman: Writing – review & editing. Attilio Iacovoni: Writing – review & editing. Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation Antonio Loforte: Writing – review & editing. Bela Merkely: Writing – review & editing. Francesco Musumeci: Writing – review & editing. Petr Nemec: Writing – review & editing. Ivan Netuka: Writing – review & editing. Mustafa Özbaran: Writing – review & editing. Evgenij V. Potapov: Data curation; Writing – review & editing. Yuri Pya: Writing – review & editing. Gregorio Rabago: Writing – review & editing. Faiz Ramjan Khan: Writing – review & editing. Hermann Reichenspurner: Writing – review & editing. Diyar Saeed: Writing – review & editing. Elena Sandoval: Writing – review & editing. Bernard Stockman: Writing – review & editing. Marc Vanderheyden: Writing – review & editing. Laurens Tops: Writing – review & editing. Thorsten Wahlers: Writing – review & editing. Michal Zembala: Writing – review & editing. Daniel Zimpfer: Writing – review & editing. Thierry Carrel: Writing – review & editing. Jan Gummert: Conceptualization; Supervision; Writing – review & editing. Bart Meyns: Conceptualization; Formal analysis; Methodology; Supervision; Writing – original draft; Writing – review & editing.

Reviewer information
European Journal of Cardio-Thoracic Surgery thanks Paul Kurlansky and the other, anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES