




# The quality of afterlife: surviving extracorporeal life support after therapy-refractory circulatory failure—a comprehensive follow-up analysis

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## Abstract

**Aims** Extracorporeal life support (ECLS) represents a popular treatment option for therapy-refractory circulatory failure and substantially increases survival. However, comprehensive follow-up (FU) data beyond short-term survival are mostly lacking. Here, we analyse functional recovery and quality of life of longer-term survivors.

**Methods and results** Between 2011 and 2016, a total of  $n = 246$  consecutive patients were treated with ECLS for therapy-refractory circulatory failure in our centre. Out of those, 99 patients (40.2%) survived the first 30 days and were retrospectively analysed. Fifty-eight patients (23.6%) were still alive after a mean FU of  $32.4 \pm 16.8$  months. All surviving patients were invited to a prospective, comprehensive clinical FU assessment, which was completed by 39 patients (67.2% of survivors). Despite high incidence of early functional impairments, FU assessment revealed a high degree of organ and functional recovery with more than 70% of patients presenting with New York Heart Association class  $\leq$  II, 100% free of haemodialysis, 100% free of moderate or severe neurological disability, 71.8% free of moderate or severe depression, and 84.4% of patients reporting to be caring for themselves without need for assistance.

**Conclusions** Patients surviving the first 30 days of ECLS therapy for circulatory failure without severe adverse events have a quite favourable outcome in terms of subsequent survival as well as functional recovery, showing the potential of ECLS therapy for patients to recover. Patients can recover even after long periods of mechanical support and regain physical and mental health to participate in their former daily life and work.

**Keywords** ECLS; ECMO; Cardiogenic shock; Cardiocirculatory failure; Outcome; Quality of life

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## Introduction

Extracorporeal life support (ECLS), also referred as veno-arterial extracorporeal membrane oxygenation (va-ECMO), has been established as an ultimo ratio therapy for critically ill patients suffering from severe cardiocirculatory failure and prolonged cardiopulmonary resuscitation (CPR) with otherwise marginal prognosis.<sup>1</sup> In case of emergency, ECLS cannula can be implanted percutaneously even in remote situations with no need for an operating room and ECLS can grant immediate full circulatory

support.<sup>2–4</sup> Today, survival rates of ECLS patients range between 41% and 47% at 30 day or hospital discharge for a patient cohort with an otherwise dismal survival.<sup>2–8</sup>

Although reported short-term outcomes are quiet encouraging, ECLS therapy remains a high-cost treatment, while the long-term benefit remains uncertain and controversial.<sup>9</sup> Comprehensive data on long-term survival after ECLS therapy are still lacking, and especially analysis of the quality of life and functional status of the patients after hospital discharge has only just begun.<sup>10</sup> However, restoration of functional status and reintegration in social and even

work life should be defined as one of the main goals for the therapy of patients suffering from critical illness.<sup>11</sup> As a consequence, new studies focusing on the long-term effects of ECLS therapy and the functional as well as psychosomatic status of the patients are urgently needed.

In the following, we therefore present a comprehensive follow-up analysis on outcome of patients undergoing ECLS for therapy-refractory cardiocirculatory failure in our department, looking beyond survival and analyse functional recovery and quality of life of longer-term survivors.

## Methods

### Ethics

The reported study followed the principles of the Declaration of Helsinki and was approved by the local ethics committee of the Heinrich-Heine-University Düsseldorf, Germany (Study ID: 5145). All patients gave their informed consent for the scientific use of anonymized patient data prior to inclusion in the study.

### Patients and study design

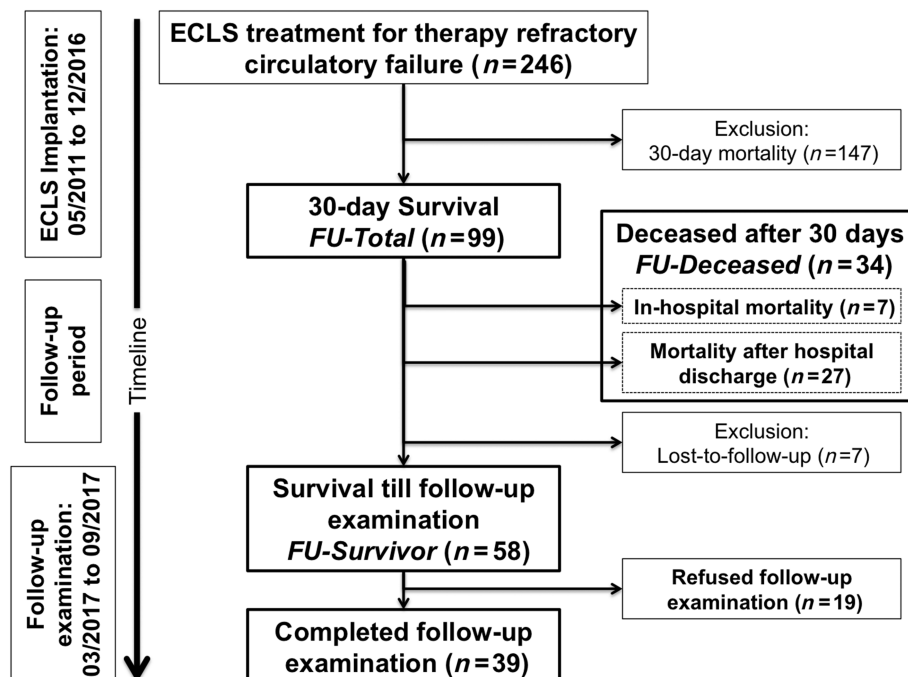
Between May 2011 and December 2016, all consecutive adult patients ( $n = 246$ ) being treated with femoral ECLS for non-cardiac surgical related therapy-refractory cardiogenic

shock or cardiac arrest with ongoing CPR at our department were retrospectively reviewed. Only patients suffering from primary cardiocirculatory failure with confirmed cardiac origin were included. Patients with postcardiotomy shock syndrome as well as all ECLS patients having died before the first 30 days of therapy were excluded from the study and the corresponding functional longer-term evaluation. The remaining ( $n = 99$ ) patients were included and underwent prospective follow-up examination (Figure 1).

### Follow-up examinations

Follow-up examinations were performed from March to September 2017 at invited clinical visits according to a standardized and predefined institutional study protocol. During follow-up visits, comprehensive health status covering organ functions as well as psychosocial aspects was evaluated. Besides clinical examination and 6 min walk test (6MWT), patients completed an extensive questionnaire evaluating functional status, psychosomatic factors, employment, and social life. Potential depression was assessed by the Beck Depression Inventory-II (BDI-II), and detailed neurological and cognitive status was evaluated by the German versions of the National Institutes of Health Stroke Scale (NIHSS) and the Montreal Cognitive Assessment (MoCA) test in cooperation with experienced neurologists.<sup>12</sup> Autonomy in daily life was evaluated using the modified Rankin Scale (mRS) and health-related quality of life (HRQL) by the 36-Item Short

**Figure 1** Patient selection and study population. ECLS, extracorporeal life support; FU, follow-up.



Form Survey (SF-36, Version 2, German). For patients that could not be reached by phone or mail, primary care physicians and health care insurances were contacted.

## Extracorporeal life support treatment

Extracorporeal life support therapy was accomplished as reported before.<sup>2,3</sup> In brief, the femoral vessels were percutaneously cannulated using the Seldinger technique with an additional leg perfusion catheter to ensure distal perfusion. In rare cases, open femoral cannulation via surgical cut-down was performed. Consecutive treatment followed current guidelines on the management of cardiogenic shock.<sup>13,14</sup> If sustained myocardial recovery was not achievable, patients were assessed for ventricular assist device (VAD) implantation or heart transplantation following institutional standards.<sup>2</sup>

## Statistics

Statistics were calculated by SPSS Statistics 26 (IBM Corporation, Armonk, NY). All results are presented in the corresponding tables as mean values with the standard deviation respectively percentages of the whole. Effects of clinical parameters such as laboratory values, concomitant diseases, and observed adverse events during the peri-implantation

interval were examined by cox regression in order to identify potential risk factors for post-30 day mortality. Furthermore, analysis of functional status and HRQL questionnaires was performed by ordinal logistic and linear regression analysis. Results were assumed as statistically significant for  $P < 0.05$ .

## Results

### Short-term effects of extracorporeal life support therapy

Between May 2011 and December 2016, a total of 246 patients underwent ECLS therapy for therapy-refractory cardiogenic shock or cardiac arrest with ongoing CPR. Ninety-nine patients (FU-Total, 40.2%) survived the first 30 days and were included for further analysis as defined before (*Figure 1*). Of those,  $n = 58$  (FU-Survivor, 58.6%) were still alive at the time of the follow-up examination whereas  $n = 34$  patients (FU-Deceased, 34.3%) had died. Information about the status of the remaining  $n = 7$  patients (7.1%) were missing (lost to follow-up).

In order to identify potential risk factors for mortality in patients surviving the initial 30 days after ECLS implantation, analyses of patient characteristics at implantation time (*Table 1*) and peri-implantation as well as discharge variables (*Table 2*) were performed. Mean age of 30 day survivors was

**Table 1** Patient characteristics at initial implantation of extracorporeal life support

| Variables                            | FU-Total (n = 99) | FU-Survivor (n = 58) | FU-Deceased (n = 34) | Hazard ratio [95% CI] | P-value |
|--------------------------------------|-------------------|----------------------|----------------------|-----------------------|---------|
| Age, years                           | 54 ± 15           | 52 ± 16              | 58 ± 14              | 1.02 [1.00; 1.05]     | 0.05    |
| Male gender, n (%)                   | 77 (77.8)         | 42 (72.4)            | 29 (85.3)            | 0.47 [0.18; 1.22]     | 0.12    |
| CPR, n (%)                           | 71 (71.7)         | 43 (71.1)            | 24 (70.6)            | 0.88 [0.42; 1.85]     | 0.74    |
| eCPR, n (%)                          | 21 (21.2)         | 10 (17.2)            | 10 (29.4)            | 1.79 [0.85; 4.76]     | 0.13    |
| Remote implantation, n (%)           | 38 (38.4)         | 26 (44.8)            | 8 (23.5)             | 0.43 [0.19; 0.96]     | 0.04    |
| <b>Aetiology</b>                     |                   |                      |                      |                       |         |
| ACS, n (%)                           | 59 (59.6)         | 32 (55.2)            | 22 (64.7)            | 1.42 [0.70; 2.87]     | 0.33    |
| CM/myocarditis, n (%)                | 29 (29.3)         | 19 (32.8)            | 8 (23.5)             | 0.63 [0.29; 1.40]     | 0.26    |
| Other, n (%)                         | 11 (11.1)         | 7 (12.1)             | 4 (11.8)             | 1.08 [0.38; 3.07]     | 0.89    |
| <b>Concomitant diseases (n = 98)</b> |                   |                      |                      |                       |         |
| Diabetes mellitus, n (%)             | 23 (23.2)         | 11 (19.3)            | 12 (35.3)            | 1.97 [0.97; 3.99]     | 0.06    |
| Hypertension, n (%)                  | 39 (39.4)         | 21 (36.8)            | 16 (47.1)            | 1.58 [0.80; 3.11]     | 0.19    |
| Previous stroke, n (%)               | 13 (13.1)         | 6 (10.5)             | 6 (17.6)             | 1.49 [0.61; 3.61]     | 0.38    |
| PAD, n (%)                           | 10 (10.1)         | 4 (7.0)              | 5 (14.7)             | 1.77 [0.68; 4.57]     | 0.24    |
| Lung disease, n (%)                  | 11 (11.1)         | 7 (12.3)             | 4 (11.8)             | 0.98 [0.35; 2.78]     | 0.97    |
| HLP, n (%)                           | 13 (13.1)         | 9 (15.8)             | 3 (8.8)              | 0.62 [0.19; 2.03]     | 0.43    |
| Nicotine abuse, n (%)                | 24 (24.2)         | 12 (21.1)            | 11 (32.4)            | 1.51 [0.73; 3.10]     | 0.26    |
| Renal failure, n (%)                 | 12 (12.1)         | 7 (12.3)             | 4 (11.8)             | 1.18 [0.41; 3.36]     | 0.76    |
| <b>Laboratory values</b>             |                   |                      |                      |                       |         |
| Lactate, mmol/L                      | 8.25 ± 5.76       | 7.80 ± 5.70          | 7.81 ± 6.13          | 1.01 [0.95; 1.07]     | 0.72    |
| Lactate clearance, h                 | 47.2 ± 48.3       | 42.6 ± 48.4          | 45.0 ± 43.7          | 1.00 [1.00; 1.01]     | 0.53    |
| NSE, ng/mL                           | 65.40 ± 37.10     | 35.46 ± 29.17        | 56.04 ± 40.89        | 1.02 [1.01; 1.03]     | <0.01   |
| AST, U/L                             | 829 ± 1317        | 760 ± 1235           | 971 ± 1535           | 1.00 [1.00; 1.00]     | 0.30    |
| ALT, U/L                             | 437 ± 839         | 350 ± 807            | 414 ± 922            | 1.00 [1.00; 1.00]     | 0.56    |

ACS, acute coronary syndrome; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; CM, cardiomyopathy; CPR, cardiopulmonary resuscitation; eCPR, extracorporeal cardiopulmonary resuscitation; FU, follow-up; HLP, hyperlipoproteinaemia; NSE, neuron-specific enolase; PAD, peripheral artery disease.

**Table 2** Peri-implantation and discharge characteristics

| Variables                     | FU-Total (n = 99) | FU-Survivor (n = 58) | FU-Deceased (n = 34) | Hazard ratio [95% CI] | P-value |
|-------------------------------|-------------------|----------------------|----------------------|-----------------------|---------|
| ECLS support duration, h      | 156 ± 115         | 150 ± 107            | 165 ± 127            | 1.00 [1.00; 1.00]     | 0.41    |
| Severe adverse events, n (%)  | 73 (73.7)         | 42 (72.4)            | 26 (76.5)            | 1.34 [0.61; 2.97]     | 0.47    |
| Neurological events, n (%)    | 31 (31.3)         | 11 (19.0)            | 15 (44.1)            | 3.13 [1.58; 6.28]     | <0.01   |
| Bleeding, n (%)               | 11 (11.1)         | 6 (10.3)             | 4 (11.8)             | 1.06 [0.37; 3.02]     | 0.91    |
| Visceral ischaemia, n (%)     | 7 (7.1)           | 0 (0.0)              | 7 (20.6)             | 7.50 [3.14; 17.88]    | <0.01   |
| Limb ischaemia, n (%)         | 15 (15.2)         | 6 (10.3)             | 8 (23.5)             | 2.23 [1.00; 4.95]     | 0.05    |
| Sepsis, n (%)                 | 21 (21.2)         | 9 (15.5)             | 12 (35.3)            | 2.55 [1.26; 5.18]     | 0.01    |
| Haemodialysis, n (%)          | 52 (52.5)         | 25 (43.1)            | 23 (67.6)            | 2.45 [1.19; 5.03]     | 0.02    |
| Failed ECLS weaning           |                   |                      |                      |                       |         |
| VAD, n (%)                    | 26 (26.3)         | 10 (17.2)            | 16 (47.1)            | 2.23 [1.12; 4.43]     | 0.02    |
| VAD + HTx, n (%)              | 3 (3.0)           | 2 (3.4)              | 1 (2.9)              | 0.76 [0.10; 5.56]     | 0.79    |
| Hospital stay, days           | 34.6 ± 31.8       | 29.6 ± 28.1          | 45.2 ± 36.8          | 1.01 [1.00; 1.02]     | 0.04    |
| ICU, days                     | 31.7 ± 25.3       | 26.6 ± 25.1          | 42.7 ± 23.9          | 1.02 [1.01; 1.03]     | <0.01   |
| Mechanical ventilation, days  | 21.8 ± 19.7       | 14.9 ± 13.9          | 33.1 ± 23.5          | 1.03 [1.02; 1.05]     | <0.01   |
| Tracheotomy, n (%)            | 48 (48.5)         | 21 (36.2)            | 23 (67.6)            | 2.93 [1.42; 6.05]     | <0.01   |
| Discharge                     |                   |                      |                      |                       |         |
| Home, n (%)                   | 2 (2.0)           | 1 (1.7)              | 1 (2.9)              | 1.40 [1.19; 10.32]    | 0.74    |
| Other hospital, n (%)         | 69 (69.7)         | 45 (77.6)            | 18 (52.9)            | 0.40 [0.21; 0.79]     | <0.01   |
| Rehab clinic, n (%)           | 21 (21.2)         | 12 (20.7)            | 8 (23.5)             | 1.04 [0.47; 2.30]     | 0.92    |
| Clinical status at discharge  |                   |                      |                      |                       |         |
| Invasive ventilation (n = 98) |                   |                      |                      |                       |         |
| Non, n (%)                    | 64 (64.6)         | 46 (79.3)            | 13 (38.2)            |                       |         |
| Intermittent, n (%)           | 2 (2.0)           | 1 (1.7)              | 1 (2.9)              | 3.00 [0.39; 23.10]    | 0.29    |
| Continuous, n (%)             | 32 (32.3)         | 11 (19.0)            | 19 (55.9)            | 4.61 [2.26; 9.40]     | <0.01   |
| Kidney function (n = 96)      |                   |                      |                      |                       |         |
| No impairment, n (%)          | 27 (27.3)         | 14 (24.1)            | 9 (26.5)             |                       |         |
| Oral diuretics, n (%)         | 27 (27.3)         | 20 (34.5)            | 7 (20.6)             | 0.72 [0.27; 1.93]     | 0.51    |
| i.v. diuretics, n (%)         | 25 (25.3)         | 19 (32.8)            | 4 (11.8)             | 0.46 [0.14; 1.49]     | 0.19    |
| Haemodialysis, n (%)          | 17 (17.2)         | 4 (6.9)              | 12 (35.3)            | 3.12 [1.30; 7.48]     | 0.01    |
| mRS                           |                   |                      |                      |                       |         |
| ≤3, n (%)                     | 66 (66.7)         | 46 (79.3)            | 18 (52.9)            |                       |         |
| ≥3, n (%)                     | 33 (33.3)         | 12 (20.7)            | 16 (47.1)            | 3.10 [1.57; 6.11]     | <0.01   |

CI, confidence interval; ECLS, extracorporeal life support; FU, follow-up; HTx, orthotopic heart transplantation; i.v., intravenous; ICU, intensive care unit; mRS, modified Rankin Scale; VAD, ventricular assist device.

54 ± 15 years with patients who died after the 30 day period being significantly older than their counterparts [FU-Survivor: 52 ± 16 years, FU-Deceased: 58 ± 14 years, hazard ratio (HR) = 1.02,  $P = 0.05$ ]. ECLS was applied at a remote hospital in a total of  $n = 38$  patients with a significant increased incidence in the FU-Survivor group (HR = 0.43,  $P = 0.04$ ). Most common cause of circulatory failure was acute coronary syndrome (59.6%), and most common concomitant diseases were arterial hypertension (39.4%), nicotine abuse (24.2%), and diabetes (23.2%) (Table 1). In contrast to that, increased serum concentration of neuron-specific enolase at ECLS implantation was associated with impaired survival after 30 days (HR = 1.02,  $P < 0.01$ ).

Although ECLS support duration itself did not impact on the survival after 30 days, occurrence of related severe adverse events such as neurological events (HR = 3.13,  $P < 0.01$ ), visceral ischaemia (HR = 7.50,  $P < 0.01$ ), limb ischaemia (HR = 2.23,  $P = 0.05$ ), sepsis (HR = 2.55,  $P = 0.01$ ), and dependence on haemodialysis (HR = 2.45,  $P = 0.02$ ) were associated with an increased morbidity (Table 2). Similar effects were observed in patients with failed ECLS weaning and need for VAD implantation (HR = 2.23,  $P = 0.02$ ) and prolonged hospitalization as well as stay on intensive care unit and mechanical ventilation time. At time of hospital

discharge (home, other hospital, or rehabilitation clinic), need of continuous invasive ventilation (HR = 4.61,  $P < 0.01$ ), haemodialysis (HR = 3.12,  $P = 0.01$ ), as well as increased degree of dependence assessed by the mRS (HR = 3.10,  $P < 0.01$ ) were associated with an increased risk for impaired survival.

### Comprehensive follow-up

Between March and September 2017, FU-Survivors were invited for a comprehensive follow-up examination of the physiological as well as psychosomatic status and HRQL at our department. In total,  $n = 39$  patients (67.2%) were willing to participate and could be examined. The remaining patients refused to participate, mostly due to convenience issues (lack of time, distance to study site, unreasonableness regarding necessity of follow-up examination). One patient refused to answer the questionnaires and took part in the clinical examination only. The mean follow-up period was  $32.4 \pm 16.8$  months. Patients who underwent heart transplant ( $n = 4$ ) were excluded from the electrocardiogram and echocardiography.

### Clinical data

Clinical assessment revealed sinus rhythm in 97.1% of the examined patients with a mean left ventricular ejection fraction of  $50.1 \pm 12.9\%$ . Mean New York Heart Association (NYHA) class was  $2.0 \pm 0.9$  with more than 70% of patients with NYHA class  $\leq$  II (Table 3). Only one patient (2.6%) had suffered from cerebrovascular events since hospital discharge. Furthermore, no new myocardial infarction had occurred; however, seven patients (18.4%) underwent percutaneous coronary interventions. Laboratory results showed compensated liver and kidney function with not a single patient dependent on haemodialysis.

### Psychosomatic status and health-related quality of life

At time of follow-up examination, patients were dependent on  $7.0 \pm 3.9$  different prescribed oral drugs (Table 4). About one quarter of the patients resumed employment with a full-time job, and even 28.9% felt fully integrated in their work life. More than every second patient (57.9%) reported that he felt fully integrated in his social life again, which was underlined by 84.4% of patients being able to independently care for themselves ( $mRS \leq 2$ ) as well as satisfactory results for 6MWT ( $67.46 \pm 21.50\%$  of normal level). Depression assessed by BDI-II questionnaire revealed a mean score of  $9.28 \pm 7.23$  with 71.8% of patients scoring below the threshold of depression ( $BDI-II \geq 14$ ). The mean NIHSS score

**Table 3** Clinical data assessed at the follow-up examination ( $n = 39$ )

| Variables  | Outcome         |
|--|-----------------|
| Age, years   | $52 \pm 16$     |
| Male gender, $n$ (%)                                   | 30 (76.9)       |
| NYHA class, /1   | $2.0 \pm 0.9$   |
| Electrocardiogram                                      |                 |
| Sinus rhythm, $n$                                      | 34 (97.1)       |
| Atrial fibrillation, $n$                               | 1 (2.9)         |
| Echocardiography                                       |                 |
| Ejection fraction (Simpson), %                         | $50.1 \pm 12.9$ |
| LVEDD, mm  | $52.6 \pm 10.6$ |
| TAPSE, mm  | $20.2 \pm 2.44$ |
| Haemodialysis, $n$                                     | 0 (0.0)         |
| Events since hospital discharge                        |                 |
| Myocardial infarction, $n$ (%)                         | 0 (0.0)         |
| Stroke, $n$ (%)  | 1 (2.6)         |
| Interventions since hospital discharge                 |                 |
| Percutaneous coronary intervention, $n$ (%)            | 7 (18.4)        |
| Ventricular assist device, $n$ (%)                     | 0 (0.0)         |
| Heart transplantation, $n$ (%)                         | 1 (2.6)         |
| Laboratory values                                      |                 |
| Cystatin C, mg/L                                       | $1.14 \pm 0.68$ |
| Glomerular filtration rate, mL/min/1.73 m <sup>2</sup> | $61.7 \pm 25.7$ |
| Creatinine, mg/dL                                      | $1.36 \pm 0.61$ |
| Urea, mg/dL  | $47.4 \pm 35.5$ |
| Bilirubin, mg/dL                                       | $0.48 \pm 0.29$ |
| AST, U/L   | $25.5 \pm 10.0$ |
| ALT, U/L   | $29.9 \pm 16.7$ |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; LVEDD, left ventricular end-diastolic diameter; NYHA, New York Heart Association functional classification of heart failure; TAPSE, tricuspid annular plane systolic excursion.

**Table 4** Health-related quality of life assessed at follow-up examination ( $n = 38$ )

| Variables                           | Outcome           |
|-------------------------------------|-------------------|
| Quantity of prescribed drugs, $n$   | $7.0 \pm 3.9$     |
| Employment                          |                   |
| Full-time, $n$ (%)                  | 10 (26.3)         |
| Part-time, $n$ (%)                  | 1 (2.6)           |
| Retired, $n$ (%)                    | 14 (36.8)         |
| Feels fully integrated in           |                   |
| Social life, $n$ (%)                | 22 (57.9)         |
| Work life, $n$ (%)                  | 11 (28.9)         |
| Functional and psychological status |                   |
| mRS, /1                             | $1.46 \pm 1.10$   |
| 6 min walk test, % of normal level  | $67.46 \pm 21.50$ |
| BDI-II score, /1                    | $9.28 \pm 7.23$   |
| MoCA score, /1                      | $21.72 \pm 4.75$  |
| NIHSS score, /1                     | $0.82 \pm 1.05$   |
| SF-36                               |                   |
| Physical functioning, /1            | $52.4 \pm 30.8$   |
| Role physical, /1                   | $53.3 \pm 46.6$   |
| Bodily pain, /1                     | $75.2 \pm 27.1$   |
| General health, /1                  | $51.8 \pm 19.5$   |
| Vitality, /1                        | $48.3 \pm 21.6$   |
| Social functioning, /1              | $64.1 \pm 29.8$   |
| Role emotional, /1                  | $60.5 \pm 47.7$   |
| Mental health, /1                   | $69.6 \pm 18.1$   |
| Physical component summary, /1      | $40.3 \pm 11.1$   |
| Mental component summary, /1        | $46.5 \pm 48.6$   |

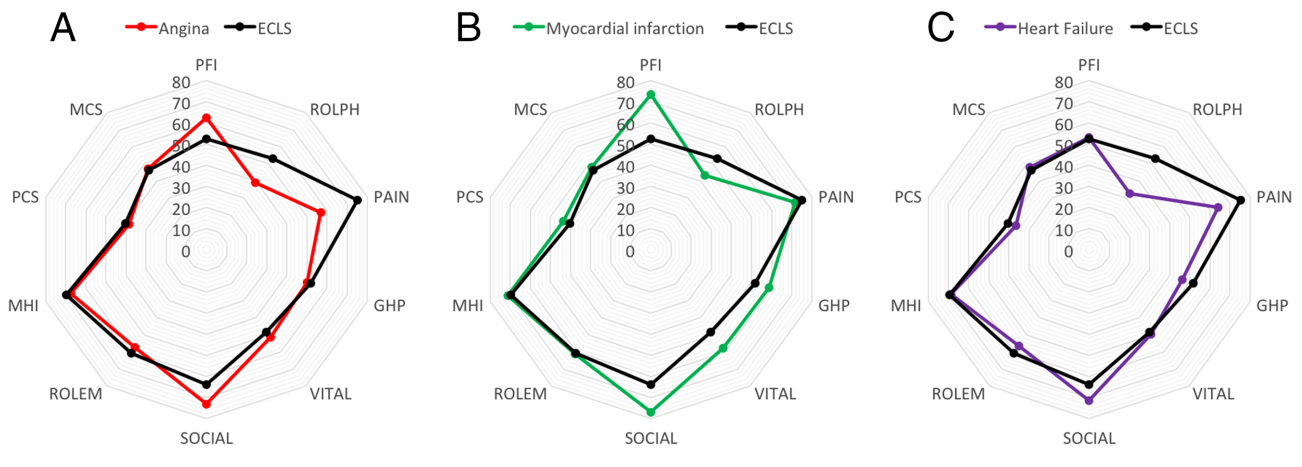
BDI-II, Beck Depression Inventory-II; MoCA, Montreal Cognitive Assessment; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SF-36, Short Form-36.

of the cohort was  $0.82 \pm 1.05$  with about one half of the patient having none and the other half suffering from only minor stroke symptoms. However, MoCA screening test indicated a mild impaired cognitive function of the study cohort with only 20.5% of patients having a score of 26 or above. Assessment of quality of life by the SF-36 questionnaire revealed that the mean score of every item was within the normal range classified as 40–60. Nonetheless, compared with an international reference population, we observed little impairment compared with patients suffering from myocardial infarction and similar to even increased results compared with angina pectoris and heart failure patients (Figure 2).<sup>15</sup>

## Discussion

Extracorporeal life support offers a promising therapy for patients suffering from therapy-refractory cardiocirculatory failure and prolonged CPR with otherwise marginal prognosis.<sup>1,3,8</sup> However, information about long-term effects and especially assessment of psychosocial status and HRQL are by now still rare.<sup>10</sup> Therefore, we invited our corresponding patient cohort of short-term survivors for a comprehensive follow-up examination. Despite high incidence of early functional impairments, our results revealed a high degree of organ and functional recovery with more than 70% of patients presenting with NYHA class  $\leq$  II, 100% free of haemodialysis,

**Figure 2** Means values of Short Form-36 (SF-36) domains. ECLS, extracorporeal life support; GHP, general health; MCS, mental component summary; MHI, mental health; PAIN, bodily pain; PCS, physical component summary; PFI, physical functioning; ROLEM, role emotional; ROLPH, role physical; SOCIAL, social functioning; VITAL, vitality. (A) Comparison of ECLS cohort ( $n = 38$ ) with an international control cohort of angina pectoris patients ( $n = 1836$ ). (B) Comparison of ECLS cohort ( $n = 38$ ) with an international control cohort of myocardial infarction patients ( $n = 2086$ ). (C) Comparison of ECLS cohort ( $n = 38$ ) with an international control cohort of heart failure patients ( $n = 1586$ ).<sup>15</sup>



100% free of moderate or severe neurological disability, 71.8% free of moderate or severe depression, and 84.4% of patients reporting to be caring for themselves without need for assistance. Therefore, patients can recover even after long periods of mechanical support and regain physical and mental health to participate in their former daily life and work, which is quite encouraging considering their primary marginal prognosis.

About two of every three patients that survived the initial 30 days after ECLS implantation were still alive at the time of follow-up examination, indicating a long-term survival of our whole cohort of 246 patients of about 24%. This is comparable with reported 1 year data in the literature.<sup>10,16</sup> In addition, median survival of patients suffering from congestive heart failure, even for age 65 to 69 years, is less than 4 years with a 5 year mortality of about 75% today, which is also comparable with our results.<sup>17</sup> Comparison of the FU-Survivor and FU-Deceased groups revealed relatively few differences between the patients and implantation characteristics. As expected, patients suffering from adverse events during ECLS treatment experienced an impaired outcome.<sup>4,16,18</sup> Nonetheless, our results showed that patients without serious adverse events during support might have a relatively good chance to recover and regain physical and psychosocial strength even after long periods of temporary mechanically circulatory support. Therefore, incidence of severe adverse events during ECLS therapy may act as a predictor of the long-term prognosis of the patients.

Thirty-nine patients participated in the comprehensive follow-up examination in order to investigate the longer-term outcome after ECLS. Clinical examinations revealed good clinical status in the vast majority of all patients with only small impairments of the daily life. Especially the low incidence of atrial fibrillation surprises for a cohort of

patients with a history of cardiac diseases and a mean age of more than 50 years.<sup>19</sup> Moreover, we observed not a single patient suffering from chronic kidney failure. Kidney failure is a common morbidity of critically ill as well as heart failure patients and was observed in more than every second patient surviving the initial 30 days after ECLS implantation.<sup>20,21</sup> At discharge, 17.2% were still dialysed, which underlines the high potential of recovery of organ function after ECLS support.<sup>22</sup>

At follow-up, patient took about seven different oral drugs per day, which is once again comparable with congestive heart failure patients.<sup>23</sup> Eleven patients resumed their occupation and felt fully integrated in their work life. In contrast to that, 14 patients had been retired and the remaining patients were currently unemployed. Nonetheless, more than every second patients felt fully reintegrated in their social life again, which is quite remarkable for such a cohort of patients. Level of dependence was also quite low with the majority of patients not needing any assistance in their daily life. Furthermore, depression, another common comorbidity of critically ill patients, patients surviving CPR, and especially heart failure patients, was rarely seen either.<sup>24–26</sup>

Although NIHSS revealed good result too, a remarkable proportion of patients still suffered from cognitive deficits. This might be related to the relatively long periods of mechanically ventilation and sedative drugs, as well as potential hypoxia during the index event.<sup>11</sup> Cardiac surgery patients, especially those who underwent aortic arch surgery, often suffer from perioperative delirium, which is also associated with cognitive disorders potentially lasting for several months before being reversible.<sup>27,28</sup> Finally, HRQL assessed by the SF-36 questionnaire confirmed acceptable results for all items and was comparable with recent published data by Guenther and colleagues of a comparable cohort of ECLS patients.<sup>10</sup>

Interestingly, besides bodily pain, best items were mental health, social functioning, and role emotional, which goes in line with our reported data of the MoCA and BDI-II scores. While SF-36 data of the ECLS cohort were in general impaired compared with an international cohort of myocardial infarction patients, results were similar or even superior to angina pectoris and heart failure patients.<sup>29</sup>

## Limitations

Although this is one of the largest comprehensive follow-ups in terms of survival and functional status of patients treated with ECLS for cardiocirculatory failure, this study still has several limitations. Due to the retrospective design, there are methodological limitations as compared with randomized trials. Furthermore, every patient was examined only once in the follow-up period leading to different follow-up durations. Seven patients were lost to follow-up, and additional 19 of the surviving patients refused to participate in the follow-up examinations. Although refusal to participate in the study was mostly due to convenience issues, the functional status of these patients remains unclear most likely provoking a selection bias. In addition, psychosomatic and HRQL data from the different questionnaires originates from patient self-assessment, and therefore, it has to be interpreted with caution. Nonetheless, this study shows that recovery after ECLS therapy is quite promising in a cohort of patients being otherwise most likely deceased due to therapy-refractory circulatory failure and return to normal life after such an incisive event and subsequent complicated clinical course is possible for a large proportion of patients.

## Conclusions

Treatment of therapy-refractory cardiocirculatory failure with ECLS can offer patients a chance of not only surviving this

life-threatening event but even regain physical and mental health to participate in their former daily life and work. By this comprehensive follow-up investigation, we were able to demonstrate that patients surviving the initial critical phase after the primary event of cardiac failure without experiencing severe ECLS-related adverse events such as neurological complications, visceral or limb ischaemia, and acute kidney failure can recover even after long periods of mechanically support. Although only a small proportion of the whole cohort may survive the first 30 days, survivors have the chance to experience high quality of afterlife, which is a remarkable success, especially with regard to the fatal prognosis of those patients without ECLS therapy.

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## Conflict of interest

None declared.

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