Outcomes after postcardiotomy venoarterial extracorporeal membrane oxygenation in young patients: An individual patient data meta-analysis

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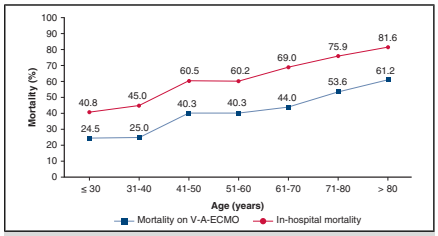
ABSTRACT

Objective: We aimed to evaluate the early and midterm mortality of young patients treated for cardiogenic shock with venoarterial extracorporeal membrane oxygenation (VA-ECMO) after adult cardiac surgery.

Methods: Studies reporting the outcome after postcardiotomy VA-ECMO in adult patients were identified through a systematic review of the literature. Individual patient-level data were provided by the authors of 10 studies.

Results: Data on 1268 patients treated at 25 hospitals were included in this study. Adjusted analysis identified 40 years of age as a cutoff value for in-hospital and midterm mortality. Patients aged >40 years had significantly greater in-hospital mortality (1129 patients, crude rates 68.8% vs 43.1%, adjusted odds ratio, 3.267; 95% confidence interval, 1.970-5.425) and mortality at 24-month (109 patients, crude rates 73.7% vs 45.0%, adjusted hazard ratio, 3.530, 95% confidence interval, 2.571-4.844). Twelve (11.0%) patients aged ≤40 years received a ventricular assist device and heart transplantation, whereas this strategy was adopted in 33 (2.9%) patients aged >40 years ($P < .001$). Eventually, 7 (6.4%) patients aged ≤40 years and 12 (1.1%) patients aged >40 years underwent heart transplantation ($P < .001$). Heart transplantation tended to decrease in-hospital mortality in patients aged ≤40 years (14.3% vs 45.1%, $P = .138$), whereas this difference reached statistical significance in patients aged >40 years (25.0% vs 69.3%, $P = .002$).

Conclusions: The present findings suggest that early and midterm mortality after postcardiotomy VA-ECMO is significantly lower in patients aged ≤40 years compared to older patients. However, mortality remains substantial also among these young patients and heart-replacement therapies are infrequently performed in this subset of patients likely because of severe perioperative complications. (JTCVS Open 2025;28:278-95)



Mortality after postcardiotomy VA-ECMO support in different age strata.

CENTRAL MESSAGE

Mortality after postcardiotomy VA-ECMO is significantly lower in patients aged ≤40 years compared with older patients. However, mortality also remains substantial among these young patients.

PERSPECTIVE

Mortality after postcardiotomy VA-ECMO is significantly lower in patients aged ≤40 years compared with older patients. However, mortality also remains substantial among these young patients, and heart-replacement therapies are infrequently performed in this subset of patients likely because of severe perioperative complications.

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Abbreviations and Acronyms

CI = confidence interval
IPD = individual patient data
OR = odds ratio
VAD = ventricular assist device
VA-ECMO = venoarterial extracorporeal membrane oxygenation

Acute heart failure is not rare after adult cardiac surgery and often requires venoarterial extracorporeal membrane oxygenation (VA-ECMO) support. Patients treated with this mechanical circulatory support method are at increased risk of morbidity and mortality.[1,2] Elderly patients have increased early and midterm mortality.[3,4] Therefore, advanced age is a key issue in the decision-making process whether to start VA-ECMO support in patients with limited life expectancy. On the contrary, data on the early and midterm outcome of younger patients are scarce. In these young patients, VA-ECMO support may be used as a bridge to ventricular assist device (VAD) implantation and/or heart transplantation, but data on this issue also are scarce. The outcome of young patients requiring postcardiotomy VA-ECMO is investigated in the present individual patient data (IPD) meta-analysis.

METHODS

A literature search was performed in August 2022 through PubMed, Scopus, and Google Scholar for systematic review to identify studies on postcardiotomy VA-ECMO for the present IPD meta-analysis. Patients who had VA-ECMO implanted before surgery were excluded from this study. This IPD meta-analysis was registered in the PROSPERO (International Prospective Register of Systematic Reviews) registry (CRD42022359392). Studies in English language were independently screened by 2 investigators (F.B., G.M.) using the terms "postcardiotomy" and "ECMO" or "ECLS." One or more authors of articles suitable for inclusion in the present IPD meta-analysis were contacted 3 times by e-mail, and they were provided with a study protocol with the definition criteria of variables of interest as well as with an Excel datasheet with prespecified covariates. Data were checked for completeness and congruency. Patients from these studies who did not fulfill the inclusion criteria were excluded from the analysis. The quality of the studies was assessed according to the National Heart, Lung, and Blood Institute Study Quality Assessment Tools for case series studies.[5]

Study population, interventions, comparison, and outcomes of the present study are summarized in Table E1. This study was accomplished following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[6] (Table E2). Institutional review board permission was not asked because of the meta-analytic nature of this analysis evaluating de-identified clinical data.

Studies were included in this analysis if they fulfilled the following inclusion criteria: (1) studies providing data on patients who required VA-ECMO after any cardiac surgery procedure, including heart transplantation; (2) studies providing data on in-hospital mortality after postcardiotomy VA-ECMO; (3) studies including patients >18 years old; (4) prospective or retrospective observational studies; (5) studies whose results were published in English language as a full article; (6) studies including at least 10 patients; (7) studies reporting on arterial lactate levels at the time of VA-ECMO cannulation; and (8) articles published since 2015.

Studies were excluded from this analysis if they (1) did not provide information on the configuration of ECMO used; (2) did not provide information on the timing and site of cannulation of VA-ECMO; (3) did not provide data on arterial lactate levels at VA-ECMO cannulation; (4) included pediatric patients; (5) reported on the use of ECMO other than venoarterial configuration; and (6) included patients with preoperative VA-ECMO.

The criteria for case series studies proposed by the National Heart, Lung, and Blood Institute Study Quality Assessment Tools were used for grading the quality of the included studies.[5] The definition criteria of baseline risk factors, operative variables, data on VA-ECMO support and outcomes are summarized in Table E3.

Outcomes

The primary outcome of this study was all-cause in-hospital mortality, ie, all-cause death occurring during the index hospitalization. The secondary outcomes were all-cause mortality on VA-ECMO, ie, death from any

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TABLE 1. Patients' characteristics, operative data, and outcomes of patients who required postcardiotomy VA-ECMO support in different age strata

Variables	≤30 y n = 49	31-40 y n = 60	41-50 y n = 124	51-60 y n = 231	61-70 y n = 393	71-80 y n = 332	>80 y n = 49	P value
Heart transplant center	40 (81.6)	55 (91.7)	99 (79.8)	179 (77.5)	284 (72.3)	267 (80.4)	40 (81.6)	.013
Male gender	33 (67.3)	42 (70)	87 (70.2)	162 (70.1)	271 (69)	217 (65.4)	33 (67.3)	.913
eGFR, mL/min/1.73 m^2	97 (56)	83 (53)	72 (45)	68 (36)	64 (33)	58 (35)	63 (21)	.752
Arterial lactate, mmol/L	7.4 (6.7)	6.2 (6.2)	7.7 (.6)	7.5 (8.1)	6.9 (7.1)	7.2 (7.1)	6.5 (4.6)	<.001
Coronary artery disease	5 (10.2)	11 (18.3)	47 (37.9)	105 (45.5)	194 (49.4)	195 (58.7)	29 (59.2)	<.001
Type A aortic dissection	0 (0)	6 (10)	11 (8.9)	21 (9.1)	33 (8.4)	22 (6.6)	3 (6.1)	.387
Preoperative acute neurologic event	1 (2.0)	3 (5.0)	5 (4.0)	15 (6.5)	20 (5.1)	21 (6.3)	6 (12.1)	.363
Previous cardiac surgery	22 (44.9)	20 (33.3)	39 (31.5)	49 (21.2)	91 (23.2)	65 (19.6)	11 (22.4)	<.001
Urgent/emergency surgery	14 (28.6)	25 (41.7)	64 (51.6)	128 (55.4)	200 (50.9)	163 (49.1)	24 (49)	.033
Isolated CABG	1 (2.0)	6 (10.0)	28 (22.6)	54 (23.4)	90 (22.9)	94 (28.3)	13 (26.5)	<.001
Any CABG	11 (22.4)	11 (18.3)	47 (37.9)	104 (45)	194 (49.4)	203 (61.1)	27 (55.1)	<.001
Aortic valve procedure	27 (55.1)	27 (45.0)	53 (42.7)	71 (30.7)	154 (39.2)	110 (33.1)	18 (36.7)	.009
Tricuspid valve procedure	7 (14.3)	15 (25.0)	20 (16.1)	31 (13.4)	57 (14.5)	46 (13.9)	3 (6.1)	.190
Pulmonary valve procedure	2 (4.1)	1 (1.7)	1 (0.8)	1 (0.4)	0 (0)	1 (0.3)	0 (0)	.007
Mitral valve procedure	14 (28.5)	26 (43.3)	43 (34.7)	90 (39)	146 (37.2)	113 (34)	16 (32.7)	.604
VSD or ventricular wall repair	3 (6.1)	1 (1.7)	3 (2.4)	9 (3.9)	16 (4.1)	11 (3.3)	1 (2.0)	.833
Myectomy	2 (4.1)	0 (0)	1 (0.8)	2 (0.9)	2 (0.5)	0 (0)	0 (0)	.032
Aortic surgery	12 (24.5)	14 (23.3)	91 (26.6)	50 (21.6)	85 (21.6)	45 (13.6)	6 (12.2)	.014
Aortic arch surgery	3 (6.1)	3 (5.0)	7 (5.6)	15 (6.5)	20 (5.1)	14 (4.2)	1 (2.0)	.857
Other procedures	7 (14.3)	8 (13.3)	1 (0.8)	9 (3.9)	7 (1.8)	7 (2.1)	3 (6.1)	.001
VA-ECMO at primary surgery	30 (61.2)	37 (61.7)	78 (62.9)	136 (59.4)	237 (60.5)	205 (61.9)	35 (71.4)	.836
Central VA-ECMO	29 (59.2)	29 (48.3)	54 (43.5)	98 (42.4)	154 (39.2)	145 (43.7)	26 (53.1)	.110
VA-ECMO duration, d	5.7 (10.4)	5.0 (6.2)	5.0 (7.8)	5.3 (7.0)	5.0 (5.9)	4.0 (6.3)	2.9 (5.58)	.002
IABP during VA-ECMO	16 (32.7)	21 (35.0)	56 (45.2)	97 (42.0)	152 (38.7)	143 (43.2)	22 (44.9)	.291
Heart transplantation or VAD implantation after VA-ECMO	7 (14.3)	5 (8.4)	9 (7.2)	16 (7)	7 (1.9)	1 (0.3)	0 (0)	<.001
Outcomes								
Mortality on VA-ECMO	12 (24.5)	15 (25)	50 (40.3)	93 (40.3)	173 (44)	178 (53.6)	30 (61.2)	<.001
In-hospital mortality	20 (40.8)	27 (45.0)	75 (60.5)	139 (60.2)	271 (69.0)	252 (75.9)	40 (81.6)	<.001
24-mo mortality	20 (41.4)	28 (48.1)	78 (65.6)	144 (64.8)	280 (73.5)	261 (81.5)	41 (88.7)	<.001

Continuous values are reported as mean and standard deviation (in parentheses). Categorical values are reported as counts and percentages (in parentheses). *eGFR*, Estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology (CKD-EPI) equation; *CABG*, coronary artery bypass grafting; *VSD*, ventricular septal defect; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *VAD*, ventricular assist device.

cause without possibility of weaning from VA-ECMO support or fatal end-organ injury, as well as midterm mortality.

Statistical Analysis

Categorical variables are reported as counts and percentages. The normal distribution of continuous variables was assessed using the Shapiro-Wilk's test. Continuous variables that were not normally distributed are reported as median and interquartile range. Missing data regarded only preoperative creatinine levels in 35 patients and were not replaced in the analyses. Differences between age strata were evaluated using the linear-by-linear association test and by the Kruskal-Wallis test. Midterm mortality was evaluated using the Kaplan-Meier method. Unadjusted cutoff point of age for in-hospital mortality was first identified using the Youden test. However, the outcomes were likely affected by the individual risk factors and interinstitutional results. Therefore, in order to identify a correct cutoff of patients' age, this was first dichotomized at different cutoff values and then divided patients' age in strata adjusting its prognostic impact for individual risk factors and interinstitutional differences. Multilevel mixed-effects logistic regression was used to identify the independent predictors and to estimate the probabilities of in-hospital mortality and mortality on VA-ECMO considering the cluster effect of each participating hospital. Regression analysis first included all covariates listed in Table 1. The final regression model for in-hospital mortality was performed with a backward elimination procedure (probability of stay = 0.05; probability of

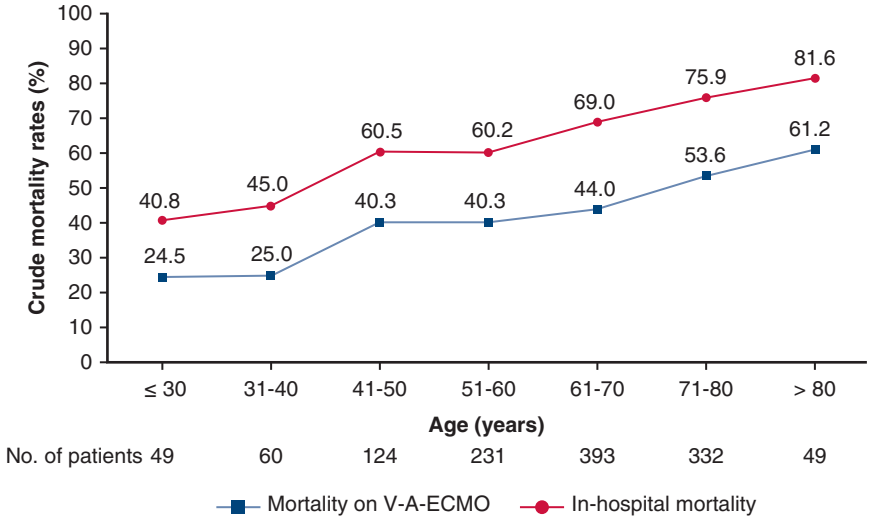

FIGURE 1. Crude rates of in-hospital mortality on postcardiotomy VA-ECMO support and during the index hospitalization in different age strata. *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation.

entry = 0.10). Likelihood ratio test as well as estimation of the receiver operating characteristics curve and the evaluation of difference between the ROC curves with the DeLong test were used to assess the difference of the results of the multilevel mixed-effect logistic regression and those of the conventional logistic regression. Risk estimates of outcomes at each age strata were adjusted in multiple variables multilevel mixed-effects logistic regression and parametric survival regression were reported as odds ratios (ORs) and hazard ratios with their 95% confidence intervals (CIs). The reference category for these analyses was age ≤30 years. The 95% CI of the mean adjusted risk of in-hospital mortality was plotted for different age strata as well. Once an age cutoff was identified, we evaluated whether heart replacement therapies were performed, and the early and midterm outcomes of these young patients compared to older patients. Statistical analyses were performed using Stata (version 15.1, StataCorp LLC, College Station, Texas, USA) statistical software.

RESULTS

A systematic review of the literature yielded 273 articles, and 31 of them were considered potentially suitable for the present analysis. Complete data on pre-, intra-, and postoperative variables of 1238 patients, but on preoperative creatinine (missing data in 35 patients) treated at 25 hospitals were available for the present IPD meta-analysis (Figure E1) from the investigators of 10 studies.[1,7-15] These investigators provided IPD for all prespecified clinical and operative variables and outcomes. The characteristics and quality of the included studies are summarized in Table E4. Baseline characteristics, operative data, and VA-ECMO related variables are reported in Table 1. Multivariable multilevel mixed-effect analysis showed that older age was an independent risk factor for in-hospital mortality (OR, 1.039; 95% CI, 1.028-1.051, $P < .001$) (Table E5). The Youden test identified an unadjusted age cutoff of 64 years (in-hospital mortality 75.2% vs 56.5%, $P < .001$, sensitivity 61%, specificity 61%). Patients were stratified in the following age strata: ≤30, 31-40, 41-50, 51-60, 61-70, 71-80, and >80 years. Crude hospital mortality rates were 40.8%, 45%, 60.5%, 60.2%, 69%, 75.9%, and 81.6%, respectively ($P < .001$) (Figure 1). Crude rates of mortality on VA-ECMO support showed a similar trend ($P < .001$) (Figure 1). Multivariable multilevel mixed-effect analysis showed that patients aged >40 years had significantly increased risk of in-hospital mortality along with female gender, increased arterial lactate at VA-ECMO initiation, previous cardiac surgery, aortic arch surgery, and other cardiac procedures (Table 2). The distribution of 95% CI of the mean adjusted risk of in-hospital mortality in different age strata confirmed that such a risk was higher in patients aged >40 years (Figure 2). The results of regression analysis with the backward elimination method are reported in Table 3. The difference between the ROC curve of the multivariable multilevel mixed-effect regression and that of the logistic regression models were statistically significant (0.742; 95% CI, 0.713-0.770 vs 0.719; 95% CI, 0.689-0.748, $P < .001$).

The cutoff for increased risk of mortality on VA-ECMO support was 60 years (Table E6). Crude overall mortality rates at 24-month were 41.4%, 48.1%, 65.6%, 64.8%, 73.5%, 81.5%, and 88.7%, respectively ($P < .001$). Consonant with the risk of in-hospital mortality, the risk of mortality at 24-month was significantly increased in patients aged >40 years (Table E7).

Patients' age was dichotomized according to 40 years, ie, ≤40 years old (109 patients) and >40 years old (1129 patients). Patients aged >40 years had significantly greater in-hospital mortality (68.8% vs 43.1%, $P < .001$), mortality on VA-ECMO support (46.4% vs 24.8%, $P < .001$), and mortality at 24 months (73.7% vs 45.0%, $P < .001$).

TABLE 2. Results of multilevel mixed-effects logistic regression for prediction of in-hospital mortality

Variables	*P* value	Adjusted odds ratio	95% confidence interval
Age, y			
≤30	–	Reference	–
31-40	.425	1.434	0.590-3.485
41-50	.006	3.093	1.379-6.940
51-60	.006	2.915	1.354-6.277
61-70	<.001	4.968	2.329-10.599
71-80	<.001	6.868	3.139-15.025
>80	<.001	10.080	3.539-28.708
Female gender	.012	1.471	1.090-1.985
eGFR (per each mL/min/ 1.73 m^2)	.132	0.997	0.992-1.001
Arterial lactate (per each mmol/ L)	<.001	1.116	1.081-1.153
Coronary artery disease	.382	0.820	0.525-1.279
Type A aortic dissection	.939	0.969	0.440-2.136
Preoperative acute neurological event	.064	0.969	0.965-3.626
Previous cardiac surgery	.013	1.544	1.095-2.177
Urgent/emergency surgery	.720	1.056	0.783-1.425
Isolated CABG	.980	1.007	0.583-1.740
Any CABG	.870	1.039	0.655-1.647
Aortic valve procedure	.183	0.770	0.524-1.131
Tricuspid valve procedure	.653	1.103	0.718-1.694
Pulmonary valve procedure	.157	1.967	0.021-1.867
Mitral valve procedure	.882	1.032	0.682-1.560
VSD or ventricular wall repair	.668	1.190	0.536-2.642
Myectomy	–	–	–
Aortic surgery	.980	1.010	0.471-2.167
Aortic arch surgery	.023	2.715	1.146-6.435
Other procedures	.018	3.157	1.222-8.151
VA-ECMO implanted at primary surgery	.780	0.959	0.716-1.284
IABP during VA-ECMO	.480	0.894	0.657-1.219
Central VA-ECMO	.050	1.351	1.000-1.826
Constant	.002	0.196	0.071-0.054
Participating centers	–	0.107	0.016-0.526
Likelihood ratio test vs logistic model: $P = .026$			

eGFR, Estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology (CKD-EPI) equation; *CABG*, coronary artery bypass grafting; *VSD*, ventricular septal defect. *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump.

Multilevel mixed-effect regression analysis showed that patients aged >40 years had a significantly increased risk of in-hospital mortality (adjusted OR, 3.267; 95% CI, 1.970-5.425) and mortality at 24 months (adjusted hazard ratio, 3.530; 95% CI, 2.571-4.844).

Overall, 45 (3.6%) patients underwent VAD implantation (29 patients, 2.3%) and/or heart transplantation (19 patients, 1.5%) and their in-hospital mortality was 46.7% compared with 67.3% of patients who did not undergo replacement therapy ($P = .004$). Two-year mortality rates were 54.1% versus 71.8%, respectively ($P = .002$). Among patients who underwent VAD implantation, in-hospital mortality was 58.6% compared with 66.7% of patients who did not undergo VAD implantation ($P = .359$), and 2-year mortality was 63.1% versus 71.3%, respectively ($P = .124$). Among patients who underwent post-VA-ECMO heart transplantation, in-hospital mortality was 21.1% compared with 67.3% in patients who did not undergo heart transplantation ($P < .001$). Two-year mortality in patients who underwent heart transplantation was 31.6% versus 71.8% among those who did no undergo post-VA-ECMO heart transplantation ($P < .001$).

Regarding the policy of postcardiotomy VA-ECMO support as a bridge to heart replacement therapies, 12 (11.0%) patients aged ≤40 years underwent VAD and/heart transplantation after postcardiotomy VA-ECMO, whereas this strategy was adopted in 33 (2.9%) patients aged >40 years ($P < .001$). Eventually, 7 (6.4%) patients aged ≤40 years and 12 (1.1%) patients aged >40 years underwent heart transplantation ($P < .001$). Heart transplantation after postcardiotomy VA-ECMO was associated with a decreased in-hospital in patients aged ≤40 years (14.3% vs 45.1%, $P = .138$) and patients aged >40 years (25.0%

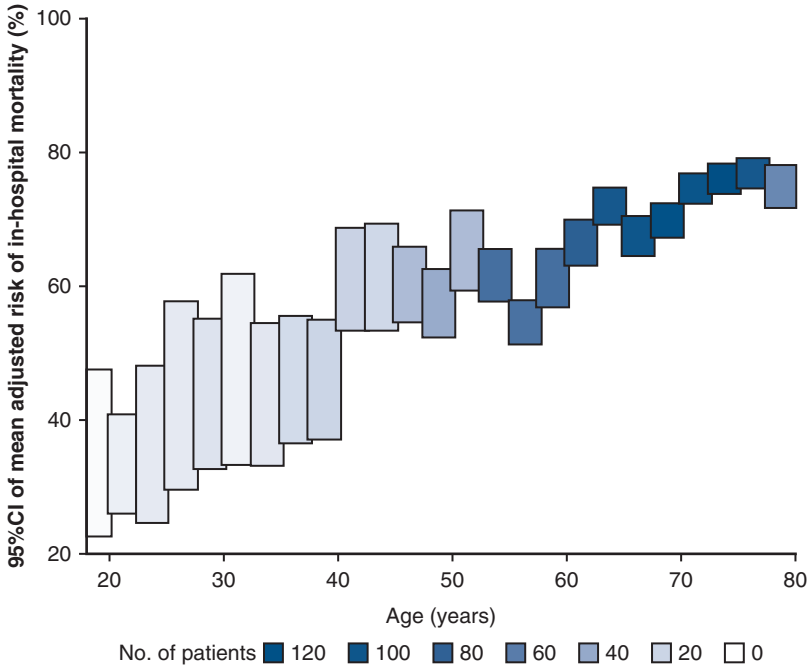

FIGURE 2. Binned scatterplot of showing the distribution of 95% confidence interval (CI) of the mean adjusted risk of in-hospital mortality in different age strata.

vs 69.3%, $P = .002$), but the difference reached statistical significance only among older patients.

DISCUSSION

The main findings of the present study analysis are the following: (1) patients younger than 40 years old who are postcardiotomy VA-ECMO have lower in-hospital and midterm mortality compared with older patients; (2) despite the better outcome, mortality remains significant in this subset of young patients; and (3) heart-replacement therapies are infrequently used in these young patients with long life expectancy.

Formulation of an age cutoff to identify patients with a low risk of adverse events is difficult within heterogenous

TABLE 3. Results of multilevel mixed-effects logistic regression with backward selection for prediction of in-hospital mortality

Variables	*P* value	Adjusted odds ratio	95% confidence interval
Age, y			
≤30	–	Reference	–
31-40	.455	1.377	0.600-3.191
41-50	.005	2.964	1.398-6.285
51-60	.003	2.878	1.421-5.826
61-70	<.001	4.756	2.382-9.499
71-80	<.001	6.446	3.170-13.109
>80	<.001	9.327	3.441-25.286
Female gender	.004	1.519	1.340-2.025
Arterial lactate (per each mmol/L)	<.001	1.122	1.089-1.157
Preoperative acute neurologic event	.050	1.916	1.000-3.675
Previous cardiac surgery	.012	1.501	1.093-2.061
Aortic arch surgery	.006	2.946	1.373-6.322
Other procedures	.010	3.085	1.308-7.278
Constant	<.001	0.152	0.074-0.314
Participating centers	–	0.125	0.033-0.476
Likelihood ratio test vs logistic model: $P = .006$			

settings of referral pathway, baseline risk factors, unmeasured proportion of iatrogenic injuries and/or suboptimal intraoperative myocardial protection strategies, and interinstitutional differences in terms of expertise with ECMO therapy. This led to a marked difference in terms of the cutoff of age estimated by the Youden test unadjusted for multiple confounders (64 years) compared with that (40 years) estimated by multilevel mixed-effects regression analysis considering the cluster effect of participating hospitals and multiple confounders (Figure 1). Despite the small proportion of patients aged ≤40 years, the risk of early and midterm mortality is evident when the outcome of these young patients is compared with age strata of patients aged between 40 and 60 years (Figures 1 and 2). This is likely related to the potential greater failure to rescue among older patients. The risk profile of patients aged ≤40 years is certainly different compared with patients aged >40 years because of a lower prevalence of baseline comorbidities such as coronary artery disease and renal failure, but they more frequently underwent repeat cardiac surgery, aortic valve surgery, and aortic surgery (Table 1). We do not have specific data on procedures for grown-up congenital heart disease, but we believe that frequently might have been the case among these young patients.

The use of VA-ECMO as bridge to heart transplant is a common practice among patients with heart failure, but its use after cardiac surgery is not common. Burgos and colleagues[16] demonstrated that in a heterogeneous cohort of patients with Interagency Registry for Mechanically Assisted Circulatory Support I and II and acute refractory cardiac arrest, the use of temporary VA-ECMO as a bridge to transplant achieved excellent in-hospital (83%) and 1-year (90%) survival in relatively young patients (mean age 46.0 years). Berger and colleagues[17] reported that patients bridged from ECMO to urgent left VAD due to refractory cardiogenic shock had similar long-term quality of life and mortality to elective left VAD recipients. Overall, there is a growing body of evidence of VA-ECMO as a valid bridge strategy to VAD implantation and/or heart transplantation.[5,18] However, these studies did not specifically address the value of heart-replacement therapies in patients who cannot be weaned from postcardiotomy VA-ECMO or have persistent severe heart failure after weaning.

A meta-analysis confirmed the low rate of heart transplantation or VAD implantation after postcardiotomy VA-ECMO support.[19] VAD was used after VA-ECMO in 2.3% of patients and heart transplantation in 1.9% of patients as reported in 21 studies.[19] We have previously observed that only 3.2% of patients postcardiotomy VA-ECMO received heart transplant or VAD.[4] Yet, these patients demonstrated a greater 5-year survival (42.9% vs 27.2%),[4] a difference that was not statistically significant in multivariate analysis likely due to the small sample size. These findings are consonant with the results of the present study, and they suggest that advanced therapies may confer survival benefits in appropriately selected patients. However, despite the young age of the patients herein evaluated, VAD implantation or heart transplantation was employed as a replacement therapy only in 11.0% patients aged ≤40 years and in 2.9% patients aged >40 years. These findings are certainly related to the preoperative comorbidities and, even more, to possible end-organ injury which developed intraoperatively or during VA-ECMO support. Therefore, the low proportion of patients undergoing replacement therapies might simply reflect the critical conditions requiring postcardiotomy VA-ECMO also among young patients.

The main limitation of this study is the retrospective nature of the included studies. Second, post-hoc power analysis showed that the sample size was not enough large to reject the null hypothesis of clinical efficacy of heart transplantation after postcardiotomy VA-ECMO. The analysis with a sample size ratio of 0.064 (beta = 0.8 and alpha = 0.05) showed that we would have needed a cohort of patients not undergoing heart transplant of 285 patients and a cohort of 19 patients undergoing heart transplant. Consonant with these results, a power analysis of a cohort ratio of 1 and a reduction of the risk of 10% would have required 376 patients in each cohort. The small number of patients who underwent heart replacement therapies in this series prevented also a reliable interaction analysis. Third, multilevel mixed-effects regression methods were employed to adjust for the cluster effect of the participating hospitals, but a bias related to interinstitutional differences in terms of referral pathways, volume and ECMO expertise might have still affected the present results. Fourth, we do not have data about anticoagulation strategies and VA-ECMO weaning protocols. We believe that multilevel regression analysis might have adjusted the results for these inter-institutional differences. Finally, this IPD meta-analysis was planned to investigate post-VA-ECMO mortality, and we are not able to provide data on other early adverse events.

CONCLUSIONS

The present IPD meta-analysis showed that the early- and midterm mortality rates after postcardiotomy VA-ECMO support were lower in patients aged ≤40 years compared with older patients. However, mortality remains substantial also among these young patients. Heart-replacement therapies are infrequently performed in this subset of patients likely because of severe perioperative complications.

Conflict of Interest Statement

Dr Kaserer received honoraria for lecturing from Bayer AG Switzerland and CSL Behring GmbH. Dr Cho is supported by Hyperfine, Inc, for SAFE MRI ECMO study. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Biancari F, Dalén M, Fiore A, et al. Multicenter study on postcardiotomy venoarterial extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*. 2020; 159(5):1844-1854.e6. https://doi.org/10.1016/j.jtcvs.2019.06.039
2. 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(1):31-36. https://doi.org/10.1097/MAT.0000000000000160
3. Biancari F, Saeed D, Fiore A, et al. Postcardiotomy venoarterial extracorporeal membrane oxygenation in patients aged 70 years or older. *Ann Thorac Surg*. 2019;108(4):1257-1264. https://doi.org/10.1016/j.athoracsur.2019.04.063
4. Biancari F, Perrotti A, Ruggieri VG, et al. Five-year survival after post-cardiotomy veno-arterial extracorporeal membrane oxygenation. *Eur Heart J Acute Cardiovasc Care*. 2021;10(6):595-601. https://doi.org/10.1093/ehjacc/zuaa039
5. National Heart, Lung, Blood Institute. Study quality assessment tools. Accessed October 15, 2022. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools
6. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. https://doi.org/10.1136/bmj.n71
7. L'Acqua C, De Tisi C, Lerva G, Ballotta A. Postcardiotomy VA ECMO in adult patients: italian single center experience in 2021. *Int J Artif Organs*. 2022;45(10): 799-800. https://doi.org/10.1177/03913988221112685
8. Sahli SD, Kaserer A, Braun J, et al. Predictors associated with mortality of extracorporeal life support therapy for acute heart failure: single-center experience with 679 patients. *J Thorac Dis*. 2022;14(6):1960-1971. https://doi.org/10.21037/jtd-21-1770
9. Alhijab FA, Tantawy TM, Ismail HH, et al. Venoarterial extracorporeal membrane oxygenation for postcardiotomy cardiogenic shock: the impact of cannulation strategy on survival. *Perfusion*. 2023;38(7):1444-1452. https://doi.org/10.1177/02676591221114954
10. Al-Kawaz M, Shou B, Prokupets R, Whitman G, Geocadin R, Cho SM. Mild hypothermia and neurologic outcomes in patients undergoing venoarterial extracorporeal membrane oxygenation. *J Card Surg*. 2022;37(4):825-830. https://doi.org/10.1111/jocs.16308
11. Hernández-Pérez FJ, Álvarez-Avelló JM, Forteza A, et al. Initial outcomes of a multidisciplinary network for the care of patients with cardiogenic shock. *Rev Esp Cardiol*. 2021;74(1):33-43. https://doi.org/10.1016/j.rec.2020.03.010
12. Laimoud M, Alanazi M. The clinical significance of blood lactate levels in evaluation of adult patients with veno-arterial extracorporeal membrane oxygenation. *Egypt Heart J*. 2020;72(1):74. https://doi.org/10.1186/s43044-020-00108-7
13. Djordjevic I, Deppe AC, Sabashnikov A, et al. Concomitant ECMO and IABP support in postcardiotomy cardiogenic shock patients. *Heart Lung Circ*. 2021; 30(10):1533-1539. https://doi.org/10.1016/j.hlc.2021.03.276
14. Samalavicius R, Norkiene I, Scupakova N, et al. Evaluation of risk factors for adverse outcome in extracorporeal membrane oxygenation-supported elderly postcardiotomy patients. *Perfusion*. 2020;35(1_suppl):50-56. https://doi.org/10.1177/0267659120907746
15. Alonso-Fernandez-Gatta M, Merchan-Gomez S, Gonzalez-Cebrian M, et al. Levosimendan in veno-arterial extracorporeal membrane oxygenator supported patients: impact on the success of weaning and survival. *Artif Organs*. 2021;45 (7):717-725. https://doi.org/10.1111/aor.13899
16. Burgos LM, Chicote FS, Vrancic M, et al. Veno-arterial ECMO ventricular assistance as a direct bridge to heart transplant: a single center experience in a low-middle income country. *Clin Transpl*. 2024;38(6):e15334. https://doi.org/10.1111/ctr.15334
17. Berger R, Hamdoun H, Sandoval Boburg R, et al. Quality of life following urgent LVAD implantation for ECMO therapy in cardiogenic shock: a long-term follow-up. *Medicina*. 2021;57(8):747. https://doi.org/10.3390/medicina57080747
18. DeFilippis EM, Clerkin K, Truby LK, et al. ECMO as a bridge to left ventricular assist device or heart transplantation. *JACC Heart Fail*. 2021;9(4): 281-289. https://doi.org/10.1016/j.jchf.2020.12.012
19. Biancari F, Perrotti A, Dalén M, et al. Meta-analysis of the outcome after postcardiotomy venoarterial extracorporeal membrane oxygenation in adult patients. *J Cardiothorac Vasc Anesth*. 2018;32(3):1175-1182. https://doi.org/10.1053/j.jvca.2017.08.048

Key Words: extracorporeal membrane oxygenation, ECMO, ECLS, cardiac surgery postcardiotomy, age, LVAD, heart transplant

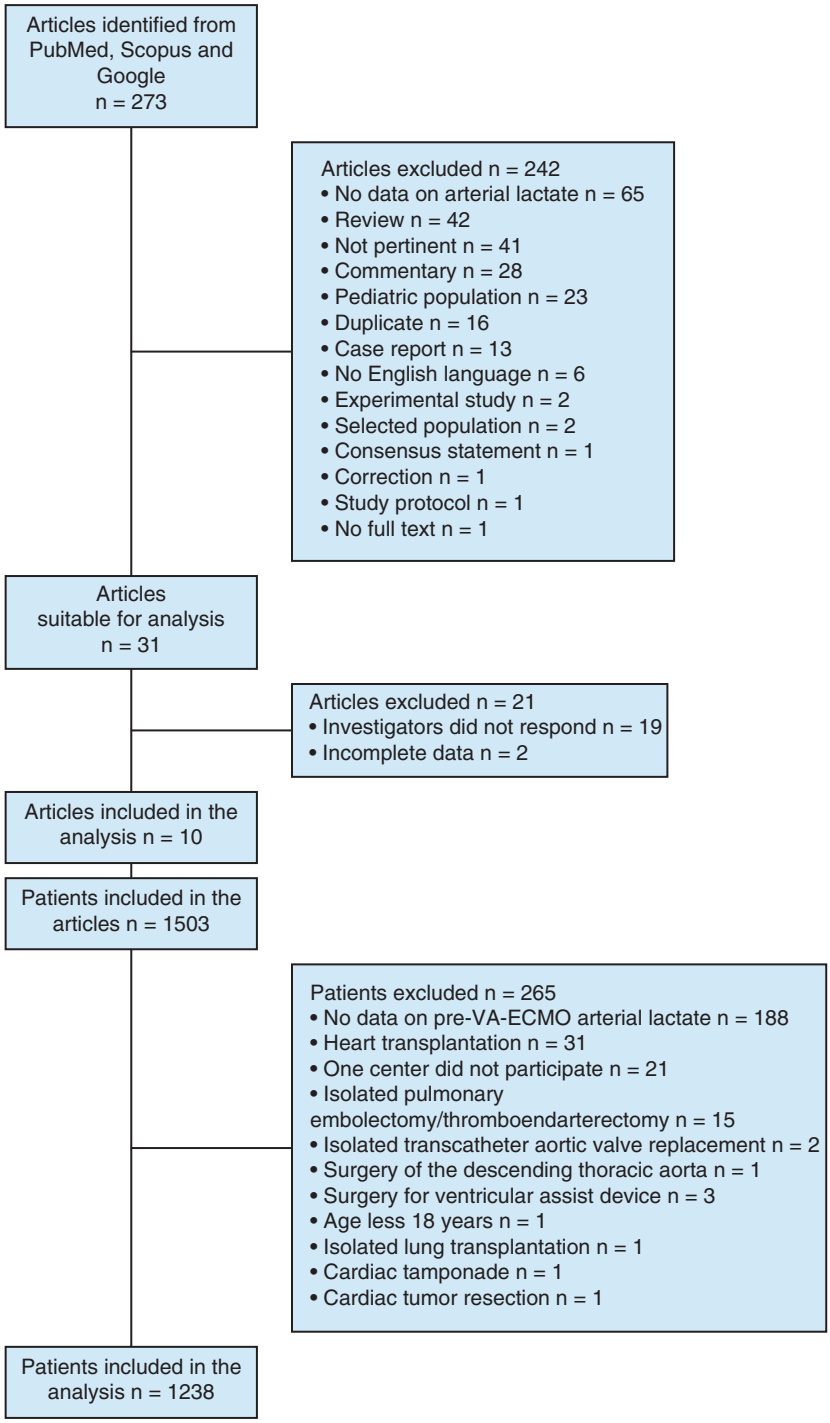

FIGURE E1. Study flowchart. *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation.

TABLE E1. Population, intervention, comparison, and outcomes of the present study

Population	Patients with cardiogenic shock after adult cardiac surgery
Intervention	Postoperative venoarterial extracorporeal membrane oxygenation
Comparison	Outcomes of venoarterial extracorporeal membrane oxygenation therapy in patients aged $\leq$ 40 years vs older patients
Outcomes	Mortality during venoarterial extracorporeal membrane oxygenation and during the index hospitalization

TABLE E2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) information

Section and topic	Item #	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	Page 1
Abstract			
Abstract	2	See the prisma 2020 for abstracts checklist.	Page 1
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (eg, for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (eg, participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 2
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4
Effect measures	12	Specify for each outcome the effect measure(s) (eg, risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6

(Continued)

TABLE E2. Continued

Section and topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (eg tabulating the study intervention characteristics and comparing against the planned groups for each synthesis [item #5]).	Page 5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (eg, subgroup analysis, meta-regression).	–
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	–
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	–
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	–
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	–
Study characteristics	17	Cite each included study and present its characteristics.	Suppl. Mat.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Suppl. Mat.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (eg, confidence/credible interval), ideally using structured tables or plots.	Page 7 and tables
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Suppl. Mat.
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (eg, confidence/credible interval) and measures of statistical	Page 5

(Continued)

TABLE E2. Continued

Section and topic	Item #	Checklist item	Location where item is reported
		heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 7
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	–
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	No missing data
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	–
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 9
	23b	Discuss any limitations of the evidence included in the review.	Page 10,11
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	Page 9,10
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	None
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 2
Competing interests	26	Declare any competing interests of review authors.	Page 2
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 2

TABLE E3. Definition criteria of baseline characteristics, operative variable, VA-ECMO treatment strategy and outcomes

Heart transplant center	Center providing VA-ECMO therapy having a heart transplant program
Age	Age at the time of index cardiac surgery in years
Estimated glomerular filtration rate	It was estimated according to the MDRD equation based on the serum concentration of creatinine before primary cardiac surgery. This does not refer to creatinine value before VA-ECMO cannulation
Coronary artery disease	It refers to coronary artery disease that required previous or current coronary artery revascularization (either coronary surgery or percutaneous coronary intervention) or evidence of coronary artery disease not requiring revascularization
Type A aortic dissection	Index cardiac surgery performed for acute aortic dissection involving the ascending aorta
Preoperative acute neurologic event	Any stroke or unconsciousness status immediately before the index cardiac surgery
Previous cardiac surgery	Prior cardiac surgery procedure on the heart valves, coronary arteries, ascending aorta/aortic arch and/or cardiac walls requiring opening of the pericardium
Arterial lactate at VA-ECMO cannulation	Level of arterial lactate before cannulation or at initiation of VA-ECMO
Type of surgery	Type of index cardiac surgery procedure
Aortic arch surgery	Surgery with partial or total repair of the aortic arch
VA-ECMO implanted at primary surgery	VA-ECMO implanted during the index cardiac surgery procedure
Late VA-ECMO implantation	VA-ECMO implanted after transferal from the operating room
IABP during VA-ECMO	Use of intra-aortic balloon pump anytime during VA-ECMO therapy
Central VA-ECMO	Cannulation of the ascending aorta or aortic prosthesis
Peripheral VA-ECMO	Cannulation for VA-ECMO access through any peripheral artery
Duration of VA-ECMO	Length of VA-ECMO therapy considering also the duration of multiple VA-ECMO runs
Duration of ICU stay	Length of stay in the intensive care unit, considering also any readmission.
Death on VA-ECMO	Death from any cause during VA-ECMO therapy, without any possibility of weaning from ECMO
Hospital death	All-cause death occurring during the index hospitalization

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; *MDRD*, Modification of Diet in Renal Disease; *IABP*, intra-aortic balloon pump; *ICU*, intensive care unit.

TABLE E4. Characteristics and quality of studies included in the present individual patient data meta-analysis according to the National Heart, Lung, and Blood Institute Study Quality Assessment Tools for case series studies

Variables	Al-Kawaz 2022	Alhijab 2023	Alonso-Fernandez-Gatta 2021	Biancari 2020	Djordjevic 2021	Hernández-Pérez 2021	L'Acqua 2022	Laimoud and alanazi 2020	Sahli 2022	Samalavicius 2020
No. of patients*	50	101	34	781	172	32	17	61	215	40
No. of patients included in the analysis	47	86	31	624	145	22	16	56	172	39
Multicenter study	No	No	No	Yes	No	No	No	No	No	No
Prospective study	No	No	No	No	No	No	No	No	No	No
NHLBI study quality criteria										
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the study population clearly and fully described, including a case definition?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
3. Were the cases consecutive?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were the subjects comparable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
5. Was the intervention clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	No
7. Was the length of follow-up adequate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Were the statistical methods well-described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Were the results well-described?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Quality rating	Good	Good	Good	Good	Good	Good	Fair	Good	Good	Fair

NHLB, National Heart, Lung, and Blood Institute. *The overall number of patients requiring postcardiotomy venoarterial extracorporeal membrane oxygenation as included in the original article.

TABLE E5. Results of multilevel mixed-effects logistic regression for prediction of in-hospital mortality

Covariates	*P* value	Adjusted odds ratio	95% confidence interval
Age (per each year)	<.001	1.039	1.028-1.051
Female gender	.013	1.461	1.083-1.971
eGFR (per each mL/min/1.73 m^2)	.148	0.997	0.992-1.001
Arterial lactate (per each mmol/L)	<.001	1.116	1.081-1.153
Coronary artery disease	.343	0.806	0.516-1.259
Type A aortic dissection	.965	0.982	0.446-2.166
Preoperative acute neurological event	.093	0.982	0.91-3.424
Priorcardiac surgery	.009	1.583	1.122-2.232
Urgent/emergency surgery	.721	1.056	0.783-1.424
Isolated CABG	.938	1.021	0.592-1.763
Any CABG	.828	1.052	0.664-1.668
Aortic valve procedure	.978	0.774	0.527-1.138
Tricuspid valve procedure	.618	1.115	0.726-1.712
Pulmonary valve procedure	.126	0.174	0.019-1.637
Mitral valve procedure	.866	1.036	0.686-1.566
VSD or ventricular wall repair	.656	1.199	0.540-2.662
Myectomy	–	–	–
Aortic surgery	.978	1.011	0.470-2.175
Aortic arch surgery	.027	2.656	1.119-5.305
Other procedures	.024	2.946	1.150-7.052
VA-ECMO implanted at primary surgery	.827	0.968	0.723-1.295
Central VA-ECMO	.051	1.349	0.999-1.823
Constant	<.001	0.074	0.027-0.208
Participating centers	–	0.108	0.023-0.506
Likelihood ratio test vs logistic model: $P = .021$			

eGFR, Estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology (CKD-EPI) equation; *CABG*, coronary artery bypass grafting; *VSD*, ventricular septal defect; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation.

TABLE E6. Results of multilevel mixed-effects logistic regression for prediction of mortality on postcardiotomy VA-ECMO support considering strata of patients' age

Covariates	*P* value	Adjusted odds ratio	95% confidence interval
Age, y			
31-40	.963	1.023	0.391-2.675
41-50	.061	2.205	0.964-5.042
51-60	.146	1.800	0.814-3.978
61-70	.023	2.473	1.135-5.389
71-80	.001	3.767	1.696-8.362
>80	<.001	5.738	2.153-15.289
Female gender	.429	1.119	0.847-1.479
eGFR (per each mL/min/1.73 m^2)	.973	1.000	0.995-1.004
Arterial lactate (per each mmol/L)	<.001	1.141	1.108-1.175
Preoperative acute neurological event	.046	1.803	1.010-3.228
Coronary artery disease	.454	0.852	0.560-1.296
Type A aortic dissection	.891	0.950	0.437-1.950
Previous cardiac surgery	.322	0.851	0.618-1.171
Urgent/emergency surgery	.718	0.947	0.707-1.270
Isolated CABG	.428	1.234	0.734-2.074
Any CABG	.806	0.946	0.611-1.467
Aortic valve procedure	.826	0.960	0.670-1.377
Tricuspid valve procedure	.612	1.111	0.740-1.668
Pulmonary valve procedure	.802	1.267	0.200-8.021
Mitral valve procedure	.410	1.179	0.797-1.745
VSD or ventricular wall repair	.157	1.721	0.811-3.651
Myectomy	.556	1.751	0.271-11.320
Aortic surgery	.216	1.568	0.769-3.197
Aortic arch surgery	.075	1.908	0.937-3.887
Oher procedures	.653	1.202	0.540-2.676
VA-ECMO implanted at primary surgery	.279	1.169	0.881-1.550
Central VA-ECMO	.867	1.027	0.753-1.400
Constant	<.001	0.089	0.031-0.254
Participating centers	–	0.349	0.129-0.941
Likelihood ratio test vs logistic model: $P < .001$			

eGFR, Estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology (CKD-EPI) equation; *CABG*, coronary artery bypass grafting; *VSD*, ventricular septal defect; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation.

TABLE E7. Results of multilevel mixed-effects parametric survival regression for prediction of 24-month mortality

Covariates	*P* value	Adjusted hazards ratio	95% confidence interval
Age, y			
31-40	.445	1.273	0.686-2.362
41-50	<.001	2.672	1.566-4.560
51-60	<.001	2.860	1.708-4.791
61-70	<.001	4.935	3.001-8.115
71-80	<.001	6.797	4.078-11.328
>80	<.001	12.224	6.696-22.318
Female gender	.141	1.136	0.958-1.347
eGFR (per mL/min/1.73 m^2)	.001	0.995	0.992-0.998
Arterial lactate (per mmol/L)	<.001	1.142	1.123-1.161
Coronary artery disease	.016	0.721	0.552-0.941
Type A aortic dissection	.456	0.862	0.584-1.272
Preoperative acute neurological event	<.001	2.489	1.761-3.516
Previous cardiac surgery	<.001	1.840	1.533-2.208
Urgent/emergency surgery	.557	0.947	0.790-1.135
Isolated CABG	.780	1.046	0.761-1.439
Any CABG	.117	1.241	0.947-1.627
Aortic valve procedure	.001	0.666	0.529-0.839
Tricuspid valve procedure	.498	1.089	0.851-1.394
Pulmonary valve procedure	.556	1.381	0.471-4.051
Mitral valve procedure	.284	1.148	0.891-1.478
VSD or ventricular wall repair	.385	1.214	0.783-1.881
Myectomy	.001	4.442	1.780-11.082
Aortic surgery	.201	1.304	0.868-1.959
Aortic arch surgery	<.001	2.358	1.584-3.509
Other procedures	.001	2.056	1.351-3.127
VA-ECMO implanted at primary surgery	.214	0.971	0.939-1.322
Central VA-ECMO	<.001	1.570	1.296-1.898
Constant	<.001	0.005	0.006-0.260
Participating centers	–	0.979	0.527-1.823
Likelihood ratio test vs logistic model: $P < .001$			

eGFR, Estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology (CKD-EPI) equation; *CABG*, coronary artery bypass grafting; *VSD*, ventricular septal defect; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation.