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Mid-term mechanical circulatory support: comparison of single-centre data with the EUROMACS registry†

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Abstract

OBJECTIVES: Mechanical circulatory support (MCS) is an established therapy for end-stage heart failure. The EUROMACS registry was created to promote research in patients with MCS and became a committee of the European Association for Cardio-Thoracic Surgery (EACTS) in 2014. Since 1 January 2011, increasing numbers of European centres implanting durable MCS have reported their patient data to EUROMACS. The aim of this study is to compare, as an example of internal quality control, data from a single centre (Bern) with those from the EUROMACS database with respect to mortality rates and preoperative patient characteristics and to describe complications in Bern.

METHODS: Patients implanted with MCS between 1 January 2011 and 30 June 2014 in participating centres were included, with extended follow-up as of 31 December 2014. Patient characteristics, operative and postoperative data, clinically significant adverse events and routine follow-up data were reported to the registry. The entire EUROMACS cohort (including the Bern data) was compared with patients from Bern only. Baseline characteristics, operative data and outcomes were compared using standard 95% confidence intervals (CIs) for means, Wilson's continuity corrected CIs for categories and Kaplan–Meier estimates with CIs.

RESULTS: Kaplan–Meier estimates show a higher survival rate in the Bern cohort than in the entire EUROMACS cohort at 6 (92%, CI 73–98, vs 66%, CI 62–69), 12 (85%, CI 57–95, vs 56%, CI 52–60) and 18 months (85%, CI 57–95, vs 51%, CI 47–55) after the index operation, respectively. This difference might be caused by the earlier implantation time in Bern (implantation at INTERMACS levels 3–4) versus that of the entire EUROMACS cohort (implantation at INTERMACS levels 2–3). The median number of follow-up records per patient was 2 in the entire EUROMACS cohort and 4 in the Bern ($P = 0.001$) cohort. During follow-up, neurological dysfunction occurred in 42% of patients, a bleeding event occurred in 42% of patients, significant infection occurred in 36% of patients and a device malfunction occurred in 31% of patients within 12 months of implantation in the Bern patients.

CONCLUSIONS: MCS is a valuable therapeutic option with excellent survival rates; nevertheless, it is associated with clinically significant complication rates. International registries are important tools that allow, as an example, internal quality control of mortality, complication and morbidity rates from a single centre compared with the EUROMACS database.

Keywords: EUROMACS • Mechanical circulatory support • Ventricular assist device

INTRODUCTION

Durable mechanical circulatory support (MCS) is an established therapy for end-stage heart failure and is used as a bridge to cardiac transplant (HTx) or, alternatively, as destination therapy, offering better survival and quality of life than optimal medical therapy [1–3]. The new generation of continuous-flow left ventricular assist devices (VADs) offer good survival rates with acceptable morbidity [4–11]. Long-term MCS is an actively developing field in modern cardiac surgery and cardiology. International registries have been established to enhance scientific insights, to address safety concerns and to implement the standard of care in patients receiving MCS.

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) was created for North America in 2005 by the Food and Drug Administration (FDA) and the National Heart, Lung and Blood Institute (NHLB), with mandatory participation of

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all centres implanting durable MCS in the USA. The 7th annual report, published in December 2015, summarized implantation experiences involving more than 15 000 VADs and ~300 total artificial hearts (TAHs) in adult patients between June 2006 and 31 December 2014, making it the largest reported cohort to date [12].

The European Registry for Mechanically Assisted Circulatory Support (EUROMACS) was established in 2009 as a collaboration between 15 European members who implant durable MCS. At the end of August 2015, EUROMACS comprised 190 members from 41 countries. Its international Internet platform (Dendrite Clinical Systems Ltd) allows data entry for adult and paediatric patients implanted with durable VADs or TAHs that have been designed for prolonged MCS of longer than 6 months, irrespective of FDA approval. Devices without the CE mark are not included.

European centres were encouraged to include all eligible patients in EUROMACS from 1st January 2011. By 3 December 2015, the database consisted of more than 1800 cases. EUROMACS became an official committee of the European Association for Cardio-Thoracic Surgery (EACTS) in 2014 and thereafter reported a continuous increase in participating centres and implantations. The first annual report summarizing the initial 825 device implantations in 741 patients (1 January 2011 to 31 December 2013) was published in 2015 [13].

MATERIALS AND METHODS

EUROMACS registry

In EUROMACS, the anonymized patient baseline, follow-up and adverse event data are transmitted from participating sites using a secure, web-based system. All centres agreed that their data be made available for scientific analyses.

Study population

Data from the entire EUROMACS registry with implantation date from January 2011 to June 2014 are included in this study, forming a cohort of 1097 implantations in 988 patients. During the same period of time, the Bernese centre submitted 36 patients to the EUROMACS registry. These patients were implanted with either a left ventricular assist device (LVAD) or biventricular assist device (BiVAD).

Baseline and follow-up data were collected between 1 January 2011 and 30 June 2014, retrospectively, and since 1 January 2013 prospectively.

We used patients' charts to collect demographic, operative and postoperative data. Death or serious adverse events (SAEs), such as major infection, major bleeding, neurological dysfunction and device malfunction (including percutaneous leads), were all reported in the database, which was updated as of 31 December 2014. Reporting of minor incidents (such as unplanned hospitalizations, non-cardiac operations, interventions, right ventricular failure, renal dysfunction, routine follow-up) was encouraged.

Written informed consent was obtained for submission of clinical data to the EUROMACS registry from all Bern patients or their legal representatives.

Patient selection, timing of implantation, device selection and optimal medical therapy are left to the discretion of the treating physicians. In this manuscript, we compare the patient characteristics, operative data and outcomes of a single centre (Bern) with the entire EUROMACS registry, and we report the major complications during the observational period.

Primary and secondary end-points

All-cause mortality was the primary end-point of this study. Secondary end-points were SAEs. The detailed definitions, described below, have been applied.

Major infection was defined as clinically relevant if antibiotic administration or surgical intervention was required. Wound dehiscence without positive blood or wound culture, antibiotics administration or vacuum dressing application was excluded.

Any bleeding into a critical organ (cerebral, pericardial), irrespective of its magnitude or of bleeding in any other location, that required transfusion of at least two units of packed red blood cells or other intervention was considered major.

Loss of function of any vital part of the implanted device's mechanical system (pump, controller, cable) posing a threat to the patient's health or life, requiring change in management or exchange was interpreted as device malfunction.

Neurological dysfunction was defined as any transient or permanent neurological deficit in clinical or imaging studies believed to be caused by a central nervous abnormality (haemorrhagic or ischaemic stroke, transient ischaemic accident, epileptic event).

Statistical analysis

Consistency checks have been made before data analysis, to address the fact that registry data could be less homogeneous than study data or single-centre data. We checked for the chronological plausibility of the follow-up records, and eliminated or corrected implausible records by queries to on-site data managers. We consider the number of follow-up records per patient as a heuristics of the completeness of the captured follow-up; thus, we calculated the frequency of follow-up records per patient. Kaplan–Meier estimates of cumulative probabilities were calculated for the primary (death) and secondary end-points using the entire EUROMACS registry and the Bern cohort. The Kaplan–Meier curves include 95% confidence intervals (CIs) as a measure of certainty because we did not truncate the curves when only one-third of patients remained to be displayed. The cohorts were compared using Kaplan–Meier estimates, standard 95% confidence intervals (CIs) for means and Wilson's continuity corrected CIs for categories. We compared the number of follow-up records for patients from Bern with that for the patients from other sites using the median test with continuity correction. All confidence intervals and *P*-values were two-sided and all calculations were made using Stata 12 (College Station, TX, USA).

RESULTS

Baseline characteristics

Detailed baseline characteristics are presented in Tables 1 and 2. At the time of analysis, the EUROMACS registry included 1097 implantations, of which 36 patients were recruited from Bern. The mean patient age of both cohorts was 52 years. A trend towards fewer female patients (17 vs 39%) in the EUROMACS cohort compared with the Bern cohort was observed and corresponded with

Table 1: Demographic data

	EUROMACS (*n* = 1097)		Bern (*n* = 36)	
	Mean, *n*, %	CI	Mean, *n*, %	CI
Age (years)	52	51–53	52	46–58
Female gender	189 (17%)	7–34	14 (39%)	24–56
Ethnic origin				
African American or Black	3 (0%)	0–12		
Asian	141 (14%)	6–31	1 (3%)	0–16
Caucasian	810 (83%)	66–93	33 (94%)	80–99
Hawaiian or other pacific islander	1 (0%)	0–12		
Weight (kg)	80	79–81	70	63–77
BSA	1.9	1.9–2.0	1.8	1.7–1.9
Body mass index	27.7	26.5–28.9	24.4	22.5–26.2
BNP preoperatively	3531	3002–4060	1778	1185–2370
Primary diagnosis				
Idiopathic dilated CM	343 (35%)	20–53	14 (39%)	24–56
Ischaemic CM	354 (36%)	21–54	10 (28%)	15–45
Dilated myopathy: myocarditis	45 (5%)	1–19	2 (6%)	1–20
Congenital heart disease	108	104–112	52	46–58
Dilated myopathy: familial	21 (2%)	0–15	5 (14%)	5–30
Comorbidities				
Frequent flyer profile	200 (20%)	9–37	14 (39%)	24–56
Temporary circulatory support	121 (12%)	4–28	3 (8%)	2–24
Haemodialysis	30 (3%)	0–16	2 (6%)	1–20
ICD device in place	592 (58%)	41–74	25 (69%)	52–83
Diabetes mellitus	249 (25%)	13–42	9 (25%)	13–43
Insulin dependent	76 (33%)	19–51	4 (44%)	28–62
Cerebrovascular event	41 (4%)	0–18	2 (6%)	1–20
Symptomatic PAD	66 (7%)	1–21	2 (6%)	1–20
Carotid artery disease	24 (2%)	0–16	1 (3%)	0–16
Medical therapy prior to implant				
Aspirin	205 (22%)	11–39	12 (33%)	19–21
ACE inhibitors	390 (40%)	25–58	14 (39%)	24–56
ARB	91 (10%)	3–25	17 (47%)	31–64
β-Blockers	438 (47%)	30–64	26 (72%)	55–85
Aldosterone antagonist	518 (55%)	38–71	22 (61%)	44–76
Phenoprocoumon	60 (6%)	1–21	18 (50%)	33–67
IV inotrope therapy				
Dobutamine	463 (47%)	31–64	5 (14%)	5–30
Milrinone	254 (26%)	13–43	1 (3%)	0–16
Levosimendan	94 (10%)	3–25	8 (22%)	11–40
Norepinephrine	207 (21%)	10–38	1 (3%)	0–16
Current device strategy				
Bridge to transplant	293 (28%)	15–46	24 (67%)	49–81
Destination therapy	182 (18%)	8–35	2 (6%)	1–20
Bridge to candidacy	475 (46%)	30–63	7 (19%)	9–37
Rescue therapy	64 (6%)	1–21	3 (8%)	2–24
Bridge to recovery	9 (1%)	0–13		

BSA: body surface area; BNP: brain natriuretic peptide; CM: cardiomyopathy; ICD: implantable cardioverter defibrillator; PAD: peripheral arterial disease; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blockers; IV: intravenous; CI: confidence interval.

a lower body surface area (BSA), body weight and body mass index (BMI).

The aetiology of heart failure was comparable in both groups with idiopathic cardiomyopathy being the leading cause, followed by ischaemic cardiomyopathy (Table 1).

New York Heart Association functional class and INTERMACS profile were the parameters used to assess the optimal timing for implantation. In the EUROMACS cohort, most patients were considered as level 2 (progressive decline) or level 3 (stable, but inotrope dependent) constituting 32 or 29%, respectively. In comparison, in the Bernese cohort, patients were predominantly considered as INTERMACS level 3 (stable but inotrope dependent) 19% or level 4 (resting symptoms, 'frequent flyer') 47%. The subjective heart failure symptomatology according to the New York Heart Association classification differed with more patients in the NYHA Class II in the Bernese cohort compared with the entire database (Table 2).

Implantation strategies appear to differ between cohorts: VADs were used as bridge-to-candidacy (46%), bridge-to-transplant (28%) or destination therapy (18%) in the EUROMACS cohort, while they were used as bridge-to-transplant (67%), bridge-to-candidacy (19%) or destination therapy (6%) in the Bernese cohort (Table 1).

Significant differences in medical therapy prior to VAD implantation were observed. Angiotensin receptor blocker (ARB) use was less in the EUROMACS cohort (10%) compared with the Bern cohort (47%), while administration of vasoactive substances (milrinone, norepinephrine, dobutamine) was more frequent in the

Table 2: Imaging and haemodynamic data

	EUROMACS (*n* = 1097)		Bern (*n* = 36)	
	Mean, *n*, %	CI	Mean, *n*, %	CI
Left ventricular systolic ejection fraction				
Very severely reduced (LVEF <19%)	368 (41%)	26–59	13 (45%)	29–62
Severely reduced (LVEF 20–29%)	396 (45%)	28–62	12 (41%)	26–59
Moderately reduced (LVEF 30–39%)	54 (6%)	1–21	3 (10%)	3–26
Mildly reduced (LVEF 40–50%)	15 (2%)	0–15	1 (3%)	0–17
New York Functional Class				
Class I	1 (0%)	0–12		
Class II	20 (3%)	0–16	7 (21%)	10–38
Class III	287 (42%)	26–60	15 (45%)	29–63
Class IV	350 (51%)	34–68	11 (33%)	19–51
INTERMACS level				
1 (cardiogenic shock)	132 (13%)	5–29	2 (6%)	1–20
2 (progressive decline)	334 (32%)	18–50	7 (19%)	9–37
3 (inotrope-dependent)	300 (29%)	16–47	7 (19%)	9–37
4 (resting symptoms)	218 (21%)	10–38	17 (47%)	31–64
5 (exertion intolerant)	35 (3%)	0–17	3 (8%)	2–24
Haemodynamics				
Heart rate	89	88–90	79	71–86
Systolic blood pressure	98	97–100	93	86–99
PA systolic BP	50	49–51	51	43–59
PCWP	24	23–25	25	21–28
Pulmonary vascular resistance	308	286–329	243	147–339
Cardiac index	2	2–2	2	2–2
TAPSE	14	14–15	15	13–16

PA: pulmonary artery; BP: blood pressure; PCWP: pulmonary capillary wedge pressure; CI: confidence interval.

EUROMACS cohort. A trend towards less β-blockade and aldosterone antagonist therapy in the EUROMACS cohort was revealed, but did not reach statistical significance.

Operative and postoperative data

No difference in the use of pulsatile or rotary pump VADs between cohorts was observed. Of the total, 82 and 81% of patients were implanted with left VADs in the EUROMACS and Bernese cohorts, respectively, whereas in the latter no implantation of sole right VAD or a TAH was conducted. The stay in the intensive care unit was significantly shorter in the Bernese versus EUROMACS cohort, while the overall length of hospital stay was similar (Table 3).

Survival analysis

Kaplan–Meier estimates demonstrate a higher survival rate in the Bernese versus EUROMACS cohort at 6 (92%, CI 71–98, vs 59%, CI 55–62), 12 (84%, CI 56–95, vs 53%, CI 49–57) and 18 months (84%, CI 56–95, vs 47%, CI 42–52) after the operation, respectively. From 2 years onwards, the CIs no longer overlap; 84% survival in the Bernese (CI 55–95) versus 44% in the entire cohort (CI 38–49) at 24 months, and 84% (CI 56–95) vs 31% (CI 22–40) at 30 months (Fig. 1). In the relatively small Bernese cohort, 3 patients died during follow-up: 2 of intracranial haemorrhage after 111 or 253 days on MCS, and 1 of fulminant right ventricular failure after 93 days. In the EUROMACS cohort 369 patients died during follow-up.

Survival analysis according to the INTERMACS levels

Kaplan–Meier analysis of the EUROMACS cohort, grouped by INTERMACS level prior to implantation, demonstrated a correlation between INTERMACS level and both early (<30 days) and long-term survival. INTERMACS levels 1 and 2 patients exhibited high mortality in the first 6 postoperative months and might stabilize afterwards, but the number of patients at risk is small (Fig. 2).

Follow-up

The median follow-up time in days was 107 [interquartile range (IQR) 25–402] for EUROMACs and 151 [IQR 71–300] for Bern.

The median of the number of follow-up records per patient was significantly lower in the EUROMACS cohort (2 [IQR 0–5]) compared with the Bernese cohort (4 [IQR 1–10]; $P = 0.001$). We thus decided not to compare complication rates between cohorts, but to describe the complications seen in Bern in detail.

Complications in Bern

In the Bernese cohort, 67% (CI 45–81) and 58% (CI 34–77) of patients remained free of neurological dysfunction for the first 6 and 12 months postimplantation, respectively. No additional neurological events after the first 12 months were recorded, resulting in a neurological dysfunction event rate of 0.63 per patient year. Most central nervous thromboembolic events were transient ischaemic attacks (seven patients; 64%), and stroke

Table 3: Operative and postoperative data

	EUROMACS (*n* = 1097)		Bern (*n* = 36)	
	Mean, *n*, %	CI	Mean, *n*, %	CI
Cardiopulmonary bypass time	108	104–112	106	93–119
Device type				
LVAD	878 (82%)	65–92	29 (81%)	63–91
BiVAD	120 (11%)	4–27	7 (19%)	9–37
RVAD	61 (6%)	1–20		
TAH	15 (1%)	0–14		
Type of pump flow				
Rotary	938 (95%)	81–99	31 (86%)	70–95
Pulsatile	45 (5%)	1–19	5 (14%)	5–30
ICU/CCU stay	20	18–22	12	4–20
Step-down care stay	20	17–22	4	1–7
Length of stay	40	37–43	41	29–52

LVAD: left ventricular assist device; BiVAD: biventricular assist device; RVAD: right ventricular assist device; TAH: total artificial heart; ICU: intensive care unit; CCU: cardiac care unit; CI: confidence interval.

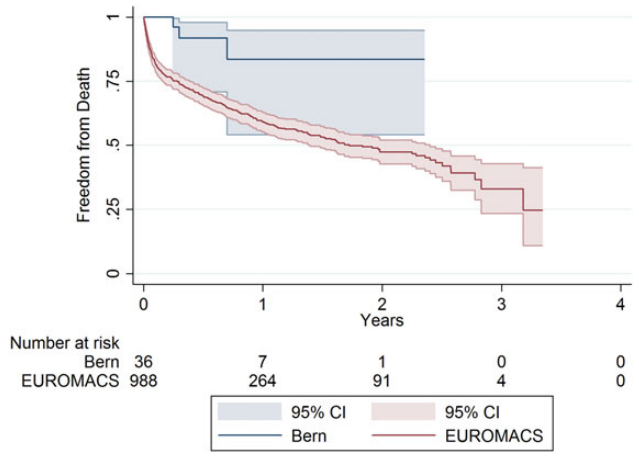

Figure 1: Kaplan–Meier survival analysis of the Bernese compared with the whole EUROMACS cohort. CI: confidence interval.

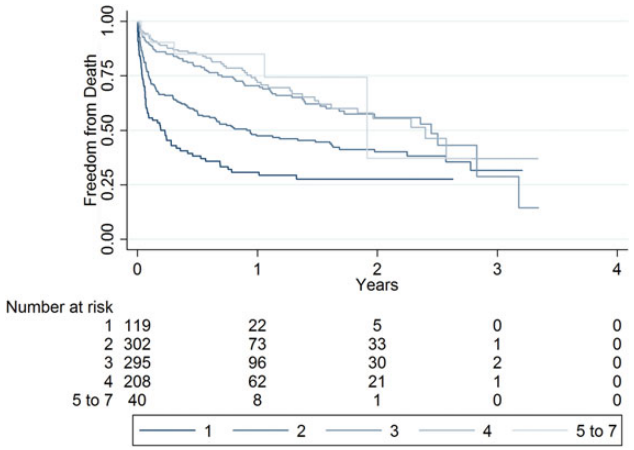

Figure 2: Kaplan–Meier survival analysis of the whole EUROMACS database dependent on the INTERMACS status at the time of implantation.

occurred in 4 patients (36%). Intracranial bleeding was present in 2 patients (6%) leading in both cases to death. One 'psychiatric episode', which could not be differentiated from a transient ischaemic attack, and one case of peripheral neural damage were considered as neurological events and resolved without sequelae.

Most infections occurred during the first 30 days following implantation. Of the total, 76% (CI 58–87) of patients and 64% (CI 41–81) of patients were free of infection at 30 days and 2 years of follow-up, respectively, resulting in 0.63 infection events per patient year. The site of infection was unknown (seven events in 5 patients) or arose at the pump or cable sites (five events in 4 patients), or in the pulmonary tract (4 patients). Generalized reactions, such as sepsis or SIRS, were also observed (4 patients). No pump exchange or explant was performed as a result of infection in the Bernese cohort during follow-up.

Freedom from bleeding occurred in 82% (CI 64–92), 66% (45–80) and 58% (34–76) of patients after 30 days, 6 and 12 months, respectively, with a bleeding event rate of 0.77 per patient year. Eleven mediastinal bleeding events occurred in 6 patients, all during hospitalization for the index operation. Ten gastrointestinal bleeding events occurred in 7 patients during follow-up (in or out of hospital). Bleeding events of the central nervous system are discussed separately.

Device malfunction rate accumulated during the entire observational period with 94% (CI 78–98), 77% (CI 56–89), 70% (CI 44–85) and 56% (CI 24–79) of patients free of malfunction at 30 days, 6, 12 and 24 months of follow-up, respectively, resulting in 0.72 device malfunction events per patient year. No patient required pump exchange or explant.

The corresponding Kaplan–Meier estimates are depicted in Fig. 3.

DISCUSSION

Survival

Primary end-point (death) occurred in 3 patients in the Bernese cohort over the entire period of follow-up, representing a survival rate of 92, 85 and 85% for 6, 12 and 24 months, respectively. This compares favourably with the data in both the 7th INTERMACS annual report (survival of 80% after 1 year and 70% after 2 years of

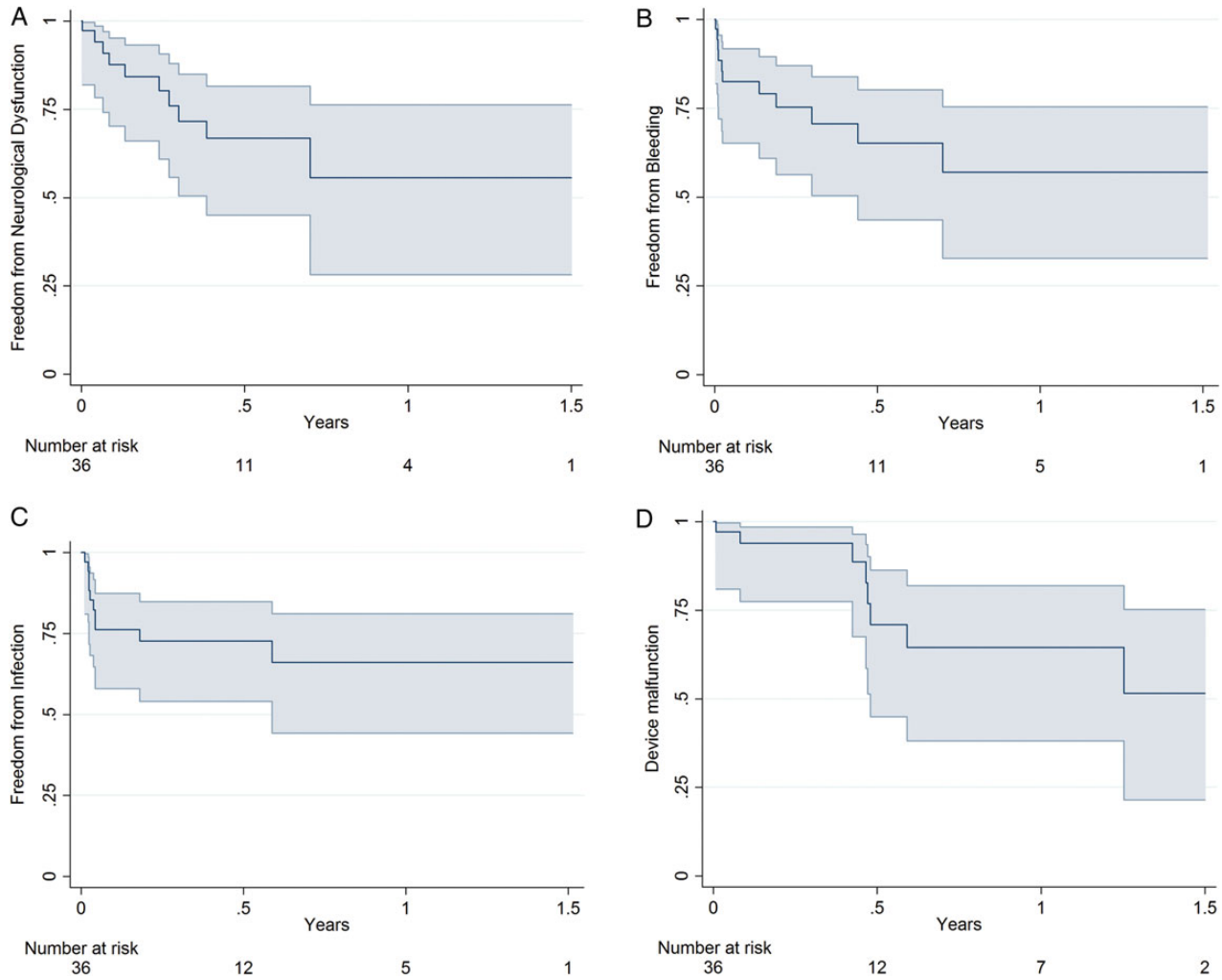

Figure 3: (**A**) Time to first event analysis of neurological dysfunction of the Bernese cohort. (**B**) Time to first event analysis of clinically significant bleeding. (**C**) Time to first event of clinically significant infection. (**D**) Time to first event of device malfunction. CI: confidence interval.

follow-up) [12] and 1st EUROMACS annual report (survival of 88.7% after 30 days, 68.4% after 1 year, 59.1% after 2 years and 57.3% after 3 years), these being the two largest contemporarily reported cohorts [13]. Relating to the significant differences between the Bernese and EUROMACS cohorts, we consider the early implantation strategy the most plausible cause. For the Bernese cohort, the decision to implant MCS before the occurrence of irreversible organ damage, which occurs with INTERMACS levels 3 and 4, allowed elective implantation in optimized clinical conditions and haemodynamic status. Clinical status was optimized primarily based on volume status (as reflected by lower natriuretic peptide levels at the time of implant in the Bernese cohort) and haemodynamic status (significantly fewer patients were inotrope dependent and patients trended towards lower pulmonary vascular resistance in the Bernese cohort). Emergency implantations in INTERMACS levels 1 and 2 were avoided, due to the known association of inotrope support prior to implant with adverse outcome [14]. Significantly more patients in the Bernese cohort required angiotensin antagonists, and a strong trend for greater β-blocker and aldosterone antagonist use was observed in this patient group, which could translate into a favourable neurohormonal balance prior to implantation, similar to the influence of optimal medical therapy in chronic heart failure. Furthermore, with a small patient population, the Bernese cohort allows tighter control of follow-up with very accurate documentation of any adverse events compared with high-volume institutions. Figure 4 shows the timing and frequency of the follow-up visits, with 4.5 follow-up records per patient in the Bernese group, compared with 3.0 per patient in the EUROMACS cohort. Consequently, possible deleterious complications could be addressed early. Therefore, we hypothesize that the Bernese strategy, including earlier VAD implantation, results in more events, yet leads to lower mortality.

Gender

We would like to comment on an interesting finding, which could relate to favourable survival. In the pivotal trials for MCS devices, as well as in large cohort studies, female gender seems to be underrepresented. Several reasons for this have been proposed, including differences in aetiology, clinical presentation, disease course and conservative choice of treatment options in this population. According to available data, women have equal benefits from VAD implantation despite worse baseline characteristics [15–17]. As almost 40% of the patients in the Bernese group are female and are implanted early according to the above-mentioned strategy, we anticipated that they would obtain at least the same benefits as their male counterparts. As our overall survival appears to be

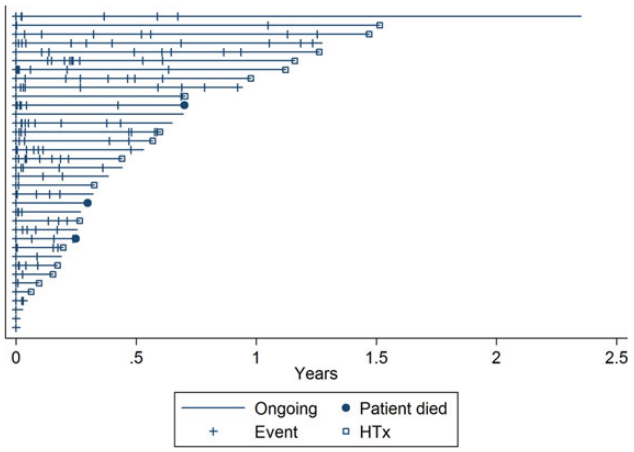

Figure 4: Bern data timing of the follow-up and events from implantation onwards.

superior to that reported in the large cohort studies, benefits for survival in women may be even more pronounced.

Complications

In the Bernese cohort, a relatively high initial rate of cerebrovascular events in the first 3 postoperative months was observed (with the majority being transient ischaemic attacks or non-disabling strokes). Stabilization of cerebrovascular events occurs after 6 months, with no further events in the long-term follow-up. The high initial rate of events may be attributable to the complexity of management in the early perioperative period. Standard medical therapy in the Bernese centre consists of low-dose platelet inhibitors and oral anticoagulation with vitamin K antagonists targeted at an international normalized ratio (INR) of 1.8–2.5, and monitoring of platelet aggregation (Muliplate® Analyser—Cobas; Roche Diagnostics International Ltd, Rotkreuz, Switzerland).

The recently reported incidence rate of neurological dysfunction after implantation of a VAD varies between 9.8 to 40% (0.21 thromboembolic strokes per patient year and 0.19 haemorrhagic strokes per patient year) [18, 19]. In the ReVOLVE trial, neurological dysfunction accounted for the death of ∼4.3% of patients after a mean time of 145 days (with a range of 1–730 days), whereas stroke (any type) occurred in 8% patients during the observational period [10]. In the 7th INTERMACS report, neurologic events per 100 patient months were 1.17 for patients implanted during 2008–2011, and 1.71 for patients implanted during 2012–2014 (20.4% patients experienced neurologic events for INTERMACS levels 4–7 and 18% patients experienced neurological events for INTERMACS levels 1–3) [12]. In the recently published comparison of neurological outcomes between recipients of HeartWare and HeartMate II, complication rates were reported as 19% for 0.44 median years of follow-up and 16% for 0.95 median years of follow-up, respectively [20]. No direct comparison can be made between these groups and our patient cohort due to different definitions of SAEs. Nonetheless, given that most Bernese events resolved without sequelae, the disproportion in onset of neurological dysfunction is not pronounced.

During the whole follow-up, only one reoperation for pump exchange occurred in the Bernese cohort. Other reported malfunctions could be managed conservatively with exchange of controller, battery or device cable. This may contribute to survival benefits as pump exchange due to any cause confers high mortality [21, 22].

Bleeding, especially gastrointestinal bleeding, is the most prevalent reason for patient readmission after implantation of MCS [23]. This was also the case in the Bernese cohort, with most of the bleeding events occurring within the first 30 days after the operation and comprising mainly mediastinal bleeding. In the late postoperative period, the gastrointestinal tract was the most frequent site of bleeding. Two deaths due to cerebral bleeding in the Bernese cohort occurred after 111 and 253 days on MCS. Although direct comparison is difficult due to differences in reporting and applied definitions, these values correspond well with the reported 0.4 bleeding events per patient year (28% entire population) with a further 0.06 events per patient year (5%). Similarly findings to the Bernese cohort were also reported for gastrointestinal bleeding; 14.8% in the ReVOLVE Trial, 12.7% in the publication of Slaughter *et al*. and 26% of operative bleeding in the publication of Pagani *et al*. The Bernese cohort results were also in line with the 7th INTERMACS report; 9.41 bleeding events for 100 patient-months (implantations during 2008–2011) and 7.79 (implantations during 2012–2014) were reported [10, 12, 24, 25].

Interestingly, the only case of pump thrombosis occurred in the VAD implanted in the right ventricle on the implantation day, which resulted in reoperation and pump exchange. This patient had already been implanted with a left VAD 4 weeks prior, and an upgrade to BiVAD was needed due to electrical storm. No other pump thrombosis was reported (in comparison to 6.7% in the ReVOLVE trial), which may result from the relatively aggressive antithrombotic regimen which can cause more bleeding events, but without impact on the overall mortality.

We conclude that international registries provide valuable data, which may, in turn, lead to new insights, approaches and discussions. In particular, comparison of the single-centre experience with the entire EUROMACS database generates interesting observations and reveals differences in the approaches and outcomes of MCS therapy. As shown with this study, benchmarking of local versus international data is clearly feasible. In the Bernese centre, we value the early implantation strategy in relatively stable patients, which may improve survival rates. However, the rate of complications after MCS implantation remains considerable.

Statistical tools are being developed in EUROMACS, which will enable clinicians to produce graphic outcomes of their hospital, compared with 'all of Euromacs' for any chosen parameter.

Strengths and limitations

This is the first manuscript that compares the experience of a single centre with the entire EUROMACS database.

The most important limitation of this study is that we did not feel confident to compare the secondary end-points seen in Bernese patients with the entire EUROMACS cohort, since the median of the number of follow-up records per patient differs significantly between the whole EUROMACS cohort and the Bern cohort ($P = 0.025$). Due to the very tight outpatient control in Bern, with strict reporting of all the events to the database, the complete dataset was created with no patients lost during follow-up. Overall, the different implantation timing and patient selection in Bern compared with the entire EUROMACS cohort indicates that the clinical strategy used in Bern is appropriate. In addition, promising alternatives and improved insight concerning the treatment of MCS patients can be gained both from registries, such as EUROMACS, data alone and through comparison with single centres.

The study of a small population is certainly a significant limitation, which may cause selection bias. There was no attempt to compare morbidity in our group to the general population due to a hypothesized more lenient follow-up in other centres, which might have resulted in under-reporting of adverse events.

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