Mortality Predictors in Elderly Patients With Cardiogenic Shock on Venoarterial Extracorporeal Life Support. Analysis From the Extracorporeal Life Support Organization Registry*

Mortality Predictors in Elderly Patients With Cardiogenic Shock on Venoarterial Extracorporeal Life Support. Analysis From the Extracorporeal Life Support Organization Registry*

Mariusz Kowalewski, MD[1–3]
Kamil Zieliński, MD[4]
Giuseppe Maria Raffa, MD[5]
Paolo Meani, MD[1,6,7]
Valeria Lo Coco, MD[1,5]
Federica Jiritano, MD[1,6,7]
Dario Fina, MD[1,8]
Matteo Matteucci, MD[1,9]
Giovanni Chiarini, MD[1,10,11]
Anne Willers, MD[1]
Jorik Simons, MD[1]
Piotr Suwalski, MD[2]
Mario Gaudino, MD[12]
Michele Di Mauro, MD[13]
Jos Maessen, MD[1,13]
Roberto Lorusso, MD[1,13]

OBJECTIVES: Because significantly higher mortality is observed in elderly patients undergoing venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock, decision-making in this setting is challenging. We aimed to elucidate predictors of unfavorable outcomes in these elderly (≥ 70 yr) patients.

DESIGN: Analysis of international worldwide extracorporeal life support organization registry.

SETTING: Refractory cardiogenic shock due to various etiologies (cardiac arrest excluded).

PATIENTS: Elderly patients (≥ 70 yr).

INTERVENTIONS: Venoarterial extracorporeal membrane oxygenation.

MEASUREMENTS AND MAIN RESULTS: Three age groups (70–74, 75–79, ≥80 yr) were in-depth analyzed. Uni- and multivariable analysis were performed. From January 1997 to December 2018, 2,644 patients greater than or equal to 70 years (1,395 [52.8%] 70–74 yr old, 858 [32.5%] 75–79 yr, and 391 [14.8%] ≥ 80 yr old) were submitted to venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock with marked increase in the most recent years. Peripheral access was applied in majority of patients. Median extracorporeal membrane oxygenation support duration was 3.5 days (interquartile range: 1.6–6.1 d), (3.9 d [3.7–4.6 d] in patients ≥ 80 yr) ($p < 0.001$). Weaning from extracorporeal membrane oxygenation was possible in 1,236 patients (46.7%). Overall in-hospital mortality was estimated at 68.3% with highest crude mortality rates observed in 75–79 years old subgroup (70.1%). Complications were mostly cardiovascular and bleeding, without apparent differences between subgroups. Airway pressures, 24-hour pH after extracorporeal membrane oxygenation start, extracorporeal membrane oxygenation duration, and renal replacement therapy were predictive of higher mortality. In-hospital mortality was lower in heart transplantation recipients, posttranscatheter aortic valve replacement, and pulmonary embolism; conversely, higher mortality followed extracorporeal membrane oxygenation institution after coronary artery bypass + valve and in decompensated chronic heart failure, and nearly 100% mortality followed in extracorporeal membrane oxygenation for sepsis.

CONCLUSIONS: This study confirmed the remarkable increase of venoarterial extracorporeal membrane oxygenation use in elderly affected by

*See also p. 156.

DOI: 10.1097/CCM.0000000000004695

refractory cardiogenic shock. Despite in-hospital mortality remains high, venoarterial extracorporeal membrane oxygenation should still be considered in such setting even in elderly patients, since increasing age itself was not linked to increased mortality, whereas several predictors may guide indication and management.

KEY WORDS: cardiogenic shock; extracorporeal membrane oxygenation; extracorporeal life support

Venoarterial extracorporeal membrane oxygenation (VA ECMO) is an established and effective therapy increasingly used in adults with refractory cardiogenic shock (RCS) (1–6). Over the last 20 years, there has been a remarkable increase of the number of elderly patients supported with extracorporeal membrane oxygenation (ECMO); we observed a 280% increase in ECMO cases in elderly patients from 2011 to 2015 as compared to cases from 2005 to 2010 (7). More advanced VA ECMO technology, more confidence with ECMO implantation and management, and the inclusion of ECMO in resuscitation protocols have favored broader indications for ECMO use. Importantly, ECMO has become a valid option for patients previously not considered for temporary circulatory support to promote organ recovery or transition to more advanced and durable therapies. At the same time, however, VA ECMO is resource-intensive and often yields a complicated post-implantation course. In most scenarios, the only objective of VA ECMO in older patients is to serve as a "bridge to recovery," because more advanced treatment modalities, such as heart transplantation or the use of durable left ventricular assist devices (LVADs), are either contraindicated or considered futile and inappropriate. Nonetheless, as the population ages, proper understanding of the use and impact of VA ECMO in patients of advanced age referred for treatment of RCS will become increasingly important to determine whether VA ECMO support should be considered in these patients. The primary aim of this analysis, therefore, was to analyze data from the international extracorporeal life support organization (ELSO) registry, to investigate trends in use ECMO and outcomes and define risk factors associated with in-hospital mortality specific to elderly patients.

METHODS

The current study was conducted according to Strengthening the Reporting of Observational Studies in Epidemiology Statement and the REporting of studies Conducted using Observational Routinely collected health Data Statement guidelines. Their respective checklists are available as **supplementary material** (Supplemental Digital Content 1, http://links.lww.com/CCM/F924).

Data Source and Study Population

Patient data were extracted from the ELSO registry, which is a worldwide voluntary registry of data related to ECMO implant in patients of all ages and with all conditions necessitating ECMO support including cardiac support, respiratory support, and cardiopulmonary resuscitation (CPR) (8). Data for the ELSO Registry are collected from the contributing centers with a standardized form querying patient demographics, diagnosis, and procedure information; ECMO technique; complications during ECMO; and survival to hospital discharge. As of December 31, 2018, 391 centers had provided adult and pediatric data to the registry with data on 19,627 VA ECMO runs in adult patients (>18 years old) with a cardiac etiology of RCS. Data from patients greater than or equal to 70 years old supported with a single run of VA ECMO for RCS between January 1997 and December 2018 were extracted from the ELSO registry. Patients supported with ECMO for extracorporeal CPR (ECPR) or respiratory dysfunction and patients with multiple ECMO runs were excluded. The requirement for informed consent was waived because the dataset was limited to nonidentifiable elements. This study was approved by the ELSO Registry Committee.

Main Goals and Definitions

We aimed to describe the prevalence of complications following VA ECMO in patients greater than or equal to 70 years old and to identify factors associated with in-hospital mortality. To study the relationship of advanced age with outcomes, we examined three cohorts grouped according to age thresholds: 70–74, 75–79, and greater than or equal to 80 years. The independent variables were grouped before analysis as follows: demographic data, *International Classification of Diseases* diagnosis codes (reviewed by two authors independently with disagreement resolved by consensus), pre-ECMO variables, pre-ECMO therapies, and ECMO course data. The pre-ECMO variables included CPR, chronic renal failure, time between ICU admission and cannulation, systolic and diastolic blood pressure values within 6 hours of cannulation, blood gases, pre-ECMO support, and ventilator settings. In-hospital mortality was the primary endpoint for the study. All complications were categorized using ELSO registry categorization and included limb complications, CNS complications, bleeding complications, kidney failure, and sepsis.

Statistical Analysis

Categorical data were compared with chi-square analysis and presented as frequencies with proportions. Continuous variables were analyzed using analysis of variance and reported as means with SDs. To assess predictor variables and major morbidity, the χ^2 was used for categorical variables. To address missing values, we used fully conditional specification (Markov chain Monte Carlo methods) for missing data (1,000 iterations) (9). Mortality, sex, primary diagnosis, pre-ECMO support, pre-ECMO cardiac arrest, age, $P\text{CO}_2$, pH after 24 hours of support, and year of treatment were employed as predictors. Variables with missing data in greater than 5% of the patients were excluded from analysis.

A piecewise model was initially used to evaluate the association between age and in-hospital mortality. An age cut-off was identified by calculating probabilities using 2×2 tables formed by the outcome and dichotomized age for all possible thresholds of age and calculating the associated χ^2 statistic. The age with the maximum χ^2 statistic was identified as the cut-off point. A simulation study demonstrated that if a cut-off point exists, maximizing the χ^2 statistic can recover a true threshold for a continuous random variable (10). To evaluate risk predictors of in-hospital mortality, variables that achieved p value of less than 0.1 in the univariable analysis were examined using multivariable analysis with forward stepwise logistic regression. Complications occurring in both groups are reported as number (%) with corresponding odds ratios (ORs) and 95% CIs. All statistical tests were performed in IBM SPSS Statistics 22 (IBM Corp, Armonk, NY). A p value of less than 0.05 was considered significant.

RESULTS

Patient Demographic Characteristics

A total of 2,644 elderly patients were included in this analysis. The number of patients over the age of 70 supported with VA ECMO in the ELSO registry increased over the study period, while mortality rates in these patients remained stable ($p > 0.05$) (**Fig. 1A**). To establish age cut-offs for analysis, a distribution of the χ^2 statistic was calculated for all possible age cut-offs. The maximum χ^2 was 4.834 with 52.8% ($n = 1395$) of patients between 70 and 74 years old, 32.5% ($n = 858$) between 75 and 79 years, and 14.8% ($n = 391$) of patients greater than or equal to 80 years old. Pre-ECMO patient profiles stratified according to age are presented in **Table 1**. The most common origin of RCS among elderly patients supported with ECMO was nonpostcardiotomy cardiogenic shock (1,557 patients, 58.9%). Among these, acute coronary syndrome was the predominant cause of cardiogenic shock in 869 patients (32.9%). Postcardiotomy shock was noted in 41.1% of patients and occurred in 340 patients (12.9%) after coronary artery bypass grafting (CABG) and in 10.2% (271 patients) after valve procedures; 746 patients (28.2%) could not be weaned from cardiopulmonary bypass.

ECMO Management and Outcomes

Peripheral cannulation was the preferred approach for VA ECMO placement and was used in 1,565 patients (59.2%). Average duration of ECMO support was 3.5 days (range 1.6–6.1 d) in the entire cohort, 4.0 days (range 1.8–6.9 d) in patients from 70 to 74 years old, 3.3 days (range 1.7–5.9 d) in 75–79-year-old patients, and 3.9 days (range 3.7–4.6 d) in patients greater than or equal to 80 years old ($p < 0.001$). Weaning from ECMO was possible in 1,236 patients (46.7%); 658 (47.2%) were 70–74 years old, 387 (45.1%) were 75–79, and 191 (48.9%) were greater than or equal to 80 years old (**Fig. 1***B*). Overall in-hospital mortality was estimated at 68.3% (1,807/ 2,644 patients) with the highest crude mortality rate observed in the 75–79-year-old subgroup (70.1%); mortality in the 70–74 years and greater than or equal to 80 years age groups were 67.0% and 67.8%, respectively (Fig. 1*A*).

When stratified by primary indication for ECMO, higher survival was observed in heart transplant recipients, after transcatheter aortic valve replacement

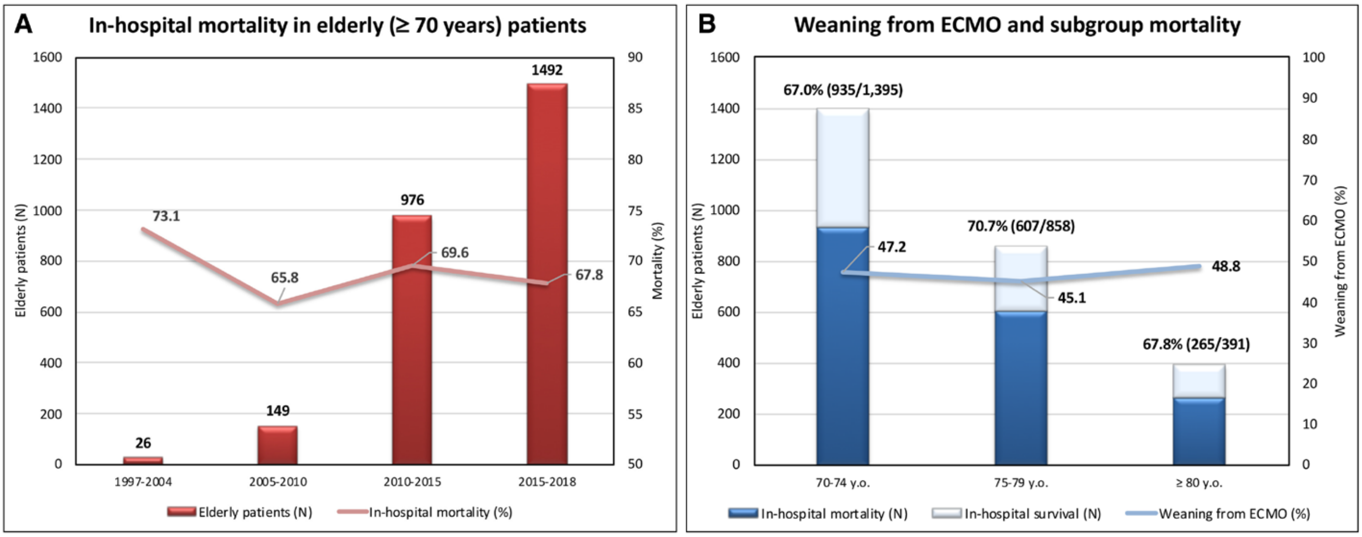

Figure 1. The in-hospital mortality rates in elderly (≥ 70 yr) patients admitted to venoarterial extracorporeal membrane oxygenation (ECMO) for refractory cardiogenic shock enrolled in the Extracorporeal Life Support Organization registry in proceeding time periods (**A**). The in-hospital weaning from ECMO support and mortality according to predefined age subgroups (**B**). y.o. = years old.

(TAVR), and in patients supported after a pulmonary embolism. Conversely, higher mortality followed ECMO institution after combined CABG and valve surgery and in patients with decompensated chronic heart failure. Nearly 100% mortality followed in ECMO institution during treatment for sepsis (**Fig. 2**, ***A*** and ***B***). There were no marked differences between the age subgroups when stratified by ECMO indication. **Supplemental Table 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/F924) lists univariable predictors of mortality in patients greater than or equal to 70 years old; among them, certain pre-ECMO variables and outcomes also predicted mortality in multivariable analysis and are listed in **Supplemental Table 2** (Supplemental Digital Content 1, http://links.lww.com/CCM/F924). Age of 75–79 years was found to be a mortality predictor in multivariable analysis; however, a borderline level of significance was observed (hazard ratio [HR], 1.37; 95% CI, 1.05–1.80; $p = 0.05$, as compared to age ≥ 80 yr: HR, 1.72; 95% CI, 1.18–2.52; $p < 0.01$). Among the remaining mortality predictors, pre-ECMO mean airway pressure, pH 24 hours after institution of ECMO, ECMO duration, and renal replacement therapy both before and during ECMO support were independently predictive of higher mortality.

Complications

Figure 3 graphically represents the extent of complications that occurred while on ECMO support for RCS. The most common complications were cardiovascular (25%). Other complications included bleeding (15%), renal (22%), mechanical (14%), and metabolic (11%) complications. Limb complications and neurologic and infectious sequelae were observed in 13% of cases. There were no marked differences in the incidence of clinically relevant complications between the age subgroups. Complication rates by age subgroup and type of complication are available as **Supplemental Figures 1–8** (Supplemental Digital Content 1, http://links.lww.com/CCM/F924).

Sensitivity Analysis

To corroborate our identification of predictors of mortality beyond the multivariable analysis, subgroup comparison was performed comparing age subgroups with etiology of RCS, type of cannulation, and duration of ECMO support (**Supplemental Fig. 9**, Supplemental Digital Content 1, http://links.lww.com/CCM/F924), and the event rates for in-hospital mortality were recalculated. The lowest mortality rates (55–58%) were achieved in the 70–74-year-old subgroup with a duration of support between 72 and 192 hours. In contrast, prolonging ECMO use beyond 192 hours, particularly in patients greater than or equal to 75, resulted in mortality rates as high as 90%. Additionally, patients on VA ECMO support for less than 96 hours had lower odds of mortality (OR, 0.79; 95% CI, 0.67–0.93; $p = 0.005$), similar odds of weaning from support (OR, 0.95; 95% CI, 0.81–1.11; $p = 0.499$), but higher odds of withdrawal

TABLE 1.

Demographic and Clinical Characteristics Along Extracorporeal Membrane Oxygenation Support Details of Elderly Patients Stratified According to Age

Variables	Overall ($n = 2,644$)	Age Group 70–74 ($n = 1,395$)	Age Group 75–79 ($n = 858$)	Age Group ≥ 80 yr ($n = 391$)	p
Male, n (%)	1684 (63.7)	896 (64.2)	539 (62.8)	249 (63.7)	0.796
Weight, kg, mean ± SD	81.0 ± 19.8	82.8 ± 20.3	80.6 ± 19.0	75.6 ± 18.8	< 0.001
Cause of cardiogenic shock, n (%)					
Postcardiotomy shock	1,087 (41.1)	541 (38.8)	375 (43.7)	171 (43.7)	0.036
CABG	340 (12.9)	170 (12.2)	134 (15.6)	36 (9.2)	0.004
Valve	271 (10.2)	123 (8.8)	86 (10.0)	62 (15.9)	< 0.001
CABG + valve	212 (8.0)	99 (7.1)	73 (8.5)	40 (10.2)	0.107
Aortic	34 (1.3)	18 (1.3)	12 (1.4)	4 (1.0)	0.862
Heart transplantation	31 (1.2)	22 (1.6)	8 (0.9)	1 (0.3)	0.111
VAD	76 (2.9)	43 (3.1)	29 (3.4)	4 (1.0)	0.074
Other	123 (4.7)	66 (4.7)	33 (3.8)	24 (6.1)	0.203
Nonpostcardiotomy shock	1,557 (58.9)	541 (38.8)	375 (43.7)	171 (43.7)	0.037
Acute coronary syndrome	869 (32.9)	854 (61.2)	483 (56.3)	220 (56.3)	0.037
Heart failure	342 (12.9)	466 (33.4)	249 (29.0)	154 (39.4)	0.001
Decompensated cardiomyopathy	106 (4.0)	221 (15.8)	97 (11.3)	24 (6.1)	< 0.001
Myocarditis	37 (1.4)	55 (3.9)	42 (4.9)	9 (2.3)	0.101
Post transcatheter aortic valve replacement	97 (3.7)	28 (2.0)	9 (1.0)	0 (0.0)	0.043
Sepsis	37 (1.4)	23 (1.6)	46 (5.4)	28 (7.2)	< 0.001
Pulmonary embolism	69 (2.6)	28 (2.0)	9 (1.0)	0 (0.0)	0.043
Hemodynamics before venoarterial ECMO, mean ± SD					
Systolic blood pressure	85.5 ± 29.5	85.3 ± 27.8	85.6 ± 30.6	86.1 ± 32.9	0.928
Diastolic blood pressure	49.3 ± 17.0	49.9 ± 15.9	48.8 ± 17.9	48.4 ± 19.0	0.358
Mean blood pressure	61 ± 18.5	61.4 ± 17.7	60.2 ± 18.7	61.1 ± 20.6	0.476
Venous O_2 saturation	61.1 ± 18.5	61.4 ± 18.3	59.2 ± 19.1	64.1 ± 18.0	0.267
Pre-ECMO blood gases, mean ± SD					
Pre-ECMO pH	7.28 ± 0.15	7.28 ± 0.14	7.28 ± 0.15	7.29 ± 0.15	0.478
Pre-ECMO HCO_3	19.9 ± 5.8	19.9 ± 5.9	19.8 ± 5.5	20.3 ± 6.1	0.443
Pre-ECMO PO_2	164.5 ± 129.7	153.9 ± 121.2	171.9 ± 136.2	187.5 ± 141.1	< 0.001
Pre-ECMO FIO_2	83.1 ± 22.9	83.0 ± 22.7	82.5 ± 23.5	84.5 ± 22.4	0.552
Pre-ECMO arterial oxygen saturation	92.6 ± 12.5	92.6 ± 11.5	92.6 ± 13.8	92.9 ± 13.1	0.948
Pre-ECMO PCO_2	41.8 ± 17.2	41.7 ± 16.2	42.6 ± 19.8	40.5 ± 13.7	0.232

(*Continued*)

TABLE 1. (*Continued*).
Demographic and Clinical Characteristics Along Extracorporeal Membrane Oxygenation Support Details of Elderly Patients Stratified According to Age

Variables	Overall (n = 2,644)	Age Group 70–74 (n = 1,395)	Age Group 75–79 (n = 858)	Age Group ≥ 80 yr (n = 391)	p
Pre-ECMO support, n (%)					
Intra-aortic balloon pump	732 (27.7)	397 (28.5)	247 (28.8)	88 (22.5)	0.046
Cardiopulmonary bypass	746 (28.2)	359 (25.7)	259 (30.2)	128 (32.7)	0.007
Nitrix oxide	149 (5.6)	83 (5.9)	56 (6.5)	10 (2.6)	0.014
Pacemaker	223 (8.4)	113 (8.1)	77 (9.0)	33 (8.4)	0.769
Inotropes	1538 (58.2)	821 (58.9)	503 (58.6)	214 (54.7)	0.326
Left VAD	96 (3.6)	58 (4.2)	33 (3.8)	5 (1.3)	0.025
ECMO support details					
Peripheral cannulation, n (%)	1,565 (59.2)	850 (60.9)	478 (55.7)	237 (60.6)	0.041
Days on ECMO, median (interquartile range)	3.5 (1.6–6.1)	4.0 (1.8–6.9)	3.3 (1.7–5.9)	3.9 (3.7–4.6)	< 0.001

CABG = coronary artery bypass grafting, ECMO = extracorporeal membrane oxygenation, VAD = ventricle assist device.

for futility (OR, 3.21; 95% CIs, 1.74–5.93; p < 0.001) as compared with patients on support for greater than 96 hours. There were no marked differences between mortality rates when ECMO was used to treat postcardiotomy versus nonpostcardiotomy cardiogenic shock or between cannulation techniques in these elderly patients.

DISCUSSION

Previous investigations comparing elderly and younger patients undergoing VA ECMO for RCS showed that in-hospital mortality is significantly higher in elderly patients (11). Not surprisingly, mortality rates vary in reports of outcomes in elderly patients supported by VA ECMO (7, 11–14). Reasons for this variation are multifactorial and include different age thresholds to define elderly patient populations, different etiologies of cardiogenic shock, and pooling together patients supported with VA ECMO and venovenous ECMO. The different risk profiles and different indications for ECMO support seem to be the most important contributors to the variation between reports. In addition, previous studies are mostly single-center experiences, which are often subjective to selection bias. Nevertheless, increasing age has been speculated as a secondary outcome predictor. Indeed, our recent study using the ELSO registry (7) showed that overall outcomes for elderly patients did not appear unacceptable, which suggested that VA ECMO might be considered to treat RCS in these patients. Patient selection, however, may play a critical role particularly for optimizing resources and the chances of favorable results. A paucity of data remains on the use of VA ECMO in such a challenging setting, and it is crucial to know what age threshold among elderly patients (e.g. > 75 yr or > 80 yr) affects their clinical outcomes. Many ECMO programs entertain somewhat arbitrary upper age limits for ECMO use. Some investigators have even suggested that age greater than 75 years should be viewed as a contraindication for ECMO support. However, a growing number of elderly patients have been treated recently, and this trend seems likely to continue. Some physicians speculate that temporary circulatory support should not be denied solely on the basis of patient age, but that the decision should be made based on reversibility, and expected duration of cardiogenic shock with

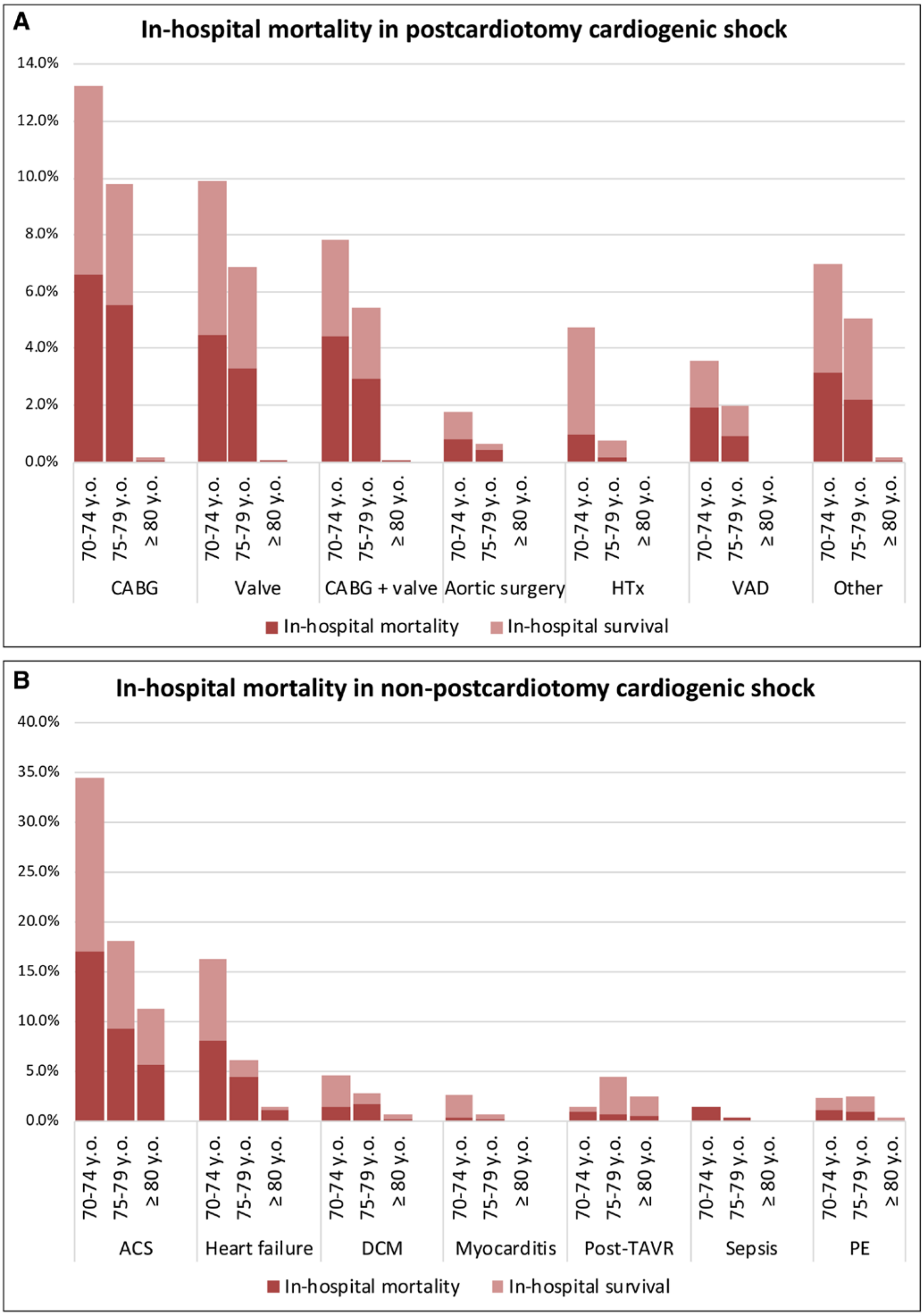

Figure 2. Analysis of in-hospital mortality stratified by the type of primary surgery (**A**) and in nonpostcardiotomy setting (**B**). ACS = acute coronary syndrome, CABG = coronary artery bypass grafting, DCM = decompensated cardiomyopathy, HTx = heart transplantation, PE = pulmonary embolism, TAVR = transcatheter aortic valve replacement, VAD = ventricle assist device, y.o. = years old.

consideration of comorbid conditions likely to impact patient survival. Indeed, elderly patients in RCS often have significant and complex comorbidities that can affect outcomes. Defining optimized decision-making criteria and optimal candidate selection for elderly patients eligible for VA ECMO due to RCS has been, until now, understudied.

Main Study Findings

The current study is the largest analysis to date of outcomes in elderly patients undergoing VA ECMO. It is also the first to address, on such scale, the trends of ECMO application and use and mortality predictors in elderly patients supported by VA ECMO for RCS. Our study showed that VA ECMO use in elderly patients is exponentially increasing; it also demonstrated that a relevant number of elderly patients undergo VA ECMO placement because of postcardiotomy cardiogenic shock, that overall in-hospital mortality in this challenging setting is not prohibitive, and that recently trends in use have been rather stable. This is most likely due to careful patient selection. When we assessed age-adjusted outcomes, even the patients with the most advanced ages (i.e. ≥ 80 yr) had in-hospital outcomes that do not discourage or contraindicate the use of ECMO for RCS in older patients. Cardiovascular complications were the most frequent adverse event, followed by bleeding, renal, and neurologic complications. Last, pre-ECMO factors, indication for ECMO support, renal complication with dialysis, and ECMO duration were negative predictors of in-hospital survival.

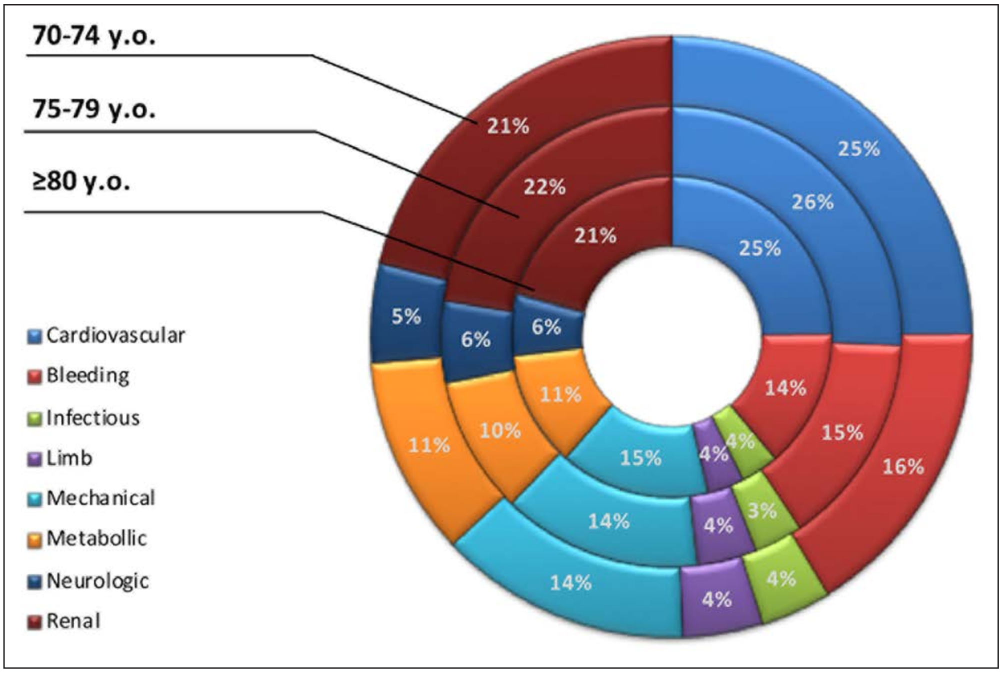

Figure 3. Overall complications rates in the ELSO registry analysis. y.o. = years old.

Temporary mechanical circulatory support (MCS) is being increasingly used in patients affected by acute heart failure (15). In an analysis of the Nationwide Inpatient Sample from 2011 to 2014 that included almost 12,000 patients undergoing short-term cardiocirculatory assistance, use of a percutaneous device increased by 1,511%, whereas use of a nonpercutaneous device increased by 101% (2). More interestingly, MCS implants increased from 39.6% to 47.2% of patients older than 65 years old among the overall study population, indicating a higher consideration of MCS use in these patients. Another recent analysis of patients treated from 2004 to 2014 showed that among MCS types, ECMO had the highest increase in use (1,421.4%). The use of other types of short-term MCS increased 1229.2%, use of percutaneous cardiocirculatory support increased 216.7%, and used of the intra-aortic balloon pump increased 140% (16).

Despite increasing use and expertise, VA ECMO is an aggressive treatment option in patients with complex conditions and is therefore associated with high complication and mortality rates (7). The search for predictors of mortality and complications is critical to improve results, resource utilization, and decision-making when treating patients with challenging conditions (17). Among several well-known factors, age has been identified as associated with less satisfactory in-hospital outcomes (**Supplemental Table 3**, Supplemental Digital Content 1, http://links.lww.com/CCM/F924) (7, 11, 12, 14, 16–22). Indeed, our recent ELSO registry analysis comparing younger (< 70 yr of age) versus older (≥ 70 yr of age) patients confirmed that elderly patients are more likely to experience complications and in-hospital mortality. However, in that study, as in this study, the in-hospital mortality rate was not discouraging, suggesting that age itself should not be considered an absolute contraindication for short-term use of VA ECMO in patients with RCS (7).

Elderly patients have a somehow peculiar profile with respect to their indications for ECMO support. Indeed, the most frequent indication for ECMO use in the current series was nonpostcardiotomy cardiogenic shock, which differs from the most frequent indication in previous series of elderly patients (18, 19, 23). Although postcardiotomy patients older than 70 years old are healthier at baseline than the general elderly population due to the fact that they were cleared to undergo major surgery, surprisingly, postoperative indications for VA ECMO placement are less common in older patients as compared to their younger counterparts (7). This may indicate that clinicians are less inclined to consider and accept the use of temporary support in elderly patients after surgery.

Our findings are relevant because they indicate that although old age is linked to limited success, age was not directly associated with an ominous prognosis. Indeed, patients in the 75–79 age group had somehow worse outcomes than patients of more advanced age, suggesting that careful selection, although not yet standardized by evidence-based data, may still lead to favorable results. We were able to identify subgroups of elderly patients with up to 50% survival with ECMO support, which is comparable with their younger counterparts. Specifically, patients who are 70–74 years old in whom the duration of support does not exceed

192 hours are most likely to benefit from ECMO support for RCS. Patients kept on ECMO for less than 96 hours have greater than 20% lower odds of mortality than those supported for more than 96 hours. Similarly, lower mortality was observed in heart transplantation recipients, post-TAVR and in patients with pulmonary embolism. On the other hand, sepsis almost always had an ominous prognosis in elderly patients, and higher mortality rates were also observed on ECMO following CABG+valve surgery.

Peripheral cannulation was used more frequently than central cannulation in the study group. This is in accordance with the findings of Sertic et al (19) who showed that central cannulation is associated with worse outcomes in older patients but may be related to poor clinical condition of the postcardiotomy patients, however. The use of VA ECMO for postcardiotomy support has been recently associated with poor results most likely because of pre-ECMO comorbidities, the impact of preoperative cardiac illnesses and complicated surgical procedures, and complications inherent to these procedures, such as bleeding (6). The use of VA ECMO for support of RCS of other etiologies may yield better results. Sertic et al (19) demonstrated that postacute myocardial infarction ECMO placement had better outcomes, which was confirmed in a postdischarge assessment. In fact, patients with an acute myocardial infarction often have undergone an escalation in support with an intra-aortic balloon pump or Impella pump (Abiomed, Inc. Danvers, MA) placed before escalation to ECMO, which is different from ECMO use in the postcardiotomy setting. Escalation may occur due to failure of MCS, vascular complications, or progression of shock with development of renal failure and rising lactates levels, which can often result in patients lingering in shock for a prolonged time.

Complications rates remain high during VA ECMO support (24–26), and our study confirmed the high frequency of major complications in elderly patients supported with VA ECMO. We confirmed that cardiovascular and end-organ perfusion adverse events are the most frequent complications, followed by bleeding and renal complications, as shown by other investigators (18, 19). These dreadful complications may result in a shorter duration of ECMO support, which may impede acceptable cardiocirculatory support or indicate an extremely low chance of recovery, prompting the attending personnel to early interruption of ongoing mechanical assistance (19). Accordingly, we observed greater than three-fold higher odds of withdrawal of support in patients with less than 96 hours of extracorporeal life support. The attitude toward withdrawal of support is also related to the almost unique bridge-to-recovery path often imminent in elderly patients with RCS supported with VA ECMO, because more advanced forms of therapy (LVADs or heart transplantation) are almost inaccessible to this patient population.

The decision to implant or continue temporary MCS is often difficult, and some clinicians may avoid or limit the indications for temporary MCS in elderly patients to reduce resource consumption by a procedure with limitedly success. From a clinical perspective, the majority of centers look at the patient's physical and neurologic status prior to the event necessitating ECMO, the severity of insult, the duration and degree of shock, the presence of prior cardiac arrest, and associated medical comorbidities when selecting potential candidates for ECMO therapy. The availability of indicators of more favorable outcomes, therefore, might be precious in guiding clinical management, either prior to or during ECMO support. High lactate levels at ECMO implant and renal failure, particularly renal failure requiring dialysis, have been shown to independently predict unfavorable results in all VA ECMO patients, but particularly in elderly patients. Our data confirm such negative predictors and add pre-ECMO circulatory state and ECMO duration as additional factors to consider. The etiology of RCS may be also associated with more favorable conditions for recovery. Patients supported with ECMO for acute cardiogenic shock have a considerable chance of survival as compared with patients who require support for acute decompensation of chronic heart failure, the presence of cardiac arrest, or prolonged low-flow time during CPR at ECMO implant, which are associated with almost no chance of survival (19, 22).

Based on our finding and insights from previous studies, improved patient selection might be feasible, taking into consideration preimplant conditions that are linked to more or less favorable outcomes (**Fig. 4**).

Limitations

This study has several limitations. The data in the ELSO registry are submitted voluntarily and limited to in-hospital events with no follow-up information.

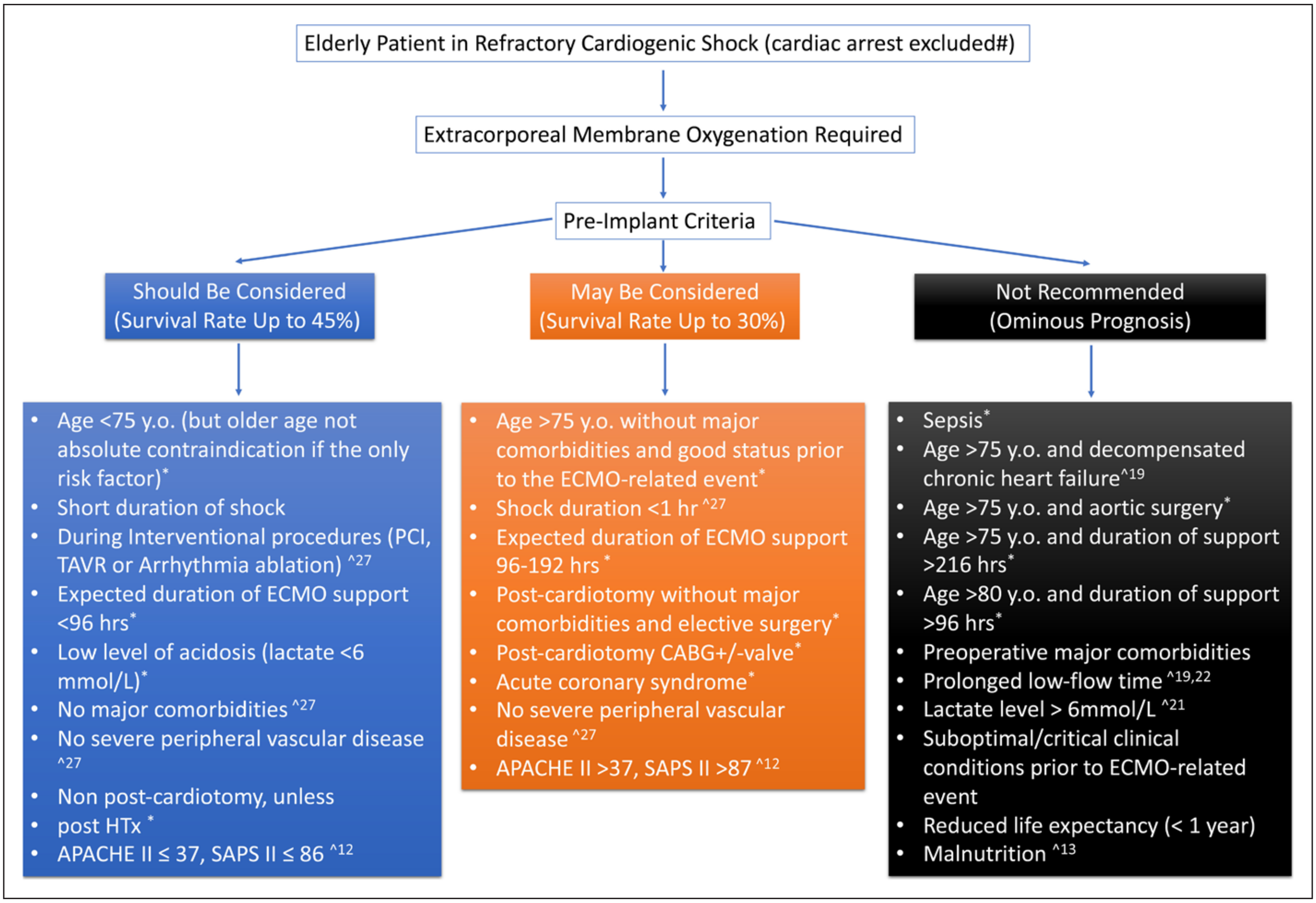

Figure 4. Summary of preimplant criteria to be considered in the extracorporeal membrane oxygenation (ECMO) decision-making in the elderly patients according to the survival probability. APACHE II = Acute Physiology and Chronic Health Evaluation II, CABG = coronary artery bypass grafting, HTx = heart transplantation, PCI = percutaneous coronary intervention, SAPS II = Simplified Acute Physiology Score II, TAVR = transcatheter aortic valve replacement, y.o. = years old.

Data on ECMO flow velocities, anticoagulation, monitoring, and the personnel involved in ECMO institution are not available. Retrospectively collected data are subject to changing definitions over time, more than 20 years in this study. There were complete data for the outcome variable of death, but arterial systolic, diastolic, and mean blood pressures; pulmonary artery systolic, diastolic, and mean blood pressures; weight; arterial oxygen saturation; peak inflation pressure after 24 hours on ECMO; and mean airway pressure after 24 hours on ECMO all had some missing data. The size of the database and our use of multiple conditional specification methods helped us to mitigate potential bias related to missing data. Nevertheless, it is possible that missing data might have affected the study findings. In addition, our findings must be interpreted with caution because the distribution of ages in the cohort was narrow, and there were few patients at the extreme ages. Indeed, limited access to elderly patients supported by ECMO should be taken into account, as many clinicians do not consider ECMO as an option in the presence of RCS of various etiologies in these patients. There was also an intentional lack of a younger control group, principally because we aimed to identify mortality predictors not affected by increasing age itself. Additionally, a previous analysis by our group addressed trends in outcomes and applications of VA ECMO in elderly versus younger patients (7). Our analysis of the ELSO registry addressed only RCS cases; we did not investigate the role and efficacy of VA ECMO in the setting of ECPR, because this had been described in a previous publication using the same registry database (20). Finally, patient survival and outcome were limited to in-hospital events because the ELSO registry does not include follow-up data collection after hospital discharge. Further clinical research of postdischarge outcomes is therefore warranted.

CONCLUSIONS

The use of VA ECMO for the treatment of RCS in elderly patients is remarkably increasing. In-hospital complication and mortality rates remain high but are not prohibitive and should not discourage ECMO use in this challenging setting. Patient status at ECMO implant, etiology, complication type, ECMO duration, and to a lesser degree advanced age are critical factors to take into consideration during decision-making prior to VA ECMO implantation.

1 *Department of Cardio-Thoracic Surgery, Heart and Vascular Centre, Maastricht University Medical Centre (MUMC), Maastricht, The Netherlands.*

2 *Clinical Department of Cardiac Surgery, Central Clinical Hospital of the Ministry of Interior and Administration, Centre of Postgraduate Medical Education, Warsaw, Poland.*

3 *Thoracic Research Centre, Collegium Medicum Nicolaus Copernicus University, Innovative Medical Forum, Bydgoszcz, Poland.*

4 *Warsaw Medical University, Warsaw, Poland.*

5 *Cardiac Surgery Unit, ISMETT, Palermo, Italy.*

6 *Cardiology Unit, Niguarda Hospital, Milan, Italy.*

7 *Cardiac Surgery Unit, University of Catanzaro, Catanzaro, Italy.*

8 *Cardiology Unit, San Donato Hospital, Milan, Italy.*

9 *Cardiac Surgery Unit, Ospedale di Circolo, University of Varese, Varese, Italy.*

10 *2nd Intensive Care Unit, Ospedale Civile, University of Brescia, Brescia, Italy.*

11 *Department of Cardio-Thoracic Surgery, Well Cornell Medicine, New York, NY.*

12 *Cardiac Surgery Unit, University Hospital, University of Chieti, Chieti, Italy.*

13 *Cardiovascular Research Institute Maastricht (CARIM), Maastricht, The Netherlands.*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

Presented, in part, at EuroELSO, London, United Kingdom, May 2021.

Dr. Lorusso is consultant and conducts clinical trial for LivaNova (London, United Kingdom), is consultant for Medtronic (Minneapolis, MN), and an Advisory Board member of PulseCath (Arnhem, The Netherlands) and Eurosets (Medolla, Italy). The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: roberto.lorussobs@gmail.com

REFERENCES

1. Bellumkonda L, Gul B, Masri SC: Evolving concepts in diagnosis and management of cardiogenic shock. *Am J Cardiol* 2018; 122:1104–1110
2. Stretch R, Sauer CM, Yuh DD, et al: National trends in the utilization of short-term mechanical circulatory support: Incidence, outcomes, and cost analysis. *J Am Coll Cardiol* 2014; 64:1407–1415
3. McCarthy FH, McDermott KM, Kini V, et al: Trends in U.S. extracorporeal membrane oxygenation use and outcomes: 2002-2012. *Semin Thorac Cardiovasc Surg* 2015; 27:81–88
4. Sauer CM, Yuh DD, Bonde P: Extracorporeal membrane oxygenation use has increased by 433% in adults in the United States from 2006 to 2011. *ASAIO J* 2015; 61:31–36
5. Maxwell BG, Powers AJ, Sheikh AY, et al: Resource use trends in extracorporeal membrane oxygenation in adults: An analysis of the nationwide inpatient sample 1998–2009. *J Thorac Cardiovasc Surg* 2014; 148:416–421 e411
6. Whitman GJ: Extracorporeal membrane oxygenation for the treatment of postcardiotomy shock. *J Thorac Cardiovasc Surg* 2017; 153:95–101
7. Lorusso R, Gelsomino S, Parise O, et al: Venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock in elderly patients: Trends in application and outcome from the Extracorporeal Life Support Organization (ELSO) Registry. *Ann Thorac Surg* 2017; 104:62–69
8. Broman LM, Taccone FS, Lorusso R, et al: The ELSO Maastricht Treaty for ECLS Nomenclature: Abbreviations for cannulation configuration in extracorporeal life support - a position paper of the Extracorporeal Life Support Organization. *Crit Care* 2019; 23:36
9. van Buuren S: Multiple imputation of discrete and continuous data by fully conditional specification. *Stat Methods Med Res* 2007; 16:219–242
10. Prince Nelson SL, Ramakrishnan V, Nietert PJ, et al: An evaluation of common methods for dichotomization of continuous variables to discriminate disease status. *Commun Stat Theory Methods* 2017; 46:10823–10834
11. Lee SN, Jo MS, Yoo KD: Impact of age on extracorporeal membrane oxygenation survival of patients with cardiac failure. *Clin Interv Aging* 2017; 12:1347–1353
12. Yeh TC, Chang HH, Ger LP, et al: Clinical risk factors of extracorporeal membrane oxygenation support in older adults. *PLoS One* 2018; 13:e0195445
13. Saito S, Nakatani T, Kobayashi J, et al: Is extracorporeal life support contraindicated in elderly patients? *Ann Thorac Surg* 2007; 83:140–145
14. Wang L, Yang F, Wang X, et al: Predicting mortality in patients undergoing VA-ECMO after coronary artery bypass grafting: The REMEMBER score. *Crit Care* 2019; 23:11
15. Vallabhajosyula S, Patlolla SH, Dunlay SM, et al: Regional variation in the management and outcomes of acute myocardial infarction with cardiogenic shock in the United States. *Circ Heart Fail* 2020; 13:e006661

16. Strom JB, Zhao Y, Shen C, et al: National trends, predictors of use, and in-hospital outcomes in mechanical circulatory support for cardiogenic shock. *EuroIntervention* 2018; 13:e2152–e2159
17. Pagani FD: Extracorporeal membrane oxygenation for septic shock: Heroic futility? *J Thorac Cardiovasc Surg* 2018; 156:1110–1111
18. Pontailler M, Demondion P, Lebreton G, et al: Experience with extracorporeal life support for cardiogenic shock in the older population more than 70 years of age. *ASAIO J* 2017; 63:279–284
19. Sertic F, Diagne D, Rame E, et al: Short-term outcomes and predictors of in-hospital mortality with the use of veno-arterial extracorporeal membrane oxygenation in elderly patients with refractory cardiogenic shock. *J Cardiovasc Surg (Torino)* 2019; 60:636–638
20. Mendiratta P, Tang X, Collins RT 2nd, et al: Extracorporeal membrane oxygenation for respiratory failure in the elderly: A review of the Extracorporeal Life Support Organization registry. *ASAIO J* 2014; 60:385–390
21. Biancari F, Saeed D, Fiore A, et al: Postcardiotomy veno-arterial extracorporeal membrane oxygenation in patients aged >/=70 years. *Ann Thorac Surg* 2019; 108:1257–1264
22. Saxena P, Neal J, Joyce LD, et al: Extracorporeal membrane oxygenation support in postcardiotomy elderly patients: The Mayo clinic experience. *Ann Thorac Surg* 2015; 99: 2053–2060
23. Salna M, Takeda K, Kurlansky P, et al: The influence of advanced age on venous-arterial extracorporeal membrane oxygenation outcomes. *Eur J Cardiothorac Surg* 2018; 53:1151–1157
24. Rastan AJ, Lachmann N, Walther T, et al: Autopsy findings in patients on postcardiotomy extracorporeal membrane oxygenation (ECMO). *Int J Artif Organs* 2006; 29:1121–1131
25. Zangrillo A, Landoni G, Biondi-Zoccai G, et al: A meta-analysis of complications and mortality of extracorporeal membrane oxygenation. *Crit Care Resusc* 2013; 15:172–178
26. Truby L, Mundy L, Kalesan B, et al: Contemporary outcomes of venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock at a large tertiary care center. *ASAIO J* 2015; 61:403–409
27. Pitsis AA, Visouli AN, Aikaterini VN: Mechanical assistance of the circulation during cardiogenic shock. *Curr Opin Crit Care* 2011; 17:425–438