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MAIN TEXT

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Outcome after veno-arterial extracorporeal membrane oxygenation in elderly patients: A 14-year single-center experience

Zdenek Provaznik[1] | Alois Philipp[1] | Thomas Müller[2] | Kozakov Kostiantyn[1] | Dirk Lunz[3] | Christof Schmid[1] | Bernhard Floerchinger[1]

[1]Department of Cardiothoracic Surgery, University Medical Center Regensburg, Regensburg, Germany

[2]Department of Internal Medicine II, Cardiology, Pneumology, Intensive Care, University Medical Center Regensburg, Regensburg, Germany

[3]Department of Anesthesia, University Medical Center Regensburg, Regensburg, Germany

Correspondence
Zdenek Provaznik, MD, Department of Cardiothoracic Surgery, University Medical Center Regensburg, Franz-Josef-Strauß-Allee 11, Regensburg 93053, Germany.
Email: zdenek.provaznik@ukr.de

Abstract

Background: Use of veno-arterial extracorporeal membrane oxygenation (VA-ECMO) in elderly patients is controversial because of presumed poor outcome. Our primary aim was to determine the influence of advanced age on short- and long-term outcome; the secondary aim was to analyze risk factors for impaired outcome.

Methods: Between January 2006 and June 2020, 645 patients underwent VA-ECMO implantation in our department. The patients were categorized into four groups:<50, 50–59.9, 60–69.9 and ≥70 years old. Data were retrospectively analyzed for short- and long-term outcome. Risk factors for in-hospital mortality and mortality during follow-up were assessed using multivariate regression analysis.

Results: VA-ECMO support duration was comparable in all age groups (median 3 days). Weaning rates were 60.8%/$n = 104$ (<50 years), 51.4%/$n = 90$ (50–59.9 years), 58.8%/$n = 107$ (60–69.9), and 67.5%/$n = 79$ (≥70, $p = 0.048$). Hospital mortality was highest in the patients aged 50–59.9 years (68%/$n = 119$), but not in the elderly patients (60–69.9, ≥70:62.1%/$n = 113$, 58,1%/$n = 68$). At discharge, the cerebral performance category scores were superior in the patients <50 years. Multivariate logistic regression analysis revealed chronic kidney failure requiring hemodialysis, duration of cardiopulmonary resuscitation, and elevated blood lactate levels before VA-ECMO, but not age as predictors of in-hospital mortality. Cox's regression disclosed age as relevant risk factor for death during follow-up. The patients' physical ability was comparable in all age groups.

Conclusion: VA-ECMO support should not be declined in patients only because of advanced age. Mortality and neurological status at hospital discharge and during follow-up were comparable in all age groups.

KEYWORDS
extracorporeal membrane oxygenation, long-term outcome, low cardiac output, resuscitation, survival

1 | INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) evolved from the cardiopulmonary bypass used in cardiac surgery.[1] Depending on set-up, ECMO can provide temporary circulatory or respiratory support. Nowadays, ECMO is an appropriate tool for cardiorespiratory support in patients who do not respond to medical therapy. In elderly patients with presumed higher morbidity and impaired prognosis, the use of ECMO is controversial and raises ethical issues concerning limitations of its application.[2]

According to the current guidelines established by the Extracorporeal Life Support Organization (ELSO), advanced age of patients with cardiac failure is considered a relative contraindication for VA-ECMO support.[3] However, there are no defined criteria for age, and decisions for or against ECMO use should be made on individual basis. Thus, the questions whether advanced age predicts worse outcome, what is the quality of life of survivors, and whether ECLS represents a bridge to recovery or just a bridge to disability for elderly patients remain unanswered.

This analysis describes 14 year-experience at the University Medical Center Regensburg in treating elderly patients with VA-ECMO. Our primary aim was to determine the influence of advanced age on short- and long-term outcome; secondary aim was to analyze risk factors for impaired outcome.

2 | MATERIALS AND METHODS

The study was approved by the Ethics Committee of the University Regensburg (study number 20-2058-104). Data were obtained from the institutional database. Between January 2006 and June 2020, 1525 patients had received ECMO support. After excluding patients bridged to transplantation or a ventricle-assist device and expelling VV-ECMO cases as well as patients switched to other ECMO configurations, 645 VA-ECMO patients were finally included. Regarding the definition of cardiac failure as indication for VA-ECMO support, we refer to previous publications.[4,5]

The patients were divided into four age groups: 18–49.9, 50–59.9, 60–69.9, and ≥70 years old. Baseline characteristics, short- and long-term outcome, complications during ECMO support, neurological outcome at discharge and follow-up were analyzed and compared with regard to patient age. Risk factors for in-hospital mortality and death during follow-up were identified. To reduce heterogeneity, patients were also grouped into those without cardiopulmonary resuscitation (CPR) or no CPR within 12 h prior to ECMO implantation (LCO patients), and patients who mandated CPR within the last 12 h or underwent ECMO implantation during external heart massage. Furthermore, a sub-analysis of VA-ECMO patients after acute myocardial infarction was carried out.

In most patients, cannulation was achieved via femoral or jugular vein and femoral or subclavian artery. Whenever possible, vessel diameter and assumed arteriosclerotic vascular lesions were examined with ultrasound prior to implantation. The inflow and outflow cannulas (15–31F) were implanted using Seldinger's technique or via open surgical access.

ECMO data were retrospectively analyzed. Median follow-up was 1104.5 days (IQR 388.0–2278.3). Follow-up data were obtained by interrogation of survivors, their relatives, or their general practitioners, and was finished in June 2020. Neurological outcome was evaluated using the cerebral performance category (CPC) score.[6] The performance status in the follow-up was assessed by means of the Eastern Co-operative of Oncology Group (ECOG) score.[7]

2.1 | Statistical methods

Continuous data are presented as mean ± standard deviation [SD] or as median with interquartile range [IQR: q1–q3] depending on the underlying distribution.

Percentage values in the text are related to the entire cohort or to the subgroup (VA-ECMO cohort) as 100%. In tables, percentage values either relate to the entire cohort or to subgroups. Categorical variables are presented as absolute and relative frequencies. Comparisons between groups were performed with the Mantel–Haenszel test for variables in ordinal distribution, and the Chi-squared test of independence for dichotomous and nominally scaled variables. The Kruskall-Wallis-Test was used for continuous data.

Risk factors for hospital mortality and death during follow-up were identified using multivariable logistic regression analysis and Cox's regression analysis. Variables for the multivariable models were preselected by univariate regressions models ($p < 0.05$). Survival in follow-up is presented graphically by Kaplan–Meier Plots. A p-value of <0.05 was considered statistically significant. Statistical analyses were done with IBM SPSS software (version 26; IBM Corp., Armonk, NY, USA).

3 | RESULTS

The age distribution of the 645 patients who had undergone VA-ECMO implantation included 171 patients in the age range of 18–49.9 years (mean 39.4 years), and 175 patients in the range of 50–59.9 years (mean 54.4 years), while 182 patients were categorized as 60–69.9 years (mean 64.3 years) and 117 patients as ≥70 years (mean 74.7 years). Table 1 demonstrates the baseline characteristics and causes of circulatory failure.

Leading cause of circulatory failure requiring VA-ECMO support in all patients was myocardial infarction. It's incidence rose with age reaching 53.3% in the 60–69.9 age group and 56.4% in the ≥70 age old patients ($p < 0.001$). In contrast, circulatory failure due to pulmonary embolism was significantly more frequent in younger patients. Other conditions leading to cardiac failure are summarized in Table 1.

Duration of VA-ECMO support was comparable between all age groups with the same median (3 days) ($p = 0.410$; range 0–51 days for 18–49.9 group; 0–15 days for ≥70 patients).

Overall, 380 patients (58.9%) could be weaned from VA-ECMO. The oldest patients had the highest weaning rate of 67.5% ($n = 79$). Worst results in this regard were noted in patients aged 50–59.9 years with a weaning rate of only 51.4%.

392 patients (60.8%) died during their hospital stay as depicted in Table 2. The in-hospital mortality of patients

TABLE 1 Characteristics and comorbidities, causes of circulatory failure

	All	<50 years	50–59.9 years	60–69.9 years	≥70 years	*p*-value
Characteristics and comorbidities						
Male sex	457/70.9%	108/63.2%	126/72.0%	140/76.9%	83/70.9%	**0.047**
Body-mass-index (median kg/m^2; IQR)		25.3 (23.1–28.3)	27.7 (24.9–31.1)	27.5 (24.6–20.0)	26.8 (23.2–29.6)	**0.001**
CPR time (median min.; IQR)		52.5 (31–74)	58 (35–70)	46 (30–65)	40 (23–55)	**<0.001**
Lactate level before ECMO (median mg/dl; IQR)		106.5 (56–155)	95.0 (51–146)	93.5 (60–133)	82.0 (51–121)	**0.04**
Diabetes	124/19.2%	14/9.2.3%	23/13.1%	55/30.2%	32/27.4%	**<0.001**
Arterial hypertension	224/34.7%	29/17.0%	51/29.1%	86/47.3%	58/49.6%	**<0.001**
History of stroke	40/6.2%	9/5.3%	10/5.7%	11/6.0%	10/8.5%	0.296
Peripheral artery disease	44/6.8%	1/0.6%	5/2.9%	32/12.6%	15/12.8%	**<0.001**
Atrial fibrillation	118/18.3%	16/9.4%	29/16.6%	44/24.8%	29/24.8%	**<0.001**
COPD	25/3.9%	2/1.2%	8/4.6%	7/3.8%	8/6.8%	0.027
Bronchial asthma	12/1.9%	2/1.2%	7/4.0%	3/1.6%	0/0.0%	0.329
Coronary artery disease	355/55.8%	48/28,1%	96/54.9%	123/67.6%	88/75.2%	**<0.001**
Hyperlipidemia	89/13.8%	8/4.7%	21/12.0%	36/19.8%	24/20.5%	**<0.001**
Smoking	96/14.9%	23/13.5%	29/16.6%	36/19.8%	8/6.8%	0.437
Chronic hemodialysis	91/14.10%	22/12.9%	27/15.4%	30/16.5%	12/10.3%	0.785
CPR group	385/59.70%	101/59.1%	97/55.4%	198/59.3%	79/67.5%	0.157
LCO group	260/40.30%	70/40.9%	78/44.6%	74/40.7%	38/32.5%	0.157
Hospital stay (median days, IQR; missing 0.5%)		11 (2–27)	10 (2–24)	9 (2–24)	13 (5–27)	0.265
Causes of circulatory failure						
Myocardial infarction	284/44.0%	52/30.4%	69/39.4%	97/53.3%	66/56.4%	**<0.001**
Aortic stenosis	13/2.0%	1/0.6%	3/1.7%	3/1.6%	6/5.1%	**0.017**
Ischemic/dilative cardiomyopathy	43/6.7%	9/5.3%	18/10.3%	13/7.1%	35/6.8%	0.532
Bleeding	19/2.9%	4/2.3%	6/3.4%	4/2.2%	5/4.3%	0.542
Cardiogenic shock other	25/3.90%	7/4.1%	7/4.0%	6/3.3.%	5/4.3%	0.970
Pulmonary embolism	71/11.00%	30/17.5%	22/12.6%	15/8.2%	4/3.4%	**<0.001**
Sepsis	38/5.9%	14/8.2%	10/5.7%	12/6.6%	2/1.7%	0.05
Ventricular dysrhythmia	60/9.30%	19/11.1%	18/10.3%	12/6.6%	11/9.4%	0.321
Myocarditis	10/1.6%	5/2.9%	4/2.3%	1/0.5%	0/0%	**0.019**
Others	82/12.70%	30/17.5%	18/10.3%	19/10.4%	15/12.8%	0.177

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).

Abbreviations: COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; LCO, low cardiac output.

≥60 years old was not increased (60–69.9 years 62.1%, $n = 113$, ≥70 years 58.1%, $n = 68$). Interestingly, the youngest patients presented with the lowest mortality (<50 years 53.8%, $n = 92$) and the patients aged 50–59.9 years died most (68.0%, $n = 119$; $p = 0.05$).

The most frequent cause of death in younger patients was cerebral ischemia or cerebral bleeding (<50 years 53.2% vs. 50–59.9 years 45.1% vs. 60–69.9 years 32.7% vs. ≥70 years 23.5%; $p < 0.001$). Elderly patients died more often due to persisting low cardiac output after weaning (<50 years 6.4% vs. 50–59.9 years 19.7% vs. 60–69.9 years 23.9% vs. ≥70 years 29.6%; $p < 0.001$).

Most implantations were performed using the Seldinger technique, with no difference among the age groups. Only 4.5% ($n = 29$) of implantations were surgical in nature, with a trend towards a higher prevalence in patients aged ≥70 years (Table 3). The canulation site did not impact the outcome.

Most ECMO implantations were accomplished on the intensive care unit (ICU). Patients aged ≥60 years underwent device placement also to a substantial amount in the catheterization laboratory (60–69.9 years 15.4% and ≥70 years 19.7% vs. <50 years 1.8% and 50–59.9 years 2.9%; $p < 0.001$). Patients who were transferred to our center after ECMO implantation at another hospital were usually younger (<65 years 35.5%, $n = 156$, vs. ≥65 years 26.8%, $n = 55$; $p = 0.03$). The number of out of hospital implantations was comparable in all age groups (Table 3).

TABLE 2 Weaning and hospital mortality

	All	<50 years	50–59.9 years	60–69.9 years	≥70 years	*p*-value
Overall						
Weaning	380/58.9%	104/60.8%	90/51.4%	107/58.8%	79/67.5%	**0.048**
Hospital mortality	392/60.8%	92/53.8%	119/68.0%	113/62.1%	68/58.1%	**0.050**
CPR group						
Weaning	195/50.6%	52/51.5%	38/39.2%	56/51.9%	49/62.0%	**0.026**
Hospital mortality	266/69.1%	66/65.3%	76/78.4%	75/69.4%	49/62.0%	0.093
LCO group						
Weaning	185/71.2%	52/74.3%	52/66.7%	51/68.9	30/78.9	0.493
Hospital mortality	126/48.5%	26/37.1%	43/55.1%	38/51.4%	19/50.0%	0.75
AMI patients						
Weaning	166/58.5%	33/63.5%	35/50.7%	53/54.6	45/68.2	0.146
Hospital mortality	176/62.0%	28/53.8%	49/71.1%	59/60.8%	40/60.6%	0.266

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).
Abbreviation: AMI, acute myocardial infarction.

TABLE 3 Implantation way, implantation place

	All	<50 years	50–59.9 years	60–69.9 years	≥70 years	*p*-value
Way of implantation						
Seldinger technique	500/77.5%	137/80.1%	137/78.3%	140/76.9%	86/73.5%	0.606
Surgery	29/4.5%	9/5.3%	4/2.3%	6/3.3%	10/8.5%	0.063
Over IABP introducer	13/2.0%	5/2.9%	5/2.9%	3/1.6%	0/0%	0.275
Via prior placed art. Introducer	103/16.0%	20/11.7%	29/16.6%	33/18.1/	21/17.9%	0.341
Implantation place						
ICU	132/20.5%	33/19.3%	48/27.4%	24/13.2%	27/23.1%	**0.008**
Out of hospital	109/16.9%	25/14.6%	38/21.7%	31/17.0%	15/12.8%	0.179
Operating room	34/5.3%	3/1.8%	8/4.6%	11/6.0%	12/10.3%	**0.015**
Emergency room	87/13.5%	35/20.5%	18/10.3%	21/11.5%	13/11.1%	**0.02**
Catheterization laboratory	59/9.1%	2/1.8%	5/2.9%	28/15.4%	23/19.7%	**<0.001**
In-hospital, another place	13/2.0%	5/2.9%	1/0.6%	3/1.6%	4/3.4%	0.278
Another hospital	211/32.7%	67/39.2%	57/32.6%	64/35.2%	23/19.7%	**0.005**

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).
Abbreviation: ICU, intensive care unit.

The analysis of complications during ECMO support revealed an increased incidence of stroke in patients aged <60. Other complications emerged with comparable incidence in all age groups (Table 4).

Univariate analysis of the clinical parameters followed by multivariate analysis showed chronic hemodialysis, resuscitation time (min), and serum lactate level prior ECMO (mg/dl) as relevant predictors for in-hospital mortality. Transport after ECMO implantation from an external hospital, was protective. Age had no relevant impact on mortality (Table 5).

A total of 253 (39.2%) of ECMO patients was discharged from hospital. Most patients presented with CPC2 (Moderate cerebral disability: conscious and sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment). The patients aged <50 years reached CPC1 level more than two times more often than the aged 50–69.9 and only one survivor aged ≥70 years was discharged having CPC1 (Good cerebral performance: conscious and alert, able to work, with normal neurological function or only slightly cerebral disability). However, even in the oldest patients aged ≥70 years the neurological status was acceptable reaching in 79.6% CPC2 (Table 7).

During follow-up, the mortality rate of VA-ECMO survivors was strongly age dependent as demonstrated by the Kaplan–Meier analysis (Figure 1, Log Rank $p = 0.025$) and multivariate Cox's regression showing only age as predictor for mortality during whole follow-up. Cox's regression focusing on 90 days follow-up revealed age as significant predictor for mortality already in this short period, in contrast it did not reach significance during 365 days follow-up. Sepsis leading to circulatory failure requiring VA-ECMO support presented as predictor for morality in the first year of follow-up (Table 6).

The performance status in follow-up was comparable in all groups, reaching ECOG scores of 0 (fully active, able to carry on all pre-disease performance without restriction) to ECOG score 1 (restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work) in 70.9% in all survivors ($p = 0.314$, Table 7). 29 patients were lost to follow-up.

3.1 | Subgroup analysis: Patients with CPR vs. patients with LCO (low cardiac output) and patients after myocardial infarction

Almost 60% of all patients on VA-ECMO underwent mechanical resuscitation prior to ECLS implantation and

TABLE 4 Complication on ECMO

	All	**<50 years**	**50–59.9 years**	**60–69.9 years**	**≥70 years**	***p*-value**
Limb ischemia	55/8.5%	20/11.7%	12/6.9%	17/9.3%	6/5.1%	0.194
Vessel perforation	12/1.9%	3/1.8%	2/1.1%	3/1.6%	4/3.4%	0.551
Major bleeding	85/13.2%	20/11.7%	22/12.6%	29/15.9%	14/12.0%	0.627
Cannula thrombosis	7/1.1%	1/0.6%	2/1.1%	1/0.5%	3/2.6%	0.351
Pericardial tamponade	1/0.2%	0/0%	1/0.6%	0/0%	0/0%	0.442
New acute kidney failure requiring hemodialysis	153/23.7%	39/22.8%	42/24.0%	45/24.7%	27/23.1%	0.975
Fatal stroke	158/24.5%	50/29.2%	55/31.4%	37/20.3%	16/13.7%	**0.001**
Fatal cerebral bleeding	14/2.2%	5/2.9%	3/1.7%	3/1.6%	3/2.6%	0.814

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).

TABLE 5 Univariate and multivariate logistic regression models on hospital mortality

	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Age	1.005 (0.994–1.017)	0.375	1.012 (0.999–1.026)	0.075
Chronic hemodialysis	1.735 (1.068–2.82)	**0.026**	2.657 (1.526–4.626)	**0.001**
Resuscitation time (min)	1.021 (1.015–1.027)	**<0.001**	1.014 (1.008–1.021)	**<0.001**
Lactate level before ECMO (missing 5.1%)	1.014 (1.011–1.018)	**<0.001**	1.011 (1.007–1.015)	**<0.001**
ECMO support duration (days)	1.001 (1.001–1.002)	**<0.001**	0.979 (0.939–1.020)	<0.309
Out of hospital implantation	0.562 (0.358–0.882)	**0.012**	0.975 (0.551–1.726)	0.930
Emergency room implantation	0.416 (0.246–0.705)	**<0.001**	1.135 (591–2.178)	0.704
Implantation in external hospital	0.438 (0.313–0.613)	**<0.001**	0.563 (367–0.863)	**0.008**

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).

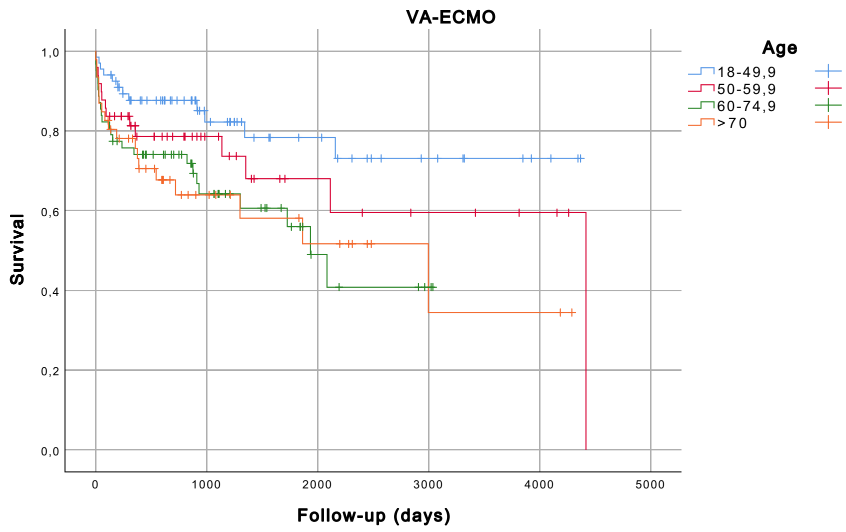

FIGURE 1 Survival in follow-up.

TABLE 6 Multivariate Cox's regression models on death in follow-up

	HR (95% CI)	*p*-value
Age	1.034 (1.006–1.062)	**0.017**
Acute myocardial infarction	1.485 (0.746–2.955)	0.260
Resuscitation time (min)	1.008 (0.95–1.020)	0.221
Chronic hemodialysis	2.050 (0.559–7.522)	0.279
Hemodialysis on ECMO	0.905 (0.365–2.249)	0.831
90 days follow-up		
Age	1.033 (1.002–1.065)	**0.034**
Sepsis requiring ECMO	4.027 (1.342–12.081)	**0.013**
365 days follow-up		
Age	1.012 (0.995–1.029)	0.172
Sepsis requiring ECMO	3.146 (1.487–6.657)	**0.003**

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).

were included in the CPR group with comparable incidences in the analyzed age groups.

CPR time was significantly longer in the younger age groups, with a median CPR period of 58 min (IQR 35–70) in patients aged 50–59.9 years. The elderly patients ≥70 years had shortest CPR times (median 40 min, IQR 23–55; $p<0.001$).

The lactate levels were high in young patients with CPR (median level in <50 years 123 mg/dl, IQR 89–169 vs. 50–59.9 years 119 mg/dl, IQR 84–161 vs. 60–69.9 years 105 mg/dl IQR 71–136 vs. ≥70 years 92 mg/dl IQR 66–121; $p<0.001$), whereas in LCO group lactate levels were comparable in all age groups (median level in <50 years 75.5 mg/dl, IQR 35–122 vs. 50–59.9 years 58 mg/dl, IQR 23–100 vs. 60–69.9 years 81.5 mg/dl IQR 43–124 vs. ≥70 years 61 mg/dl IQR 30–114; $p = 0.143$).

The weaning rate was lower in the CPR subgroup than in patients without CPR (CPR 50.6%, $n = 195$, vs. LCO 71.2%, $n = 185$; $p<0.001$). The oldest patients with CPR could be weaned more often than younger patients with CPR (weaning: <50 years 51.5% vs. 50–59.9 years 39.2% vs. 60–69.9 years 51.9% vs. ≥70 years 62%; $p<0.026$). The weaning in LCO cohorts was comparable within the age groups (weaning: <50 years 74.3% vs. 50–59.9 years 66.7% vs. 60–69.9 years 68.9% vs. ≥70 years 78.9%; $p<0.493$).

Hospital mortality rates in the two subgroups were comparable within the age groups (CPR: <50 years 65.3% vs. 50–59.9 years 78.4% vs. 60–69.9 years 69.4% vs. ≥70 years 62%; $p<0.093$; LCO: <50 years 37.1% vs. 50–59.9 years 55.1% vs. 60–69.9 years 51.4% vs. ≥70 years 50%; $p<0.154$). Overall, in-hospital mortality was higher after CPR than after LCO (69.1%, $n = 266$, vs. 48.5%, $n = 126$; $p<0.001$).

The sub-analysis of 284 patients with ECMO support following acute myocardial infarction showed comparable weaning rates and hospital mortality (weaning: <50 years 63.5% vs. 50–59.9 years 50.7% vs. 60–69.9 years 54.6% vs. ≥70 years 68.2%; $p<0.146$; mortality: <50 years 53.8% vs. 50–59.9 years 71% vs. 60–69.9 years 60.8% vs. ≥70 years 60.6%; $p<0.266$).

3.2 | Comment

Since the first ECLS application for acute respiratory failure in adults in 1972[8] (VA configuration), the value of ECMO as a rescue tool in patients with refractory cardiac and/or respiratory failure has become evident.[9] ECMO represents a valuable treatment option to restore stable hemodynamics and gas exchange in case of failing conventional therapy due to refractory cardiogenic shock. In the United States, ECMO application increased by 433% between 2006 and 2011.[10]

Different scoring systems have been devised to identify patients for extracorporeal support. Traditionally, age

TABLE 7 Cerebral performance categories scale (CPC) at discharge and eastern Co-operative oncology group status (ECOG) during follow-up

	All	<50 years	50–59.9 years	60–69.9 years	≥70 years	*p*-value
CPC1	19/7.5%	11/13.9%	3/5.3%	4/5.7%	1/2.0%	**0.040**
CPC2	180/70.6%	55/69.6%	41/71.9%	45/64.3%	39/79.6%	
CPC 3	43/16.9%	11/13.9%	9/15.8%	18/25.7%	5/10.2%	
CPC4	7/2.7%	0/0%	4/7.0%	1/1.4%	2/4.1%	
CPC5	6/2.4%	2/2.5%	0/0%	2/2.9%	2/4.1%	
ECOG follow-up						
0–1	117/70.9%	34/59.6%	27/79.4%	32/74.4%	24/77.4	0.314
2	29/17.6%	15/26.3%	5/14.7%	5/11.6%	4/12.9%	
3	19/11.5%	8/14.0%	2/5.9%	6/14.0%	3/9.7%	

Note: The bold values indicate statistically significant *p*-values ($p < 0.05$).

is included in these scoring systems as age may impact the treatment course due to associated comorbidities, as well as the reduced biological ability to recover.[11] Many reports have demonstrated, age is a strong risk factor for impaired outcome of ECLS patients. An analysis by de Waha et al. compared patient outcome after VA-ECMO in cardiogenic shock patients younger and older than 60 years. Older patients showed comparable weaning rates but clearly increased in-hospital mortality. Mid-term mortality was also higher in older patients.[11] In a study of patients with STEMI treated with VA-ECMO-support, Sheu et al. demonstrated age as an independent predictor of 30-day mortality.[12]

In our analysis confirmed by multivariate regression analysis, advanced age alone was not identified as relevant predictor for impaired VA-ECMO outcome. In patients aged ≥70 years, VA-ECMO offered immediate stabilization well and prevented secondary organ damage with acceptable hospital mortality and neurological status, comparable to patients aged 50–69.9 years. Young patients (<50 years) presented a trend towards better outcome. Therefore, this study does not suggest that age plays an important role in VA-ECMO treatment. In contrast, this study demonstrates an acceptable outcome in elderly, if thorough patient selection is applied. Our institutional policy for extracorporeal support is restrictive in elderly patients in case of severe comorbidities as well as poor overall status and prognosis, whereas young patients receive maximum support, even in cases of unfavorable prognosis. Our young patients (particularly those with previous CPR) demonstrated higher pre-ECMO lactate levels indicating prolonged cardiogenic shock. It is not surprising, that we see a somewhat worse prognosis in the patients aged 50–59.9 years. As prolonged resuscitation intervals prior to VA-ECMO implantation is no contra-indication in our younger age patients, the predominant cause of death in this group is cerebral damage.

In patients with refractory cardiogenic shock, Fux et al. demonstrated that arterial serum lactate levels and the amount of inotropes and vasopressors were independent pre-VA-ECMO predictors of 90-day mortality. The authors suggested that the severity of cardiogenic shock reflected by lactate levels and inotropic/vasopressor medication just before the start of VA-ECMO therapy is more predictive for outcome than the etiology of cardiogenic shock.[13] This suggestion corresponds with our findings. Of note, our cohort of elderly patients presented with more chronic co-morbidities, which did not impact outcome.

VA-ECMO implantation in a secondary care hospital did not yield worse results, probably related to a biased patient selection. We assume that these hospitals focused on patients with better prognosis for transport and further treatment.

More than 50% of our elderly patients underwent ECMO placement after myocardial infarction, frequently during coronary interventions in the catheterization laboratory. As the underlying cause of cardiac failure was treated immediately, the outcome of these patients was better. In contrast to this analysis of non-postcardiotomy population, our own experience with postcardiotomy VA-ECMO patients revealed age as a risk factor for death.[14] In the latter group, characteristics of postcardiotomy patients, such as presence of higher comorbidity, surgical trauma, and cardiopulmonary bypass side effects, may decrease the ability to recover after cardiac surgery, and these characteristics correlate stronger with age.[14]

The most relevant non-cardiac comorbidity regarding outcome was renal failure. In general, chronic renal failure requiring hemodialysis is more prevalent in elderly populations and is a strong risk factor for mortality in critical ill patients with or without ECMO.[15] Nevertheless, prevalence of chronic hemodialysis was comparable in all VA-ECMO age groups but represented a strong risk factor for hospital mortality. In our multivariate logistic regression analysis, acute kidney failure requiring hemodialysis did not negatively impact outcome. A study of Antonucci et al. suggested that hemodialysis is not associated with increased mortality in an adult patient population treated with VV-/VA-ECMO.[16] In contrast to chronic hemodialysis, acute renal replacement therapy should not be considered as predictor for impaired outcome in this context.

4 | CONCLUSIONS

Age alone should not be a contraindication for VA-ECMO support in patients on VA-ECMO. Even in patients aged ≥70 years, comparable hospital mortality and acceptable neurological status at hospital discharge and during follow-up can be achieved. Chronic hemodialysis, elevated lactate levels, and resuscitation time prior to ECMO represent risk factors for in-hospital mortality. During follow-up, age remains the most relevant risk factor for outcome.

4.1 | Limitations

This study has several limitations, such as its retrospective study design. Although most data were collected prospectively, some data were collected retrospectively. Despite the division of patients into two subgroups and sub-analysis of acute myocardial infarction patients, patient heterogeneity could not be completely avoided, especially in term of indications for ECMO support causing potentially selection bias.

AUTHOR CONTRIBUTIONS

Zdenek Provaznik: Concept/design, data analysis/interpretation, statistics. Alois Philipp: Concept/design, data collection. Thomas Müller, Kozakov Kostiantyn, Dirk Lunz: Data collection. Christof Schmid: Critical revision of article. Bernhard Floerchinger: Concept/design, Critical revision of article.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

ORCID

Zdenek Provaznik https://orcid.org/0000-0003-3081-0170
Kozakov Kostiantyn https://orcid.org/0000-0002-2103-9903
Bernhard Floerchinger https://orcid.org/0000-0002-4417-6345

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