Long-term survival and health-related quality of life in patients with severe acute respiratory distress syndrome and veno-venous extracorporeal membrane oxygenation support

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Abstract

Background: There is limited information about the long-term outcome of patients suffering from acute respiratory distress syndrome (ARDS) supported with veno-venous extracorporeal membrane oxygenation (VV ECMO). Most studies focused on short- to mid-term follow-up. We aimed to investigate long-term survival and health-related quality of life (HRQL) in these patients.

Methods: We report retrospective data from a single-centre registry of patients with severe ARDS treated with VV ECMO at the Interdisciplinary Medical Intensive Care Unit at the Medical Centre, University of Freiburg, Germany, between 10/2010 and 06/2019. Follow-up data of all patients that survived the index hospitalisation were collected by telephone interviews from 02/2020 till 09/2020. Long-term survival, HRQL (Short-Form Health Survey-36 (SF-36), St. Georges Respiratory Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS)) and the return to work rate were documented.

Results: In total, 289 patients were treated with VV ECMO during the study period (median age 55 years, 67% males, hospital survival 45%). After a median duration of 3.9 years, follow-up assessment was complete in 94 of 129 hospital survivors (73%). Fifty-three patients completed the HRQL assessment. Hospital survivors showed a high 6- and 12-month survival rate (89% and 85%, respectively). Estimated survival rate of those discharged alive from ICU was 68.5% (95%-CI 56.9–80.1%) after 9.7 years. These patients reported high levels of HRQL (median SF-36 total score 73) and only few pulmonary (median SGRQ total score 19) and mental limitations (median HAD-D score 2 and HAD-A score 3). In total, 80% of the patients were able to resume employment.

Conclusion: This analysis of VV ECMO patients showed favourable long-term survival and high levels of HRQL suggesting promising prospects for VV ECMO survivors.
Keywords: ECMO, Extracorporeal membrane oxygenation, Acute respiratory distress syndrome, Outcome, Survival, Long-term, Quality of life

Background

Patients with severe acute respiratory distress syndrome (ARDS) may benefit from veno-venous extracorporeal membrane oxygenation (VV ECMO) support [1–3]. A substantial increase in the use of ECMO support has been recorded over the recent years [4]. Nevertheless, the mortality of these patients remains very high [2]. In addition, patients suffer from complications as a result of their underlying disease or as a direct consequence of ECMO support, such as secondary infections, bleedings, thromboses and embolisms [5, 6]. Moreover, patients surviving complex intensive care treatment including severe ARDS therapy and ECMO support are often severely compromised even after discharge and at risk to subsequently die in the further course [7].

It is difficult to predict long-term survival of individual patients. Future quality of life is often of major interest for the patients, relatives and ICU teams. The resource-intensive and extended course of these patients, often prone to serious complications, may lead to a high level of emotionality within the treatment teams with a potential impact on therapy decisions. More evidence about long-term survival and long-term quality of life would therefore be of great value for appropriate therapy management. However, most VV ECMO outcome studies only focus on hospital survival or a short- to mid-term outcome after 6 or 12 months, respectively [7–11].

We performed an analysis of long-term survival, long-term health-related quality of life (HRQL) and the rate of return to work with an extended follow-up period in ARDS patients supported with VV ECMO. Furthermore, we analysed factors associated with hospital and mid-term survival.

Methods

Study population

We report retrospective data from a single-centre registry of adult patients with severe ARDS according to the Berlin definition (Horowitz index < 100 mmHg) [12] supported with VV ECMO. VV ECMO was initiated in cases of severe hypoxic respiratory failure or hypercapnia despite invasive mechanical ventilation as suggested by ELSO guidelines [13].

All patients treated at the Interdisciplinary Medical Intensive Care Unit at the Medical Centre, University of Freiburg, Germany, from October 2010 through June 2019 were registered. Follow-up data of all patients surviving the index hospitalisation were collected by standardized telephone interviews from February 2020 through September 2020. We followed a systematic approach for contacting the patients using the last available registration address, the patients telephone numbers, the contact information (postal and telephone) of relatives or caregivers, and the patient primary care physician. All patients who were interviewed by telephone provided written informed consent to participate in the study. The study was approved by the University of Freiburg Ethics Committee (EK-Freiburg 553/19).

Study endpoints and definitions

The primary endpoint of this study was long-term survival (Kaplan–Meier survival estimation) after hospital discharge.
chonic obstructive pulmonary disease (COPD) refer-
of the respiratory questionnaire were compared with a
severe ARDS generally biphasic positive airway pressure
rial and veno-venous cannulation are 65 and 35 per year,
part of a tertiary hospital. Typical numbers for veno-ar-
ized joined to a 30-bed medical intensive care unit and
Our centre provides a 24/7 ECMO service and is local-
was based on concordance of microbiological findings
was investigated. Assignment to pulmonary pathogens
retained by broncho-alveolar lavage and tracheal secretions
caused by HIV.
sive therapies (cut-off for cortisone: ≥ 10 mg prednisolone equivalent) and patients with immunosuppression caused by HIV.
Furthermore, pulmonary pathogen spectrum ascer-
tained by broncho-alveolar lavage and tracheal secrections
was investigated. Assignment to pulmonary pathogens was based on concordance of microbial findings with clinical signs of infection.

**ECMO centre and ECMO management**

Our centre provides a 24/7 ECMO service and is local-
ized joined to a 30-bed medical intensive care unit and part of a tertiary hospital. Typical numbers for veno-arterial and veno-venous cannulation are 65 and 35 per year, respectively.

In our institution, for mechanical ventilation (MV) in severe ARDS generally biphasic positive airway pressure (bilevel ventilation) is used. VV ECMO support was implemented in case of severe but potentially reversible respiratory failure, when lung-protective MV resulted in hypoxemia or hypercapnia following established criteria [26]. To date, lung-protective MV was defined as positive end expiratory pressure (PEEP) ≤ 15cmH2O, plateau pressure ≤ 30cmH2O, driving pressure ≤ 15cmH2O and FiO2 ≤ 50%. The management of vasopressors and fluid therapy was driven by clinical judgement of the ECMO experienced intensivist in charge and has been reported earlier [27]. Treatment algorithms and standard operating procedures were subject to optimizations during the observational period, reflecting current state-of-the-art recommendations and scientific knowledge. In particular, patient selection was adjusted with regard to comorbidities, so that patients with immunosuppression are only treated with ECMO after very careful evaluation and patients with lung fibrosis (with a few exceptions) are no longer supported with ECMO.

After initiation of VV ECMO, invasiveness of MV was reduced and ECMO flow was adjusted aiming for a peripheral oxygen saturation of 85–90% and partial pressure arterial oxygen of approximately 60 mmHg. Typical ventilator settings were: PEEP 15cmH2O, plateau pressure 25cmH2O, FiO2 50%, respiratory rate 10/min. Details on ventilator management and prone positioning procedures have been described earlier [28]. Additional information about ECMO management is available in Additional file 1.

**Statistical analysis**

Continuous variables are presented as median and inter-quartile range (IQR), categorical variables as numbers and percentages. Mann–Whitney U test was used for analysis of continuous variables, Pearson’s Chi-squared test or Fisher’s exact test for categorical variables. Logistic regression analysis using forward selection with a threshold of p < 0.05 of all clinical characteristics (excluding survival prediction scores) was performed for predictors of hospital survival and 6-month survival. Results are given as odds ratio [(OR), 95% confidence interval (CI)], and a p value of ≤ 0.05 was considered statistically significant. Primary endpoint (long-term survival after hospital discharge) was analysed using the Kaplan–Meier method. Median follow-up time was calculated as the simple median time from discharge to last follow-up point. Statistical calculations were performed using IBM SPSS statistics 25.0 (Armonk, NY: IBM Corp, 2017). Survival analysis was conducted in R (R Core Team, 2014), and figures were produced using the package ggplot2 (Wickham, 2009) and GraphPad Prism 9 (San Diego, California USA, 2020).
| Demographics                          | All \((n = 289)\) | Status after index hospitalisation | Dead \((n = 160, 55.4\%\)) | \(p\) value |
|--------------------------------------|-------------------|-----------------------------------|-----------------------------|------------|
| Age (y)                              | 55 (43–64)        | 53 (41.5–59.5)                    | 56 (45–66.8)                | 0.027      |
| Sex (male)                           | 194 (67.1\%)      | 89 (69\%)                        | 105 (65.6\%)                | 0.545      |
| BMI (kg/m\(^2\))                    | 24.5 (23.4–29.3)  | 24.5 (22.9–30.2)                  | 24.4 (23.5–27.8)            | 0.610      |
| Underlying pulmonary disease         | 87 (30.1\%)       | 32 (24.8\%)                      | 55 (34.4\%)                 | 0.078      |
| COPD                                 | 25 (8.7\%)        | 11 (8.5\%)                       | 14 (8.8\%)                  | 0.947      |
| Asthma                               | 16 (5.5\%)        | 7 (5.4\%)                        | 9 (5.6\%)                   | 0.941      |
| Lung fibrosis                        | 26 (9\%)          | 2 (1.6\%)                        | 24 (15\%)                   | <0.001     |
| Cystic fibrosis                      | 7 (2.4\%)         | 1 (0.8\%)                        | 6 (3.8\%)                   | 0.102      |
| LTOT                                 | 14 (4.8\%)        | 3 (2.3\%)                        | 11 (6.9\%)                  | 0.073      |
| Pulmonary hypertension              | 8 (2.8\%)         | 1 (0.8\%)                        | 7 (4.4\%)                   | 0.064      |
| Comorbidities                        |                   |                                   |                             |            |
| Nicotine abuse                       | 98 (33.9\%)       | 50 (38.8\%)                      | 48 (30\%)                   | 0.118      |
| Hypertension                         | 99 (34.3\%)       | 49 (38\%)                        | 50 (31.3\%)                 | 0.230      |
| Diabetes mellitus                    | 39 (13.5\%)       | 17 (13.2\%)                      | 22 (13.8\%)                 | 0.888      |
| CAD                                  | 36 (12.5\%)       | 13 (10.1\%)                      | 23 (14.4\%)                 | 0.271      |
| Chronic renal failure                | 21 (7.3\%)        | 8 (6.2\%)                        | 13 (8.1\%)                  | 0.531      |
| Chronic haemodialysis                | 2 (9.1\%)         | 1 (12.5\%)                       | 1 (7.1\%)                   | 0.674      |
| Liver cirrhosis                      | 22 (7.6\%)        | 4 (3.1\%)                        | 18 (11.3\%)                 | 0.009      |
| Immunosuppression                    | 89 (30.8\%)       | 24 (18.6\%)                      | 65 (40.6\%)                 | <0.001     |
| Oxygenation pre-ECMO                 |                   |                                   |                             |            |
| \(\text{FiO}_2\) \((\%)\)           | 1 (0.8–1)         | 1 (0.8–1)                        | 1 (0.8–1)                   | 0.271      |
| Horowitz index \((\text{mmHg})\)    | 72.5 (60.5–98.8)  | 77.1 (62.1–107)                  | 70 (59.3–95.7)              | 0.256      |
| \(D (A-a)\text{O}_2\) \((\text{mmHg})\) | 556 (422.8–596.8) | 550 (385.5–591.8)               | 570 (442.3–598)             | 0.115      |
| Duration of MV before ECMO \((\text{d})\) | 1.2 (0.3–3.5) | 1.1 (0.2–3)                      | 1.3 (0.3–5.3)               | 0.341      |
| Acute renal failure                  |                   |                                   |                             |            |
| SOFA score                           | 13 (10–15)        | 12 (10–15)                       | 13 (10–16)                  | 0.439      |
| APACHE-II score                      | 26 (20.5–32)      | 25 (19–31)                       | 27 (22–33)                  | 0.022      |
| RESP score                           | 1 (-2–3)          | 2 (-0.5–4)                       | 1 (-2–3)                    | 0.006      |
| Causes of ARDS                       |                   |                                   |                             |            |
| Pneumonia                            | 206 (71.3\%)      | 89 (69\%)                        | 117 (73.1\%)                | 0.440      |
| Aspiration                           | 25 (8.7\%)        | 10 (7.8\%)                       | 15 (9.4\%)                  | 0.626      |
| Other injuries                       | 58 (20.1\%)       | 30 (23.3\%)                      | 28 (17.5\%)                 | 0.225      |
| Pulmonary pathogen spectrum          |                   |                                   |                             |            |
| Bacterial                             | 120 (41.5\%)      | 67 (51.9\%)                      | 53 (33.1\%)                 | 0.001      |
| Viral                                 | 91 (31.5\%)       | 44 (34.1\%)                      | 47 (29.4\%)                 | 0.389      |
| Fungal                                | 56 (19.4\%)       | 16 (12.4\%)                      | 40 (25\%)                   | 0.007      |
| Pneumocystis jirovecii               | 19 (6.6\%)        | 4 (3.1\%)                        | 15 (9.4\%)                  | 0.032      |
| Procedural characteristics and outcome|                 |                                   |                             |            |
| ICU length of stay \((\text{d})\)    | 13.5 (9–23.5)     | 17.9 (11.7–32.8)                 | 11.1 (5.5–18.9)             | <0.001     |
Results

Patients and follow-up

A total of 289 patients were treated with VV ECMO at our centre in the study period (median age 55 (43–64) years, 67.1% males). These patients showed a high rate of underlying pulmonary diseases (30.1%), especially lung fibrosis (9%), and other comorbidities like immunosuppression (31%) and liver cirrhosis (7.6%, Table 1). Median SOFA score was 13 (10–15), APACHE-II score 26 (20.5–32) and RESP score 1 (–2–3) indicating a high disease severity.

Follow-up duration ranged from 1.3 to 9.7 years with a median follow-up of 3.9 (2.2–6.6) years. Follow-up was successful in 94 of 129 hospital survivors (72.8%, Fig. 1). Seventy-one (75.5%) of these patients were alive at follow-up, and 53 patients (74.6%) agreed to a HRQL assessment.

Hospital, mid-term and long-term survival

Weaning was successful in 153 of 289 ECMO patients (52.9%) and 129 patients (44.6%) survived the index hospital stay. Hospital survivors showed a high mid-term survival rate with 84 of 94 patients (89.4%) alive after 6 months and 80 of 94 patients (85.1%) alive after 12 months, respectively. Kaplan–Meier estimation showed a survival rate of 68.5% (95%-CI 56.9–80.1%) 9.7 years after ECMO support (Fig. 2, Kaplan–Meier estimation of all patients is shown in Additional file 1: figure E6).

Predictors for hospital and 6-month survival

In univariate analysis age, lung fibrosis, liver cirrhosis, immunosuppression, fungal pulmonary infection were associated with increased hospital mortality, while bacterial pulmonary infection was associated with increased hospital survival (Table 1). Logistic regression analysis revealed age, lung fibrosis, liver cirrhosis, immunosuppression and bacterial pulmonary infection as independent predictors for hospital mortality and survival, respectively (Fig. 3).

In the landmark analysis of hospital survivors with successful follow-up underlying pulmonary disease, long-term oxygen therapy, a duration of MV before ECMO of more than 7 days and the duration of ECMO support itself were associated with reduced 6-month survival
In logistic regression analysis only the duration of ECMO support was an independent predictor for 6-month mortality (odds ratio: 0.66 (95%-CI 0.01–0.91, \( p = 0.010 \)) per week (Fig. 3).

**Long-term health-related quality of life**

HRQL assessment was successful for 53 patients (one patient only completed SF-36, therefore 52 patients for SGRQ and HADS assessment) and conducted 3.9 (2.2–6.6) years after ECMO cannulation.

A great number of these patients were working at follow-up (82%; 61% continued in their previous job, 21% had to change their jobs), 8% were permanently disabled, and 10% were already without work before ECMO support (Fig. 4, a).

The SF-36 showed a high total score of 72.9 (61.7–83.8), which was within the range of the German age- and sex-adjusted reference cohort. Only the categories physical, role limitations, physical health and general health showed a higher level of limitations in the ECMO cohort (Fig. 4, b).

The level of anxiety (HAD-A) was comparable to the German reference cohort, and the level of depression (HAD-D) was even significantly lower in the ECMO cohort (Fig. 4, c).

Respiratory limitations (measured by the SGRQ) ranged between the limitations prevalent in the general population (IBERPOC) and those of a reference cohort of COPD patients (COSYCONNECT). In every single category of the SGRQ (impacts, symptoms and activity), the patients of the ECMO cohort showed significant lower levels of limitation compared to the COPD cohort but higher levels of limitation compared to the general population (Fig. 4, d).

An association between HRQL and the time to follow-up after ECMO cannulation could not be demonstrated in this cohort (Additional file 1: Table E2). With the exception of the SF-36 physical role and HAD-A, there was also no association between HRQL and the duration of ECMO support (Additional file 1: Table E3).

Reference ECMO and ARDS cohorts showed comparable levels of HRQL. The SF-36 showed a slight trend in favour for the presented ECMO cohort in the total score and in the categories physical functioning, social functioning and emotional role (Additional file 1: figure E1 and E2). The results of the SGRQ and the HAD-A were comparable, while the results of the HAD-D were slightly higher in comparative groups (Additional file 1: figure E3 and E4). Moreover, there was a trend for a higher back to work rate in the presented ECMO patients compared to the reference studies (Additional file 1: figure E5).

**Discussion**

This analysis describes, to the best of our knowledge, the longest follow-up period of VV ECMO patients reported so far and showed a remarkable long-term survival rate as well as high levels of health-related quality of life.
Patients in this cohort were similar in age and gender distribution to previous ECMO cohorts, but had a high rate of relevant comorbidities, particularly lung fibrosis, immunosuppression and liver cirrhosis, resulting in high hospital mortality.

Patients that survived initial hospitalisation showed a very high 6-month survival of nearly 90% which is comparable to the results of the CESAR trial [7]. Moreover, these patients showed a 10-year survival rate of approximately 70%.

Most analyses of survival predictors focus on a baseline analysis with respect to hospital survival or 6-month survival. To increase our understanding of factors that may affect post-discharge survival, we also performed a landmark analysis of hospital survivors. Predictors of hospital survival were age and severe pre-existing conditions such as lung fibrosis, liver cirrhosis, immunosuppression and pulmonary pathogen spectrum. These are typical factors which were associated with survival in previous ECMO studies [8, 23, 29–31] as well.

Most interestingly, our landmark analysis showed that pre-existing conditions of VV ECMO patients that survived the index hospitalisation were no longer associated with the probability of long-term survival. The only independent predictor of 6-month survival was the duration of ECMO support.

Possibly, patients with severe pre-existing conditions and a poor general state of health prior to ARDS die frequently during ECMO support and patients with less severe pre-existing conditions tend to survive. Therefore, these underlying diseases seem to play a minor role in the further course of the patients. In contrast, after the initial hospital

| Predictors of hospital survival | Odds ratio (95% CI) for survival | P value |
|-------------------------------|---------------------------------|--------|
| Age                           | 0.981 (0.964-0.999)             | 0.034  |
| Lung fibrosis                 | 0.115 (0.026-0.508)             | 0.004  |
| Liver cirrhosis               | 0.167 (0.053-0.532)             | 0.002  |
| Immunosuppression             | 0.431 (0.236-0.788)             | 0.006  |
| Bacterial pathogen            | 1.796 (1.054-3.060)             | 0.031  |
| Fungal pathogen               | 0.527 (0.264-1.052)             | 0.069  |

| Predictors of 6-month survival (landmark analysis) | Odds ratio (95% CI) for survival | P value |
|---------------------------------------------------|---------------------------------|--------|
| ECMO duration (7 days)                            | 0.658 (0.010-0.906)             | 0.010  |
| Duration of MV before ECMO                        | 0.959 (0.889-1.033)             | 0.270  |
| LTOT                                              | 0.137 (0.008-2.493)             | 0.179  |
| Pulmonary disease                                 | 0.272 (0.051-1.441)             | 0.126  |

Fig. 3 Predictors of hospital and 6-month survival. Logistic regression analysis of factor associated with hospital survival and with 6-month survival (6-month survival of primary hospital survivors—landmark analysis). Age, lung fibrosis, liver cirrhosis and immunosuppression were independent predictors for increased hospital mortality, while proof of bacterial infection was a predictor for increased survival. In the landmark analysis only the ECMO duration was an independent predictor for increased mortality. ECMO: extracorporeal membrane oxygenation; LTOT: long-term oxygen therapy; MV: mechanical ventilation.
Fig. 4 Health-related quality of life in the long-term follow-up of VV ECMO survivors. A) Distribution of patients, who were able to return to work after discharge, had to change their job or were no longer able to work. B) SF-36 of VV ECMO survivors compared to German general population (DESG1) [18]. Higher scores denote better health-related quality of life. C) HAD-D and HAD-A compared to German general population (Hinz et al.) [17]. Lower scores denote lower levels of depression and anxiety. D) SGRQ compared to the German COSYCONECT population (COPD reference cohort) [19] and the Spanish IBERPOC general population [20]. Lower scores denote lower levels of pulmonary impairment. ECMO extracorporeal membrane oxygenation; VV veno-venous.
The quality of life measured in our study cohort was even better than in previous HRQL analyses of ECMO or ARDS survivors [21, 32, 33]. One hypothesis could be a correlation between the time point of the HRQL survey and the level of remaining limitations. While the CESAR trial [7] with a 6-month follow-up reported a relatively low SF-36 score, the PRESERVE study [8] with an average follow-up of 17 months reported better SF-36 scores. A similar distribution was found for the proportion of patients that were able to return to work. However, in this study there was no correlation between the duration of follow-up and the level of HRQL. This might be due to the fact that the shortest follow-up started at 1.3 years and thus the early phase after discharge could not be assessed. To further investigate this hypothesis, a serial prospective follow-up with standardized intervals would be necessary.

In summary, these results indicate a rather good HRQL after ECMO. The median age of the patients in this study was 55 years, and they were therefore expected to continue to work for more than 10 years. Therefore, an economic consideration of the survivors is also important. Also from this point of view, the results were very encouraging, as only 8% of the patients who were working before the ARDS developed a disability and over 60% even were able to remain in their former job. This high rate of ability to work could be a result of the overall lower physical and mental limitations compared to previous studies [7, 8, 21].

The Here reported retrospective analysis, both survival and quality of life showed very encouraging long-term results. These results may help to strengthen the confidence of patients, relatives and ICU teams involved in the treatment of severe ARDS requiring ECMO support. In order to confirm these results and to explore changes in HRQL over time, large prospective studies with defined follow-up intervals should be conducted.

**Limitations**

This is a retrospective observational study, and therefore, there is a risk of selection and reporting bias, although all ECMO patients of our centre were included and the ECMO indication was based on standardized algorithms. Thus, our patients showed similar disease severity and mortality compared to previous ECMO studies. Moreover, this is a single-centre report and centre-specific processes may influence the presented results. The loss of follow-up rate is comparable to previous studies on HRQL in ECMO patients, and we therefore consider it acceptable for a retrospective analysis and a particularly long follow-up period. However, a distortion of the results due to missing data (loss of follow-up 4 years after initial hospital stay was 27%) cannot be excluded. Moreover, one quarter of the patients did not participate in the HRQL interview. Together, due to these limitations, our findings should be considered as hypothesis-generating and should not prompt clinical decision-making.

**Conclusion**

This analysis of VV ECMO patients showed an encouraging long-term survival rate with a high level of health-related quality of life and thereby demonstrates a promising perspective for ECMO survivors.

**Abbreviations**

APACHE II score: Acute Physiology And Chronic Health Evaluation; ARDS: Acute respiratory distress syndrome; BAL: Broncho-alveolar lavage; BMI: Body mass index; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; D(A-a)O2: Alveolar-arterial gradient of oxygen concentration; ECMO: Extracorporeal membrane oxygenation; FiO2: Fraction of inspired oxygen; HRQL: Health-related quality of life; IMV: Invasive mechanical ventilation; ICU: Intensive care unit; LTOT: Long-term oxygen therapy; MV: Mechanical ventilation; PEEP: Positive end expiratory pressure; RESP: Respiratory Extracorporeal Membrane Oxygenation Survival Prediction; SOFA score: Sequential Organ Failure Assessment; TS: Tracheal secretions; VV: Veno-venous.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s13054-021-03821-0.

**Additional file 1:** Figure E1–E5 and Table E1–E3: Long-term survival and health-related quality of life in patients with severe acute respiratory disease.
the corresponding author on reasonable request.

The datasets used and/or analysed during the current study are available from

Availability of data and materials

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Authors' contributions

JR and TW contributed to the conception of the study; JR, KK and TW contrib-

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tion; JR, KK and TW drafted the manuscript; XB, MJ, VZ, CNL, DD, AS, CB and

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Competing interests

Not applicable.

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Declarations

Ethics approval and consent to participate

The protocol was approved by our institution's ethical committee (EK-Freiburg

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Combes A, Hajage D, Capelli J, Demoule A, Lavoue S, Guervilly C, Da Silva D, Zafra

2. Munshi L, Walkley A, Golgher E, Pham T, Uleynek EM, Fan E. Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome: a systematic review and meta-analysis. Lancet Respir Med. 2019;7(2):163–72.

3. Ellett LJ, Kurth BM. Health related quality of life in adults in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsvorsorge. 2013;56(5–6):643–9.

4. Lutter JI, Jorres RA, Kahnert K, Schwarzkopf L, Studnicka M, Karrasch S, et al. Health-related quality of life in adult survivors of the acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526–33.

5. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–70.

6. Abrams D, Grassell G, Schmidt M, Mueller T, Brodje D. ECLS-associated infections in adults: what we know and what we don’t yet know. Intensive Care Med. 2020;46(2):182–91.

7. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalany MM, Hibbert CL, Truetsch A, Cleemans F, Cooper N, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet. 2009;374(9698):1351–63.

8. Schmidt M, Zogheib E, Roze H, Repesse X, Lebreton G, Lyut CE, Trouillet JL, Brechot N, Nieszkowska A, Schmidt M, Trouillet JL, Leprince P, et al. Brain injury during venovenous extracorporeal membrane oxygenation. Intensive Care Med. 2016;42(5):897–907.

9. Wang ZY, Li T, Wang CT, Xu L, Gao XJ. Assessment of 1-year outcomes in survivors of severe acute respiratory distress syndrome receiving extracorporeal membrane oxygenation or mechanical ventilation: a prospective observational study. Chin Med J (Engl). 2017;130(10):1161–8.

10. Grasselli G, Sciaravilli V, Tufiolo D, Russo R, Citrella F, Bichi F, Corinna Morlacci L, Scotti E, Patrini L, Gattinoni L, et al. Quality of life and lung function in survivors of extracorporeal membrane oxygenation for acute respiratory distress syndrome. Anesthesiology. 2019;130(4):572–80.

11. Chen KH, Tsai FC, Tsai CS, Yeh SL, Weng LC, Yeh LC. Problems and health needs of adult extracorporeal membrane oxygenation patients following hospital discharge: a heart lung study. Healthc. 2016;4(5):147–53.

12. Force ADT, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526–33.

13. Extracorporeal Life Support Organization (ELSO), Guidelines for Adult Respiratory Failure, August, V 1A. 2017 https://www.elseo.org/Portals/0/ELSO%20Guidelines%20For%20Adult%20Respiratory%20Failure%201A.pdf. Accessed 03 Feb 2020.

14. Tarlov AR, Ware JE Jr, Greenfield S, Nelson EC, Perrin E, Zubkoff M. The Medical Outcomes Study: An application of methods for monitoring the results of medical care. JAMA. 1989;262(7):925–30.

15. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis. 1992;145(6):1321–7.

17. Hinz A, Braehler E. Normative values for the hospital anxiety and depression scale. Acta Psychiart Sci. 1983;67(6):361–70.

19. Lutter JI, Jorres RA, Kahnert K, Schwarzkopf L, Studnicka M, Karrasch S, et al. Health-related quality of life in adult survivors of the acute respiratory distress syndrome: a meta-analysis. Intensive Care Med. 2006;32(8):1115–24.

21. Dowdy DW, Eid MP, Dennison CR, Mendez-Tellez PA, Herridge MS, Guallar DV, et al. Prediction of mortality with the Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score. Am J Resp Crit Care Med. 2014;189(11):1374–82.

23. Schmidt M, Bailey M, Sheldrake J, Hodgson C, Aubron C, Rycus PT, et al. ECLS-related mortality and multi-organ dysfunction in survivors of severe respiratory failure: the Extracorporeal Membrane Oxygenation Survival Prediction (RESP) model. Intensive Care Med. 2013;39(10):1704–13.

24. Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bellomo R, Pilcher DV, Australian, New Zealand Intensive Care Society Centre for O, Resource Management. pdf. Accessed 03 Feb 2020.

25. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis. 1992;145(6):1321–7.
25. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–29.
26. Abrams D, Ferguson ND, Brochard L, Fan E, Mercat A, Combis A, Pellegroto V, Schmidt M, Slutsky AS, Brodie D. ECMO for ARDS: from salvage to standard of care? Lancet Respir Med. 2019;7(2):108–10.
27. Staudacher DL, Gold W, Beier PM, Bode C, Wengenmayer T. Early fluid resuscitation and volume therapy in venoarterial extracorporeal membrane oxygenation. J Crit Care. 2017;37:130–5.
28. Rilinger J, Zotzmann V, Berntgen X, Schumacher C, Beier PM, Duerschmied D, Kaier K, Stachon P, von Zur MC, Zehender M, et al. Prone positioning in severe ARDS requiring extracorporeal membrane oxygenation. Crit Care. 2020;24(1):397.
29. Roch A, Hraiech S, Masson E, Grisoli D, Forel JM, Boucekine M, Morera P, Guervilly C, Adda M, Dizier S, et al. Outcome of acute respiratory distress syndrome patients treated with extracorporeal membrane oxygenation and brought to a referral center. Intensive Care Med. 2014;40(1):74–83.
30. Schmidt M, Pham T, Arcadipane A, Agerstrand C, Ohshimo S, Pellegrino V, Vuylsteke A, Guervilly C, McGuinness S, Pierard S, et al. Mechanical ventilation management during extracorporeal membrane oxygenation for acute respiratory distress syndrome. An international multicenter prospective cohort. Am J Respir Crit Care Med. 2019;200(8):1002–12.
31. Rilinger J, Zotzmann V, Berntgen X, Reig S, Beier PM, Duerschmied D, Pottgiesser T, Kaier K, Bode C, Staudacher DL, et al. Influence of immunosuppression in patients with severe acute respiratory distress syndrome on veno-venous extracorporeal membrane oxygenation therapy. Artif Organs. 2021.
32. Sylvestre A, Adda M, Maltese F, Lannelongue A, Daviet F, Parzy G, Coiffard B, Roch A, Loundou A, Baumstarck K, et al. Long-term neurocognitive outcome is not worsened by the use of venovenous ECMO in severe ARDS patients. Ann Intensive Care. 2019;9(1):82.
33. Harley O, Reynolds C, Nair P, Buscher H. Long-term survival, posttraumatic stress, and quality of life post extracorporeal membrane oxygenation. ASAIO J. 2020;66(8):909–14.

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