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Variables associated with in-hospital and postdischarge outcomes after postcardiotomy extracorporeal membrane oxygenation: Netherlands Heart Registration Cohort

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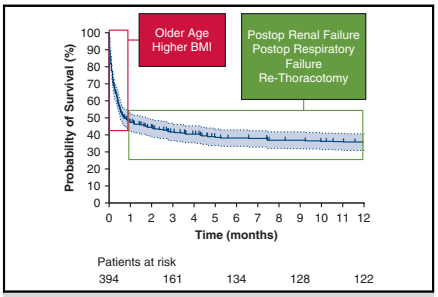
ABSTRACT

Objectives: Extracorporeal membrane oxygenation (ECMO) for postcardiotomy cardiogenic shock has been increasingly used without concomitant mortality reduction. This study aims to investigate determinants of in-hospital and postdischarge mortality in patients requiring postcardiotomy ECMO in the Netherlands.

Methods: The Netherlands Heart Registration collects nationwide prospective data from cardiac surgery units. Adults receiving intraoperative or postoperative ECMO included in the register from January 2013 to December 2019 were studied. Survival status was established through the national Personal Records Database. Multivariable logistic regression analyses were used to investigate determinants of in-hospital (3 models) and 12-month postdischarge mortality (4 models). Each model was developed to target specific time points during a patient's clinical course.

Results: Overall, 406 patients (67.2% men, median age, 66.0 years [interquartile range, 55.0-72.0 years]) were included. In-hospital mortality was 51.7%, with death occurring in a median of 5 days (interquartile range, 2-14 days) after surgery. Hospital survivors (n = 196) experienced considerable rates of pulmonary infections, respiratory failure, arrhythmias, and deep sternal wound infections during a hospitalization of median 29 days (interquartile range, 17-51 days). Older age (odds ratio [OR], 1.02; 95% CI, 1.0-1.04) and preoperative higher body mass index (OR, 1.08; 95% CI, 1.02-1.14) were associated with in-hospital death. Within 12 months after discharge, 35.1% of hospital survivors (n = 63) died. Postoperative renal failure (OR, 2.3; 95% CI, 1.6-4.9), respiratory failure (OR, 3.6; 95% CI, 1.3-9.9), and re-thoracotomy (OR, 2.9; 95% CI, 1.3-6.5) were associated with 12-month postdischarge mortality.

Conclusions: In-hospital and postdischarge mortality after postcardiotomy ECMO in adults remains high in the Netherlands. ECMO support in patients with higher age and body mass index, which drive associations with higher in-hospital mortality, should be carefully considered. Further observations suggest that prevention of re-thoracotomies, renal failure, and respiratory failure are targets that may improve postdischarge outcomes. (J Thorac Cardiovasc Surg 2022;■:1-11)



Analysis of 406 patients undergoing postcardiotomy ECMO from the Netherlands Heart Registration.

CENTRAL MESSAGE

Higher age, BMI, re-thoracotomy, and renal and respiratory failure associations with mortality suggest that optimizing patient selection and targeting complication prevention improves postcardiotomy ECMO outcomes.

PERSPECTIVE

This study supports the development of multidisciplinary dynamic strategies for patients undergoing postcardiotomy ECMO whose needs change over the clinical journey. Each strategy should be titrated on the characteristics of the local population and more attention is required during the post-ECMO and postdischarge time, with adequate follow-up programs for at least 12 months after discharge.

See Commentary on page XXX.

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Abbreviations and Acronyms
BMI = body mass index
ECMO = extracorporeal membrane oxygenation
NHR = Netherlands Heart Registration

Scanning this QR code will take you to the table of contents to access supplementary information.

Postcardiotomy cardiogenic shock occurs in 2% to 6% of cardiac surgery patients,[1] leading to consider mechanical circulatory support after cardiac surgery.[1-5] Based on the increasing complexity of cardiac surgery, the number of patients with postcardiotomy cardiogenic shock is expected to rise.[6] Postcardiotomy cardiogenic shock is associated with greater resource use, longer length of stay, and higher mortality compared with other shock etiologies[7] and extracorporeal membrane oxygenation (ECMO) remains among the most used postcardiotomy cardiogenic shock support strategies.[1,2,8] Despite the rising incidence of postcardiotomy ECMO, alongside the increasing expertise, survival rates to discharge have shown no improvements from the current rate of 20% to 40%.[2-5] Factors such as differences in health care systems, variability among institutional protocols and experiences,[9,10] resources availability, and cultural aspects could play an important role in affecting mortality rates. The availability of evidence regarding long-term outcomes and their determinants is scarce and often contradictory.[11-13] A possible approach to reducing in-hospital and long-term mortality after postcardiotomy ECMO includes identifying modifiable factors at different time points during a patient's clinical course. This would support the development of dynamic strategies to address a patient's needs at different stages of the clinical journey, guarantee a more effective personalized therapy, optimize resources, and improve in-hospital and postdischarge outcomes. Despite the growing awareness regarding the dynamicity in the clinical course of each postcardiotomy ECMO patient, the need for new approaches to select and manage these patients, the differences among health care systems and cultures, and the importance of their postdischarge care, are characterized by significant knowledge gaps.

In the Netherlands Heart Registration (NHR) procedure-related and follow-up outcomes of all invasive cardiac and cardiothoracic surgical procedures from 16 Dutch cardiac surgery units are collected. This study aimed to investigate in-hospital and postdischarge mortality of Dutch patients undergoing postcardiotomy ECMO between 2013 and 2019.[3,14] We aimed to describe patients' characteristics, in-hospital outcomes, and to identify determinants for in-hospital mortality at different time points during a patient's clinical course. Moreover, we hypothesized that postoperative multiorgan impairment could influence patients' postdischarge mortality for up to 12 months.

MATERIALS AND METHODS

NHR evaluates current surgical practice for heart disease to improve care by assessing patient data from preoperative diagnosis to work-up until several years after intervention.[15] Participating hospitals deliver a predefined dataset to the NHR in a secured online environment. This study complies with the Declaration of Helsinki, and the data use was approved by the Maastricht University Medical Centre Ethical Committee (METC 2021-2629; date of approval: April, 29, 2021) and the Medical Research Ethics Committees United (reference No. W19.270), that issued a waiver for informed consent for the current analysis of anonymized data. The NHR Scientific Steering Committee approved the study protocol.

Study Design and Population

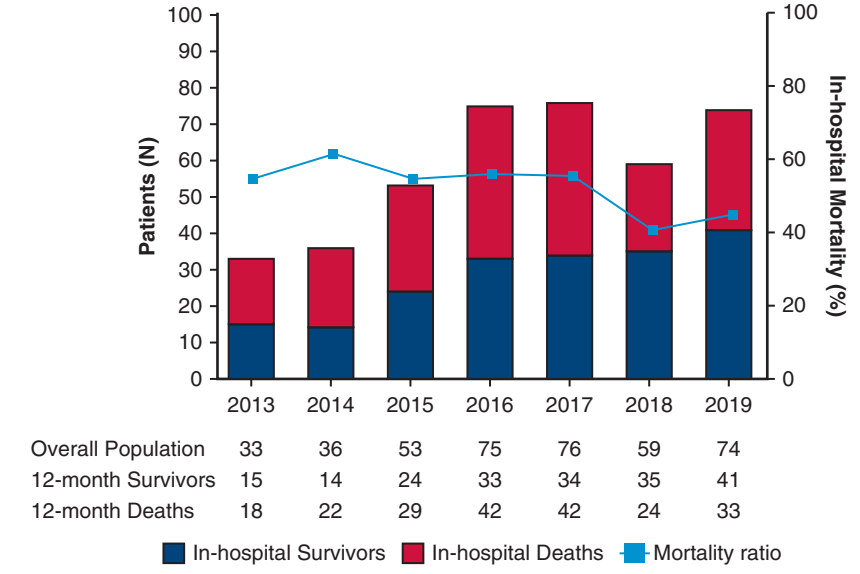
We included adults (aged ≥18 years) receiving ECMO (for a cardiac indication and performed by a cardiothoracic surgeon) during or after a cardiac surgery procedure between January 2013 and December 2019 (Appendix E1 and Figure 1). Patients were excluded if they received mechanical circulatory support devices other than ECMO (eg, durable ventricular assist devices, paracorporeal ventricular assist device, total artificial heart, or catheter-based assist devices). We studied patients and included the first ECMO run as an indexed procedure when patients had multiple runs.

Demographic and clinical variables were collected from the NHR database and defined according to the NHR handbook version 2021.0.3 (Table E1).[16] Survival status was determined after verification with the Dutch Personal Records Database or the date of the last contact. The primary outcome was in-hospital mortality. The secondary outcome was mortality at 12 months after discharge.

Statistical Analysis

Demographic and clinical variables were expressed as numbers (%) for categorical variables and median (interquartile range [IQR]) for continuous variables after evaluation for normality. Categorical data were compared with the χ^2 test. Continuous variables were analyzed using the Kruskal-Wallis test or Wilcoxon test, as appropriate. Survival was investigated with the Kaplan-Meier method.

First, we described the population characteristics, and perioperative and postoperative variables for the whole cohort and separately for in-hospital survivors and in-hospital deaths (Tables 1-3). Second, we compared patients alive or dead 12 months after discharge in in-hospital survivors only. In a multivariable binary logistic regression analysis, we considered different sets of clinical variables deemed important for the association with mortality at different time points during a patient's clinical course. Each variable set was developed based on clinical practice and literature.[3,14,17] For the association with in-hospital mortality, 3 different sets of variables were chosen: demographic data, demographic data and preoperative variables, and demographic data and preoperative and intraoperative variables. As determinants of 12-month postdischarge mortality, 4 different sets of variables were chosen: demographic data, demographic data and preoperative variables, demographic data and preoperative and intraoperative variables, and demographic data and postoperative complications. Associations are reported as odds ratios and 95% CIs. Variables with data completeness lower than 80% were excluded. To allow for the inclusion of all patients for the regression analysis, we used stochastic regression imputation with a fully conditional specification to impute the dataset. Imputations were drawn using predictive mean matching. All data were



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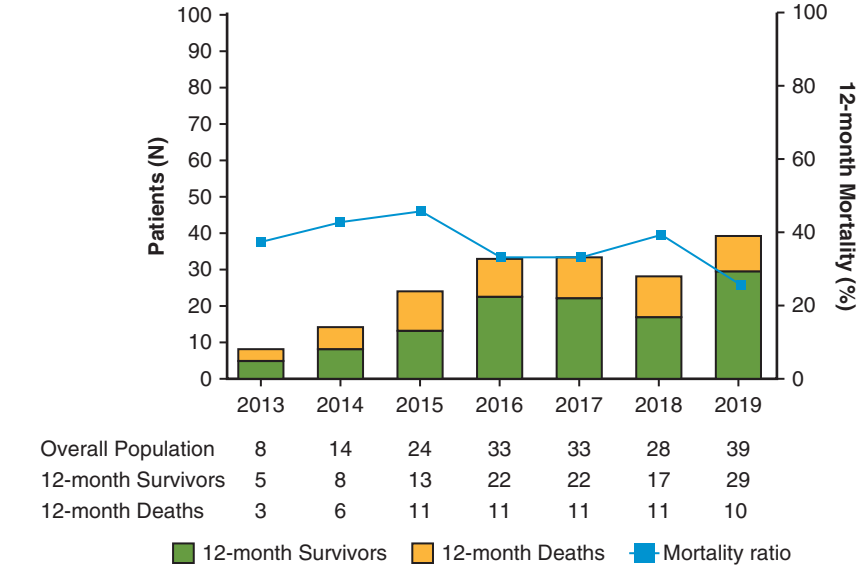

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FIGURE 1. A, Annual trend for in-hospital mortality. B, Annual trend for postdischarge 12-month mortality. Based on the structure of the Netherlands Heart Registration database, an underreporting of absolute numbers of extracorporeal membrane oxygenation implants cannot be excluded.

merged from separate de-identified files into SPSS 26.0 (IBM-SPSS Inc), Prism 8.0 (GraphPad Software Inc), and R version 4.1.2 (R Foundation for Statistical Computing) for data management and statistical analysis.

RESULTS

Baseline Characteristics, In-Hospital Mortality, and Its Determinants

In total, 697 patients received ECMO and were registered in the NHR. Of them, 270 received an isolated ECMO implantation not associated with any cardiac operation, and 21 received preoperative ECMO support (n = 21). Thus, 406 patients were studied (Figure E1). Median age was 66.0 years (IQR, 55.0-72.0 years) with women accounting for 32.8% (n = 133) (Table 1). Hospital nonsurvivors (n = 210 [51.7%]) were older ($P = .013$) and had a higher body mass index (BMI) ($P = .001$) than survivors (n = 196 [48.3%]), with comparable surgical procedures (Table 2), except for a longer extracorporeal circulation time in hospital nonsurvivors ($P = .022$). In-hospital survivors were discharged after a median of 29.0 days (IQR, 17-51 days), whereas in-hospital death occurred at a median of 5 days (IQR, 2-14 days) after surgery (Figure E2). Based on a

TABLE 1. Baseline characteristics of the overall population

Characteristic	Overall population (N = 406)	In-hospital survivors (n = 196)	In-hospital deaths (n = 210)	*P* value
Age (y)	66.0 (55.0-72.0)	64.0 (53.0-71.0)	67.0 (59.0-72.0)	.013
Sex				1.000
Female	133 (32.8)	64 (32.7)	69 (32.9)	
Male	273 (67.2)	132 (67.3)	141 (67.1)	
BMI	26.5 (24.1-29.7)	25.7 (23.6-28.4)	27.3 (24.6-30.9)	.001
Body surface area (m^2)	2.0 (1.8-2.1)	2.0 (1.8-2.1)	2.0 (1.8-2.1)	.090
Obesity defined as BMI >29.9	85 (24.4)	28 (16.8)	57 (31.5)	.002
Diabetes mellitus				.085
None	302 (82.1)	150 (85.2)	152 (79.2)	
Insulin-dependent	22 (6.0)	12 (6.8)	10 (5.2)	
Non–insulin-dependent	36 (9.8)	10 (5.7)	26 (13.5)	
Treatment unknown	8 (2.2)	4 (2.3)	4 (2.1)	
Chronic lung disease	47 (11.6)	17 (8.7)	30 (14.3)	.088
Extracardiac arterial vascular pathology	44 (10.8)	20 (10.2)	24 (11.4)	.751
Neurological dysfunction	12 (3.4)	5 (2.8)	7 (3.9)	.771
Previous cardiac surgery	109 (26.8)	57 (29.1)	52 (24.8)	.370
Active endocarditis	45 (11.1)	20 (10.2)	25 (11.9)	.637
Critical preoperative condition	136 (33.5)	61 (31.1)	75 (35.7)	.345
Unstable angina pectoris	33 (8.1)	14 (7.1)	19 (4.7)	.586
Recent myocardial infarction	92 (22.7)	45 (23.0)	47 (22.4)	.906
Postinfarct ventricular septal rupture	13 (3.2)	5 (2.6)	8 (3.8)	.578
Dialysis	1 (0.3)	0 (0)	1 (0.6)	.492
Poor mobility	15 (5.2)	11 (7.4)	4 (2.8)	.110
NYHA functional class				.889
I	48 (18.9)	27 (20.8)	21 (19.9)	
II	50 (19.7)	25 (19.2)	25 (20.2)	
III	79 (31.1)	39 (30.0)	40 (32.3)	
IV	77 (30.3)	39 (30.0)	38 (30.6)	
CCS class IV angina	41 (13.7)	21 (13.8)	20 (13.5)	.939
Urgency of the procedure				.453
Elective	154 (40.2)	78 (43.1)	76 (37.6)	
Urgent	92 (24.0)	38 (21.0)	54 (26.7)	
Emergency	93 (24.3)	42 (23.2)	51 (25.2)	
Salvage	44 (11.5)	23 (12.7)	21 (10.4)	
Weight of intervention				.075
Isolated CABG	49 (12.9)	23 (12.8)	26 (13.1)	
1 procedure other than CABG	104 (27.4)	47 (26.1)	57 (28.6)	
2 procedures other than CABG	139 (36.7)	77 (42.8)	62 (31.2)	
3 procedures other than CABG	87 (23.0)	33 (18.3)	54 (27.1)	
EuroSCORE II	10.9 (3.6-25.0)	9.12 (3.7-23.9)	12.4 (3.4-26.5)	.672
Left ventricular ejection fraction (%)	40.0 (25.0-55.0)	40.0 (25.0-55.0)	40.0 (26.0-55.0)	.474

Values are presented as median (interquartile range) or n (% as valid percentage excluding missing values). *BMI*, Body mass index; *NYHA*, New York Heart Association; *CCS*, Canadian Cardiovascular Society; *CABG*, coronary artery bypass graft; *EuroSCORE II*, European System for Cardiac Operative Risk Evaluation II score.

longer hospitalization, survivors experienced considerable rates of pulmonary infections, respiratory failure, arrhythmias, and deep sternal wound infections (Table 3).

The multivariable analyses showed that higher age and BMI (both analyzed as continuous variables) were associated with in-hospital mortality (Table 4, *models 1-4,*

TABLE 2. Procedure-related characteristics of the overall population

Characteristic	Overall population (N = 406)	In-hospital survivors (n = 196)	In-hospital deaths (n = 210)	*P* value
CABG	178 (43.3)	81 (41.3)	97 (46.3)	.368
No. of arterial grafts	1 (0-1)	1 (0-1)	1 (0-1)	.857
No. of venous grafts	2 (1-3)	2 (1-3)	2 (1-3)	.609
Off-pump CABG	7 (4.1)	4 (5.1)	3 (3.3)	.704
Valve surgery	249 (61.3)	116 (59.2)	133 (63.3)	.415
Aortic valve surgery	161 (39.7)	72 (36.7)	89 (42.4)	.265
Mitral valve surgery	127 (31.3)	60 (30.6)	67 (31.9)	.831
Tricuspid valve surgery	35 (8.6)	18 (9.2)	17 (8.1)	.726
Pulmonary valve surgery	3 (0.7)	2 (1.0)	1 (0.5)	.612
Aortic surgery	103 (25.4)	45 (23.0)	58 (27.6)	.305
Ascending aorta surgery	102 (25.1)	44 (22.4)	58 (27.6)	.253
Aortic arch surgery	25 (6.2)	12 (6.1)	13 (6.2)	1.000
Descending aorta procedure	4 (0.9)	4 (2.0)	0 (0)	.115
Other cardiac procedures	304 (74.9)	151 (77.0)	153 (72.9)	.361
Heart transplant	7 (1.7)	6 (3.1)	1 (0.5)	.060
Rhythm surgery	32 (7.9)	15 (7.7)	17 (8.1)	1.000
Correction of a cardiac aneurysm	8 (2.0)	5 (2.6)	3 (1.4)	.490
Cardiac rupture*	17 (4.2)	5 (2.5)	12 (5.7)	.277
Myectomy	5 (1.2)	2 (1.0)	3 (1.4)	1.000
Congenital cardiac surgery	6 (1.5)	4 (2.0)	2 (1.0)	.435
Pericardiectomy	3 (0.7)	0 (0)	3 (1.4)	.249
Pulmonary embolectomy	10 (2.5)	4 (2.0)	6 (2.9)	.752
Extracorporeal circulation				.711
Off-pump	21 (5.3)	12 (6.4)	9 (4.3)	
Conventional ECC	357 (89.9)	168 (89.4)	189 (90.4)	
Miniaturized ECC	11 (2.8)	4 (2.1)	7 (3.3)	
ECC type unknown	8 (2.0)	4 (2.1)	4 (1.9)	
ECC time (min)	247.0 (170.5-375.25)	207.5 (129.5-302.5)	263.0 (190.0-377.0)	.022
Crossclamp time (min)	113.5 (65.25-171.0)	84.5 (47.3-140.0)	122.0 (57.0-188.5)	.080
Circulatory arrest	49 (12.3)	20 (10.6)	29 (13.9)	.362

Values are presented as n (% as a valid percentage, excluding missing values) or median (interquartile range). *CABG*, Coronary artery bypass graft; *ECC*, extracorporeal circulation. *Ventricular septal rupture and/or free wall rupture.

Table E5), with higher BMI values in older patients (Figure E3). Of note, crossclamp time was not included due to missing data (38.4%). In-hospital and 12-month postdischarge mortality rates remained stable between 2013 and 2019 (Figure 1). Figure E4 shows in-hospital and 12-month postdischarge mortality stratified by primary surgery.

Determinants of 12-Month Postdischarge Mortality

Among hospital survivors who completed the long-term follow-up (n = 179), 63 patients died within 12 months from discharge (crude mortality rate, 35.1%). Kaplan-Meier survival curves are reported in Figure 2. Patient and procedure-related characteristics (Tables E2-E4) were comparable between the 2 groups, except for a higher preoperative New York Heart Association functional class ($P = .003$) and more frequent congenital cardiac surgery procedures in nonsurvivors ($P = .014$). However, this observation is based on only 4 in-hospital survivors who underwent congenital cardiac surgery. Postoperative complications included more respiratory (26.2% vs 7.8%; $P = .001$) and renal (44.3% vs 20.9%; $P = .002$) failure in 12-month postdischarge nonsurvivors. Furthermore, postoperative respiratory and renal failure and re-thoracotomy for cardiac reason/other were associated with higher 12-month postdischarge mortality (Table 5, *model 4,* Table E6).

DISCUSSION

The present study has 4 main findings. First, in patients undergoing postcardiotomy ECMO, in-hospital mortality remains high (51.7%), with death occurring at 5 days after surgery. Second, older age and higher BMI are associated with in-hospital mortality. Third, among patients who survived to hospital discharge, 35.1% died within 12 months. Fourth, postoperative complications such as respiratory and

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TABLE 3. Postoperative outcomes of the overall population

Outcome	Overall population (N = 406)	In-hospital survivors (n = 196)	In-hospital deaths (n = 210)	*P* value
Perioperative myocardial infarction	48 (14.1)	22 (13.3)	26 (14.9)	.756
Lung infection during admission	39 (9.9)	27 (14.5)	12 (5.8)	.006
Respiratory failure during admission	41 (10.5)	26 (14.0)	15 (7.4)	.046
Ventilation >24 h during admission	172 (46.4)	103 (56.0)	79 (38.0)	<.001
Readmission to ICU/PACU	35 (9.1)	19 (10.4)	16 (7.9)	.478
CVA during admission				
CVA with residual damage	14 (3.6)	3 (1.6)	11 (5.4)	.057
CVA without residual damage	2 (0.5)	2 (1.1)	0 (0)	.226
Renal failure during admission	120 (30.4)	55 (29.6)	65 (31.1)	.827
Gastrointestinal complications during admission	30 (7.7)	14 (7.5)	16 (7.8)	1.000
Vascular complications during admission	24 (7.1)	9 (5.5)	15 (8.7)	.293
Arrhythmia during admission	88 (22.3)	53 (28.5)	35 (16.8)	.007
Re-thoracotomy within 30 d				.186
Bleeding/tamponade	101 (31.1)	49 (31.4)	52 (30.8)	
Cardiac reason	69 (21.2)	28 (17.9)	41 (24.3)	
Other	16 (4.9)	10 (6.4)	6 (3.6)	
Deep sternal wound infection within 30 d	6 (2.1)	6 (4.1)	0 (0)	.030
Length of stay (d)	14 (4-33)	29 (17-51)	5 (2-14)	<.001
Location of in-hospital death				
Operation room			9 (5.3)	
Intensive care unit			147 (87.0)	
Ward			10 (5.9)	

Values are presented as n (% as a valid percentage, excluding missing values). *ICU*, Intensive care unit; *PACU*, postanesthesia care unit; *CVA*, cerebrovascular accident.

renal failure and re-thoracotomy are associated with 12-month postdischarge death. Overall, this shows that postcardiotomy ECMO is still associated with high mortality in the Netherlands. However, the identification of specific variables at different time points during a patient's journey may be taken into consideration as potential targets that may improve outcomes. For example, optimization and careful patient selection in case of older age and higher BMI could be applied before surgery and at ECMO implantation to reduce in-hospital mortality. Close multidisciplinary collaboration to prevent postoperative complications and adequate follow-up programs with careful monitoring of patients at risk may help to lower postdischarge mortality.

So far, a nationwide investigation on this topic was not yet performed in a European country. The NHR data confirmed stable in-hospital mortality rates over time.[5] Moreover, NHR follow-up data showed that 12-month postdischarge mortality did not improve over time, urging more focus on interdisciplinary collaboration and tailored follow-up programs. In detail, 51.7% of all patients died in the hospital, and 35.1% of hospital survivors died within 12 months after discharge. In contrast, previous studies showed in-hospital mortality of 64.4%, but 91.1% of survivors were alive at 1-year follow-up.[14,18] Although the overall 1-year survival approaches 30% in both the current and previous reports, this study highlights for the first time how the discharge timing and postdischarge care might differ based on differences in health care systems.[10] Indeed, clinical practices for postdischarge care are highly variable according to resource allocations. Certain health care systems prioritize primary in-hospital rehabilitation followed by an early discharge and further home care,[19] whereas others prefer a longer hospital stay and full in-hospital rehabilitation.[20] In both cases, a good follow-up program, starting postoperatively, should be continued after intensive care unit discharge.[21] This is even more important based on the ECMO gap observation (ie, patients with in-hospital unfavorable outcomes despite successful ECMO).[22] Interventions toward this direction should start with identifying high-risk patients before surgery and during intensive care unit stay to plan adequate programs to reduce ECMO mortality. Several studies have investigated determinants for in-hospital mortality after postcardiotomy ECMO,[17] identifying age and increased arterial lactate before ECMO as risk factors for in-hospital death.[3,14,23,24] Herein, we identified older age and higher BMI associated with in-hospital mortality, and we observed a relationship between

TABLE 4. Results of multivariable logistic regression analyses to predict in-hospital mortality*

Variable	Coefficient	SE	Odds ratio (lower 95% CI-upper 95% CI)	*P* value
Model 1: Demographic characteristics				
Age (y)	0.020	0.009	**1.021 (1.003-1.038)**	**.019**
Female sex	0.028	0.222	1.029 (0.666-1.589)	.899
BMI	0.080	0.026	**1.084 (1.029-1.142)**	**.003**
Model 2: Demographic + baseline characteristics				
Age (y)	0.021	0.009	**1.021 (1.003-1.039)**	**.022**
Female sex	0.068	0.239	1.070 (0.670-1.708)	.776
BMI	0.079	0.028	**1.082 (1.024-1.144)**	**.006**
Diabetes mellitus*	0.303	0.292	1.353 (0.764-2.399)	.300
Left ventricular ejection fraction (%)	0.007	0.008	1.007 (0.991-1.024)	.388
Creatinine (μmol/L)	0.000	0.002	1.000 (0.996-1.004)	.981
Chronic lung disease	0.511	0.341	1.667 (0.854-3.255)	.134
Extracardiac arterial vascular pathology	–0.126	0.345	0.882 (0.448-1.735)	.716
Neurological dysfunction	0.160	0.551	1.174 (0.378-3.649)	.774
Previous cardiac surgery	–0.388	0.270	0.678 (0.400-1.152)	.151
Active endocarditis	0.298	0.397	1.347 (0.619-2.930)	.453
Critical perioperative condition	0.290	0.299	1.336 (0.744-2.401)	.332
Nonelective procedure*	–0.195	0.293	0.823 (0.464-1.460)	.505
Recent myocardial infarction	0.256	0.314	1.292 (0.699-2.388)	.415
Weight of intervention: 1 procedure (other than CABG)	0.179	0.397	1.195 (0.549-2.602)	.653
Weight of intervention: ≥2 procedure	0.029	0.353	1.029 (0.515-2.058)	.935
Model 3: Demographic + baseline + procedure-related characteristics				
Age (y)	0.020	0.009	**1.020 (1.002-1.039)**	**.031**
Female sex	0.061	0.240	1.063 (0.664-1.701)	.800
BMI	0.077	0.028	**1.080 (1.022-1.142)**	**.007**
Diabetes mellitus*	0.396	0.302	1.487 (0.821-2.692)	.190
Left ventricular ejection fraction (%)	0.003	0.009	1.003 (0.986-1.020)	.760
Creatinine (μmol/L)	0.000	0.002	1.000 (0.996-1.004)	.967
Chronic lung disease	0.537	0.343	1.711 (0.874-3.350)	.117
Extracardiac arterial vascular pathology	–0.138	0.348	0.871 (0.440-1.723)	.692
Neurological dysfunction	0.188	0.537	1.206 (0.404-3.605)	.729
Previous cardiac surgery	–0.472	0.281	0.624 (0.360-1.081)	.093
Active endocarditis	0.108	0.419	1.114 (0.490-2.533)	.797
Critical perioperative condition	0.356	0.305	1.428 (0.785-2.595)	.243
Nonelective procedure*	–0.206	0.300	0.814 (0.452-1.466)	.493
Recent myocardial infarction	0.258	0.323	1.294 (0.686-2.439)	.426
Weight of intervention: 1 procedure other than CABG	0.296	0.460	1.345 (0.546-3.312)	.519
Weight of intervention: ≥2 procedures other than CABG	–0.058	0.416	0.944 (0.417-2.134)	.890
Coronary artery bypass surgery	0.193	0.266	1.213 (0.721-2.043)	.467
Valve surgery	0.211	0.282	1.235 (0.710-2.148)	.456
Aortic surgery	0.493	0.284	1.638 (0.939-2.856)	.082
Other cardiac surgery procedures	–0.114	0.264	0.892 (0.532-1.496)	.664

Bold indicates significant variables associated with in-hospital mortality. *SE*, Standard error; *CI*, confidence limit; *BMI*, body mass index; *CABG*, coronary artery bypass. *Differences in variable characterization compared with the Netherlands Heart Registration Handbook: Diabetes mellitus (presence/absence); nonelective procedure (elective/nonelective where nonelective includes urgent, emergency, and salvage procedures).

these 2 variables with increased BMI in older patients. Previous literature has reported conflicting results regarding obese patients in cardiac surgery[25] and described the so-called obesity paradox where overweight and obese patients have lower postoperative mortality.[26] However, these findings were mainly observed in populations that excluded patients with a critical preoperative state, such as typical ECMO patients.[26] Moreover, obesity was considered a relative contraindication to ECMO until a recent growing body of literature started supporting the use of ECMO in patients with obesity.[27]

Whereas BMI was rarely included in prognostic models for postcardiotomy ECMO, it might become more relevant in countries such as the Netherlands, where the prevalence

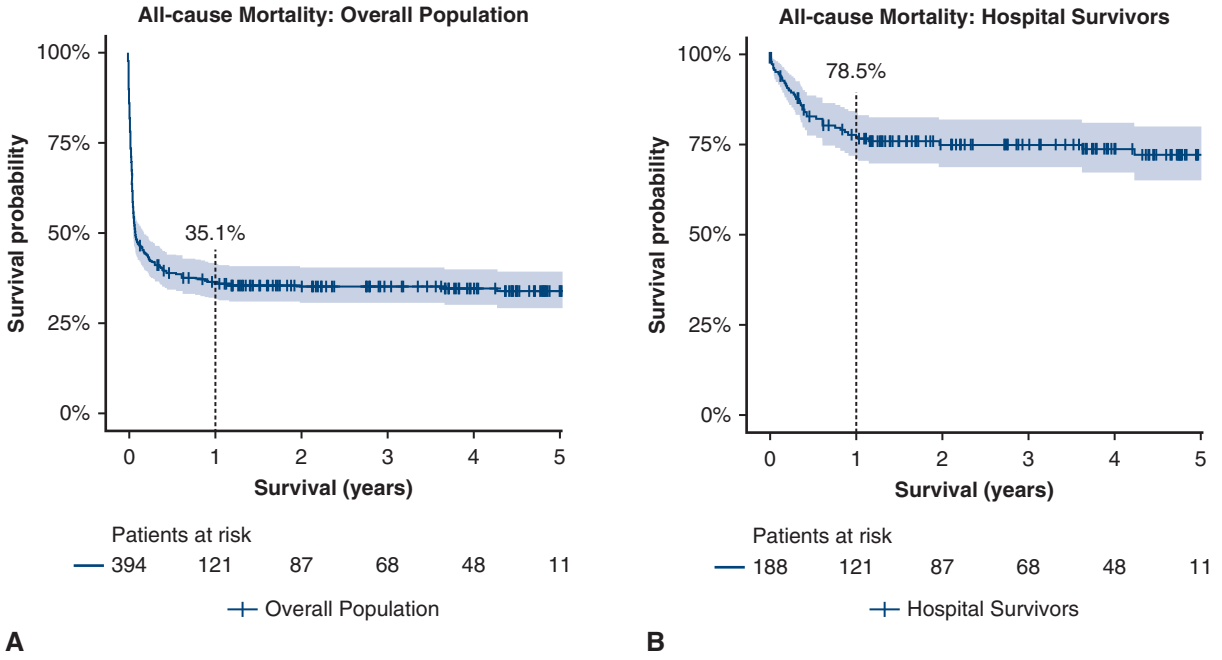

FIGURE 2. Kaplan-Meier survival curves with 95% confidence limit. A, The overall survival probability of the study cohort up to 6 years of follow-up after the indexed cardiac surgical procedure. The overall 1-year, 2-year, and 5-year survival was 35.1% (95% CI, 30.6-40.4), and 33.8% (95% CI, 29.1-39.2). B, The overall survival probability in the subgroup of hospital survivors. The overall 1-year, 2-year, and 5-year survival was 78.5% (95% CI, 72.6-85.0), 75.7% (95% CI, 69.4-82.6), and 72.8% (95% CI, 65.6-80.7).

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of obesity is high and rising.[28] Thus, more clinicians will routinely encounter older patients who are overweight and obese to consider for support with postcardiotomy ECMO. Preoperative programs aiming at weight control and health education should be advised when patients are accepted for an elective cardiac surgery operation. Moreover, an accurate patient selection process at the time of ECMO implantation should be carefully evaluated in patients with older age and higher BMI. For this purpose, further studies are warranted to stratify patients' risk based on age and weight groups and to investigate patients with obesity who are receiving postcardiotomy ECMO.

As for preoperative optimization and patient selection, determinants for postdischarge mortality should be considered for adequate postoperative management and follow-up programs. In line with previous evidence,[29,30] hospital death occurs at a median time of 5 days after surgery, but patients who survive are burdened by complications such as lung infections, respiratory failure, arrhythmia, and deep sternal wound infections. This results in a median length of stay of 29 days for survivors. Considering the growing rates of such complex patients in cardiac surgery, optimizing their management with adequate resource allocation becomes pivotal in the multidisciplinary management of each cardiac surgery service. However, preventing and treating complications is important for resource management and patients' long-term outcomes. Indeed, as demonstrated for the first time in this study, postoperative respiratory failure, renal failure, and re-thoracotomy negatively influence postdischarge 12-month mortality. Chen and colleagues[31] previously demonstrated that patients undergoing postcardiotomy ECMO are at increased risk for all-cause mortality and hospital readmission during the first year of follow-up compared with patients who did not receive ECMO. However, mortality, readmissions, and medical expenditures were similar from the second year of follow-up onward. Based on the results found by Chen and colleagues[31] and supported by our results, we can speculate that the prevention of postoperative complications might help fill this 12-month mortality gap. For this purpose, a good follow-up program should be advised during the first 12 months after postcardiotomy ECMO, especially in patients experiencing respiratory failure, renal failure, and re-thoracotomy. Although such follow-up programs for patients undergoing postcardiotomy ECMO are still rare, a lesson can be learned from the veno-venous ECMO field.[21]

Strengths and Limitations

The structured and systematic data collection performed by the NHR, the regular audits on data quality, and the large participation of Dutch cardiac surgery centers guarantee data robustness and granularity to provide a 6-year nationwide analysis of patients undergoing postcardiotomy ECMO in

TABLE 5. Results of multivariable logistic regression analyses to predict 12-month post-discharge mortality*

	Coefficient	SE	Odds ratio (lower 95% CI-upper 95% CI)	*P* value
Model 1: Demographic characteristics				
Age (y)	–0.009	0.012	0.991 (0.968-1.015)	.455
Female sex	0.024	0.339	1.024 (0.528-1.988)	.944
BMI	–0.040	0.045	0.961 (0.879-1.050)	.374
Model 2: Demographic + baseline characteristics				
Age (y)	–0.013	0.012	0.987 (0.963-1.011)	.295
Female sex	0.103	0.374	1.108 (0.533-2.305)	.783
BMI	–0.048	0.046	0.953 (0.871-1.044)	.301
Diabetes mellitus	0.792	0.451	2.207 (0.910-5.351)	.080
Left ventricular ejection fraction (%)	0.003	0.012	1.003 (0.981-1.026)	.763
Creatinine (μmol/L)	0.002	0.004	1.002 (0.995-1.009)	.613
Chronic lung disease	0.298	0.565	1.348 (0.445-4.080)	.598
Model 3: demographic + baseline + procedure-related characteristics				
Age (y)	–0.008	0.012	0.992 (0.969-1.017)	.539
Female sex	–0.042	0.347	0.959 (0.486-1.893)	.904
BMI	–0.047	0.046	0.954 (0.871-1.045)	.309
Left ventricular ejection fraction (%)	0.004	0.012	1.004 (0.981-1.027)	.757
Weight of intervention: 1 procedure other than CABG	–0.550	0.591	0.577 (0.181-1.838)	.352
Weight of intervention: $\geq$ 2 procedures other than CABG	0.367	0.506	1.443 (0.535-3.891)	.468
Model 4: Demographic characteristics + postoperative complications				
Age (y)	–0.009	0.014	0.991 (0.965-1.017)	.496
Female sex	0.093	0.382	1.098 (0.519-2.322)	.807
BMI	–0.074	0.051	0.928 (0.840-1.026)	.144
Respiratory failure	1.278	0.516	**3.589 (1.304-9.877)**	**.013**
Renal failure	0.820	0.387	**2.271 (1.062-4.853)**	**.034**
Re-thoracotomy: bleeding/tamponade	–0.075	0.463	0.928 (0.375-2.299)	.872
Re-thoracotomy: cardiac reason/other	1.063	0.415	**2.895 (1.284-6.530)**	**.010**

Bold indicates significant variables associated with in-hospital mortality. *SE*, Standard error; *CI*, confidence limit; *BMI*, body mass index; *CABG*, coronary artery bypass. *Differences in variable characterization compared with the Netherlands Heart Registration Handbook: Diabetes mellitus (presence/absence).

the Netherlands. Nevertheless, our study is observational by nature, limiting causal inferences. Underreporting of ECMO implants is also plausible. Furthermore, specific data on ECMO details such as selection criteria, ECMO protocols, arterial lactate values before and during ECMO support, time on ECMO, cannulation strategies, left ventricular unloading techniques, and centers' ECMO experience are not captured by the database and could not be included in this analysis. Based on the body of literature, it is known that several of the above-mentioned variables might influence outcomes and organ dysfunction, directly affecting both in-hospital and long-term outcomes. Data were retrieved anonymously, and no patient was linked to the original center. Therefore, controlling for the dependency of data within centers was not possible. Furthermore, an in-depth analysis of intraoperative variables, quality of life, and rehospitalization events at 12 months was not possible due to a percentage of missing data (Table E7).

CONCLUSIONS

In-hospital mortality of patients supported with postcardiotomy ECMO in the Netherlands remains high, especially in older patients with higher BMI. Moreover, 35.1% of hospital survivors die within 12 months from discharge, which was associated with postoperative respiratory or renal failure and re-thoracotomy (Figure 3). This supports the concept that action should be taken to move from a static, 1-size-fits-all clinical approach to a more dynamic strategy addressing potential determinants for mortality at different time points during a patient's journey: preoperative optimization of modifiable variables, careful patient selection at ECMO implantation, multidisciplinary collaboration to prevent postoperative complications, and adequate postdischarge follow-up programs (Figure 3). Furthermore, this new clinical approach should always be titrated to the local population, considering the characteristics of the local health care system. Further dedicated studies are warranted

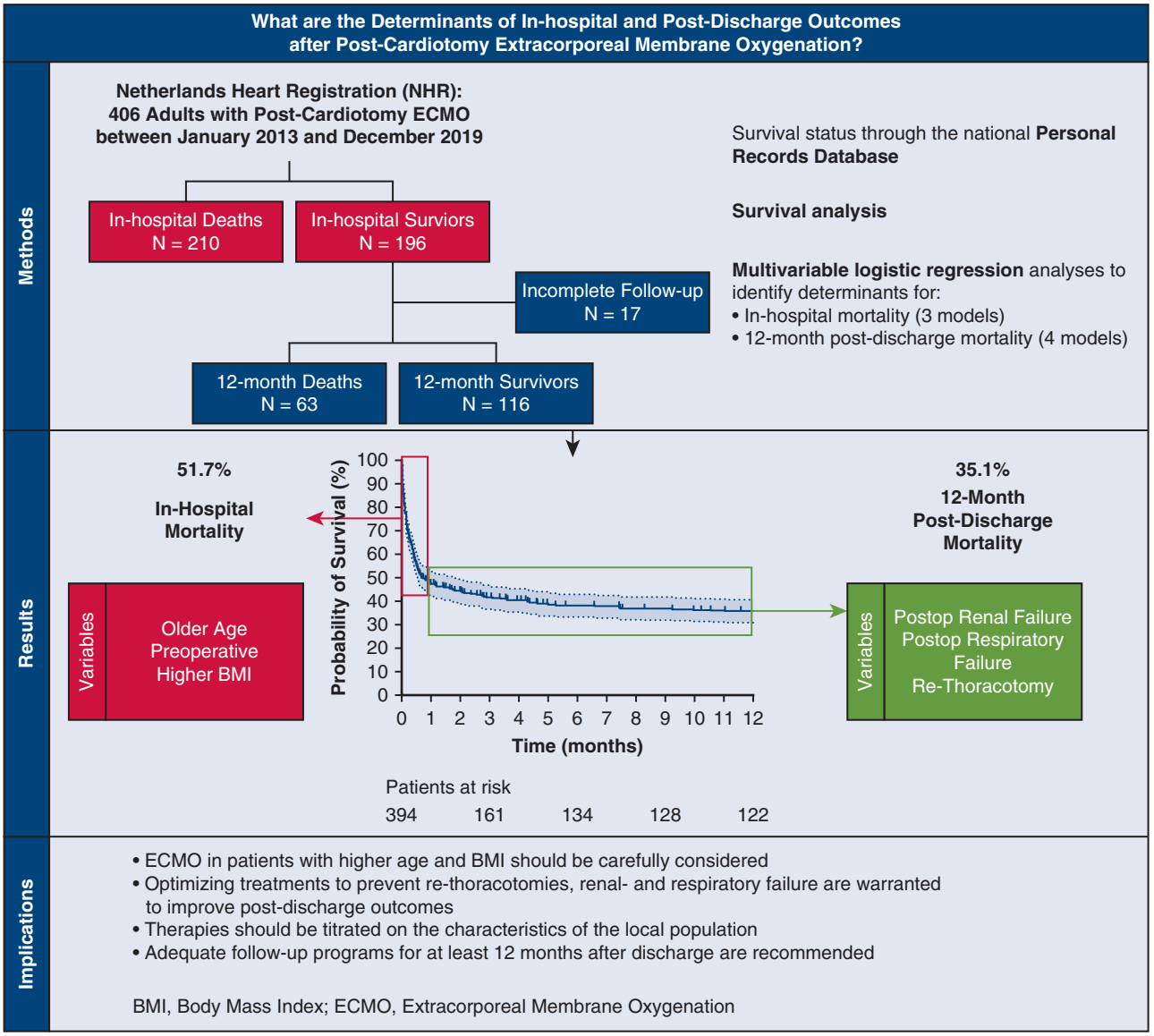

FIGURE 3. The analysis of 406 patients undergoing postcardiotomy extracorporeal membrane oxygenation (*ECMO*) from the national Netherlands Heart Registration (NHR) database showed a 51.7% in-hospital mortality and a 35.1% 12-month postdischarge mortality among hospital survivors. Older age and preoperative higher body mass index (*BMI*) were identified as determinants for in-hospital death and should be addressed through preoperative optimization and patient selection. Postoperative re-thoracotomy, and renal and respiratory failure were associated with 12-month postdischarge mortality and should be addressed through complications prevention and post-discharge follow-up programs.

to verify the feasibility and efficacy of these interventions in patients receiving postcardiotomy ECMO.

Conflict of Interest Statement

Dr Lorusso is a consultant for Medtronic, Getinge, and LivaNova as well as an advisory board member of Eurosets (honoraria paid as research funding). 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.

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Key Words: mechanical circulatory support, extracorporeal membrane oxygenation, extracorporeal life support, postcardiotomy cardiogenic shock, cardiac surgery, acute heart failure

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APPENDIX E1. SUPPLEMENTAL METHODS

The Netherlands Heart Registration

The Netherlands Heart Registration (NHR) (in Dutch: Nederlandse Hart Registratie; https://nederlandsehartregistratie.nl/) is a nonprofit organization that aims to support quality improvement and safety in cardiac care by facilitating quality registries. The NHR processes personal data of patients undergoing cardiac interventions in the Netherlands. The NHR is supported by the Healthcare Quality, Complaints and Disputes Act (Dutch: Wkkgz), which obliges health care providers to evaluate and improve their own quality. Participating hospitals are responsible for data collection and registration in a secure online environment, and remain the owner of the data they submit. The NHR analyses patient data, provides online dashboards, and reports relevant outcome indicators in yearly, publicly accessible reports. The main goal of the NHR include:

- Reliable data reports at various levels: hospital, disease state, and patient;
- Scientific research; and
- Transparency for patients, cardiologists and thoracic surgeons, external regulators, health insurers, and other stakeholders.

In the Netherlands, structural registration and monitoring of health care outcomes is performed on a compulsory basis. All cardiac surgery centers in the Netherlands (N = 16) are part of this registry and deliver data regarding all their cardiac surgery procedures.

The NHR database consists of a set of mandatory variables and a set of voluntary variables described in detail in the NHR handbook (https://nederlandsehartregistratie.nl/wp-content/uploads/2022/01/NHR_HANDBOEK-22.2.1_Cardiochirurgie_DEFINITIEF.pdf). Further details on the NHR database can be found in the following publication: Timmermans MJC, Houterman S, Daeter ED, et al. Using real-world data to monitor and improve quality of care in coronary artery disease: results from the Netherlands Heart Registration. *Neth Heart J*. April 7, 2022 [Epub ahead of print]. https://doi.org/10.1007/s12471-022-01672-0.

Patient Selection and Extraction from the NHR Cohort

The selection process was predefined before the beginning of the study in the study protocol that was approved by the NHR Scientific Steering Committee. Participant were selected from the NHR database if ALL of the following inclusion criteria apply:

- Age ≥18 years
- Cardiac surgery and extracorporeal membrane oxygenation (ECMO) implantation during the same hospitalization
- ECMO implantation defined in the NHR as
  - Variable No.: CHIR-INT-530
  - Variable name: cardiac_assist_device
  - Coding: 40
- Cardiac surgery and ECMO implantation performed between January 2013 and December 2019

Participants were excluded if ANY of the following exclusion criteria apply:

- Age <18 years
- Coding of the variable CHIR-INT-530 other than 40 in the NHR
- Missing value of the variable CHIR-INT-530 in the NHR
- Cardiac surgery performed before January 2013 or after December 2019

We selected the included population using the variable "CHIR-INT-530" (name: "Cardiac Assist Device") of the NHR database, which is defined as follows: "Placement of a cardiac assist device because of cardiac failure or complications after cardiac surgery." Within this group, the NHR database includes all cardiac assist devices such as:

- Ventricular assist device (VAD) (code: 10): Ventricular Assist Device: LVAD, RVAD, or BiVAD.
- Artificial Heart (code: 20): Total artificial heart, such as SynCardia and AbioCor.
- Catheter Based Assist Device (code: 30): For example, Impella, Tandem Heart
- ECMO (code: 40): Extra corporeal membrane oxygenation, also known as extra corporeal life support or permanent life support. This concerns only ECMO with a cardiac indication.
- Other (code: 90): other cardiac assist device that cannot be categorized in any of the previous groups. Example: Cardiac support device (eg, CorCap).

A further specification of this variable states that the following procedures should not be delivered within this variable:

- ECMO without cardiac indications,
- Removal or replacement of cardiac assist device without use of ECC (such as ECMO and intra-aortic balloon pump), and
- Placement of intra-aortic balloon pump as an isolated procedure.

Using such a variable, we selected only patients who received a cardiac assist device with code 40 (40 = ECMO). The database does not provide the specific configuration of the used ECMO, but it only allows for registration of cardiac supports, excluding respiratory supports. Therefore, we assume that all included patients received ECMO for cardiac support.

Data Collection

The following groups of data were extracted from the NHR database:

- Demographic data: Age, sex
- Patient characteristics: European System for Cardiac Operative Risk Evaluation score, length, weight, serum creatinine level, left ventricular ejection fraction, systolic artery pulmonary pressure, diabetes mellitus, chronic lung disease, extracardiac arterial vascular pathology, neurological dysfunction, previous cardiac surgery, active endocarditis, critical preoperative condition, unstable angina pectoris, recent myocardial infarction, thoracic aortic surgery, postinfarction ventricular septal rupture, dialysis, poor mobility, New York Heart Association functional class, Canadian Cardiovascular Society class IV angina, urgency of the procedure, weight of intervention, and European System for Cardiac Operative Risk Evaluation II score.
- General surgical variables: Planned intervention, intervention canceled, use of extracorporeal circulation (ECC), ECC cannulation, circulatory arrest.
- Coronary surgery: Arterial graft, number of distal arterial anastomoses, left internal thoracic artery, right internal thoracic artery, radial artery, gastroepiploic artery, other arterial graft, venous graft, number of distal venous anastomoses, and other coronary surgery.
- Valve surgery: Valve surgery, aortic valve surgery, aortic valve procedure, aortic valve implant, mitral valve surgery, mitral valve procedure, pulmonary valve surgery, pulmonary valve procedure, pulmonary valve implant, tricuspid valve surgery, tricuspid valve procedure, and tricuspid valve implant.
- Aortic surgery: Approach to aortic surgery, aortic ascending surgery, aortic arch surgery, and aortic descending procedure.
- Other cardiac surgeries: Cardiac assist device, heart transplantation, rhythm surgery, additional pacemaker/implantable cardioverter-defibrillator procedure, correction of a cardiac aneurysm, cardiac rupture closure, correction of cardiac trauma, tumor removal, myectomy, ventricular septal defect closure, atrial septal defect closure, congenital cardiac surgery, other ventricular surgery, pericardiectomy, pulmonary embolectomy, resuscitation with ECC, other cardiac surgery, and other cardiac surgery description.
- Additional noncardiac procedures: Noncardiac surgery, lung surgery, and other noncardiac surgery.
- ECC: ECC duration, crossclamp duration, circulation arrest duration, retrograde autologous priming, and hemofiltration.
- In-hospital outcomes: Deceased in hospital, deceased location, new heart surgery during admission, discharge date, perioperative myocardial infarction, arm or leg wound during admission, lung infection during admission, urinary tract infection during admission, respiratory failure during admission, ventilation >24 hours during admission, readmission to intensive care unit/postanesthesia care unit, cerebrovascular accident with residual damage during admission, cerebrovascular accident without residual damage during admission, renal failure during admission, gastrointestinal complication during admission, vascular complication during admission, and rhythm problem during recording.
- Outcomes at follow-up: Re-thoracotomy within 30 days, re-thoracotomy date, re-fixation sternum within 30 days, date of re-fixation of the sternum, deep sternal wound infection within 30 days, deep sternal wound infection to date, mortality status, and date of mortality status.

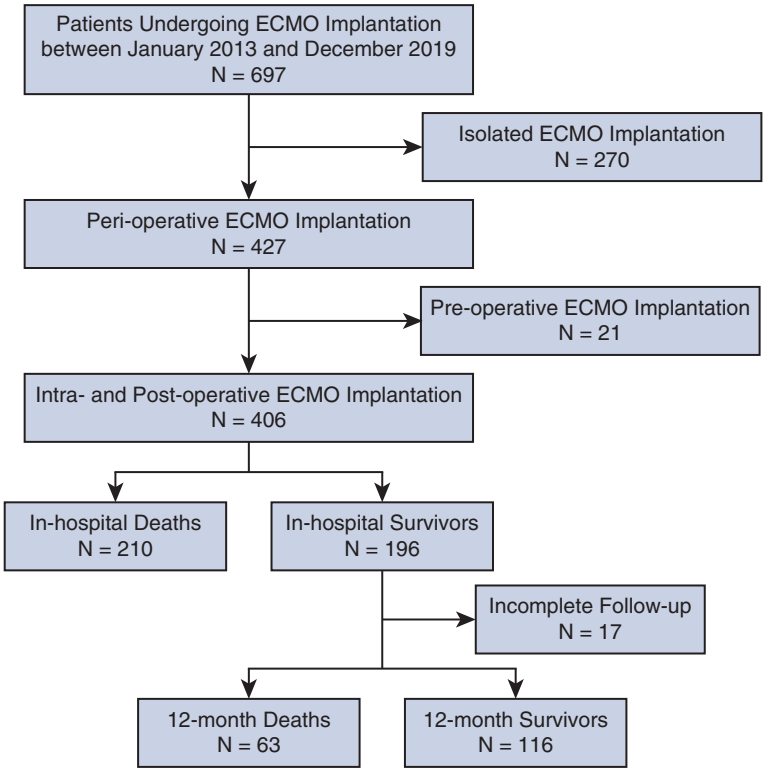


FIGURE E1. Flowsheet of the included patients. *ECMO*, Extracorporeal membrane oxygenation.

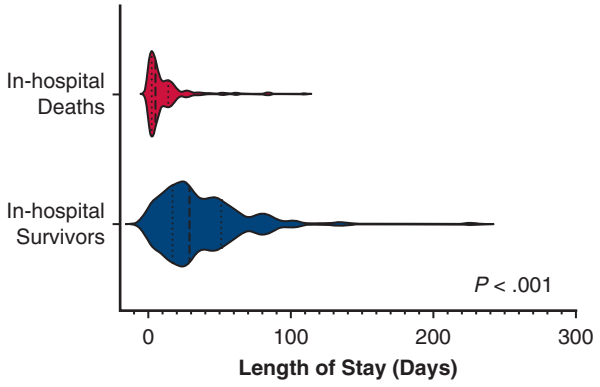
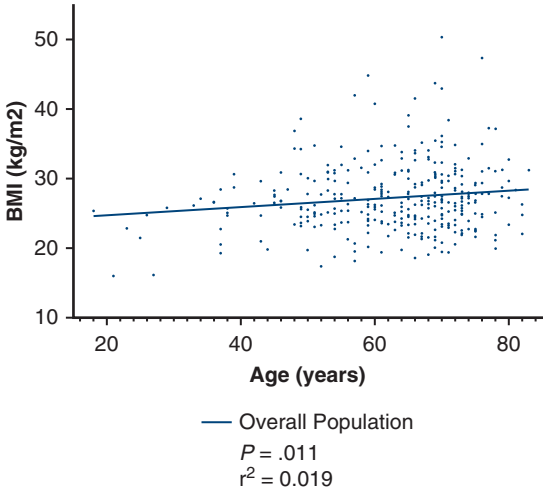
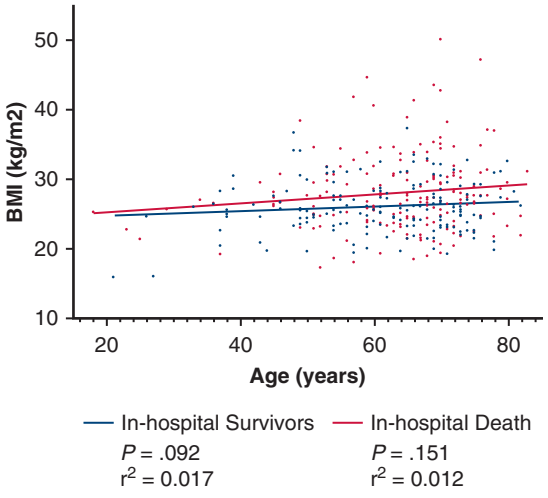


FIGURE E2. Length of stay for in-hospital survivors and nonsurvivors.

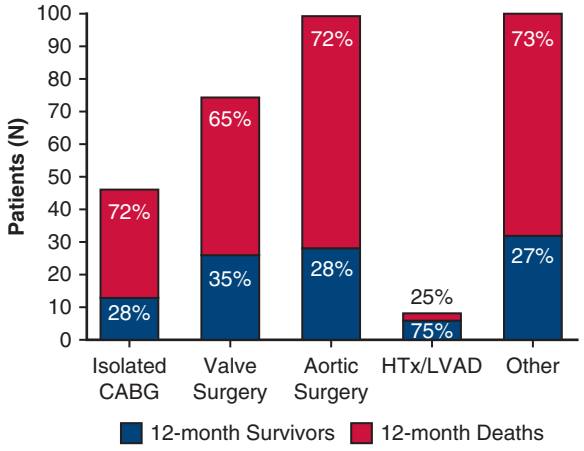


A

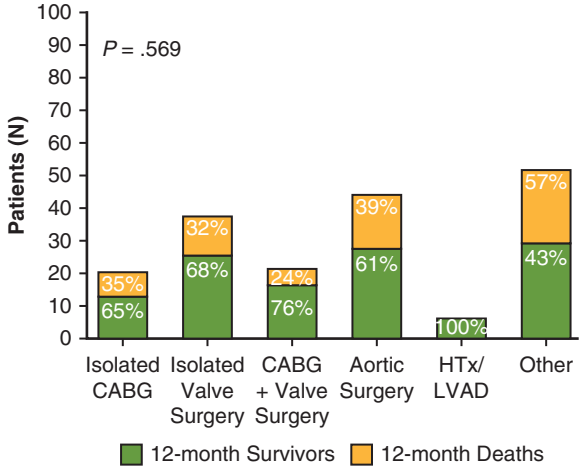


B

FIGURE E3. Scatter plot of body mass index (*BMI*) distribution according to age in the (A) overall population and (B) based on hospital survival.



A



B

FIGURE E4. Analysis of (A) in-hospital mortality and (B) postdischarge 12-month mortality stratified by the type of primary surgery. *CABG*, Coronary artery bypass grafting; *HTx*, heart transplantation; *VAD*, ventriclular assist device.

MCS

TABLE E1. Variables and outcomes definitions

Variable	Definition
In-hospital mortality	Death, regardless of cause and time, during hospitalization at the cardiac surgery center. Any death between the date of surgery and discharge after this surgery. Thus, a discharged patient who is subsequently readmitted and subsequently dies is not registered as "died in hospital." The latter also applies to a patient transferred to another hospital and dies there.
Location of in-hospital death	Operating room: Patient died in the period after arriving at the operating room and did not leave the operating room alive. Intensive care unit: Patient died in the period after arriving at the intensive care unit and did not leave the intensive care unit alive. Ward: Patient died in the period after arriving at a ward within the hospital and did not leave the ward of the hospital alive. However, the patient may have undergone surgery or been readmitted to the intensive care unit during hospitalization.
Perioperative myocardial infarction	The Society of Thoracic Surgeons definition is adopted. The definition of myocardial infarction is independent of the preoperative status of the patient.
Lung infection	Lung infection or pneumonia with positive sputum culture during the index admission.
Respiratory failure	Respiratory failure requires reintubation during the index admission.
Ventilation >24 h during admission	Mechanical ventilation support for more than 24 h after the index surgery.
Re-admission to intensive care unit/postanesthesia care unit	Re-admission to the intensive care unit or postanesthesia care unit after initial discharge from the intensive care unit/postanesthesia care unit. This does not include a stay in the medium care unit.
Cerebrovascular accident without residual damage	A neurologist determined that a cerebrovascular accident had occurred postoperatively during the index hospital admission but without residual injury at discharge. Thus, this includes a transient ischemic attack.
Cerebrovascular accident with residual damage	A neurologist has determined that a postoperative cerebrovascular accident occurred postoperatively during the index hospital admission (excluding transient ischemic attack). Cerebrovascular accident = neurologist-diagnosed permanent neurological dysfunction due to focal ischemia of the brain, spinal cord, or retina caused by acute infarction of the neurological tissue due to thrombosis, embolism, systemic hypoperfusion, or hemorrhage.
Renal failure	Renal failure is present if one or more of the following Society of Thoracic Surgeons criteria are met during the postoperative period and the index hospital admission: Renal function replacement treatment (dialysis, continuous venovenous hemofiltration) that was not present preoperatively; Highest postoperative creatinine value > 177 μmol/L and doubling of the preoperative value (as preoperative value: the value of the creatinine used to calculate the European System for Cardiac Operative Risk Evaluation score).
Gastrointestinal complications	Gastrointestinal complication occurring during the index hospital admission: Type of complication unknown: gastrointestinal complication where the type is unknown. Bleeding: Gastrointestinal bleeding requiring therapy such as transfusion, laparoscopy, or surgery. Other: Intestinal ischemia, acalculous cholecystitis.
Vascular complications	The occurrence of a vascular complication during the index hospital admission (diagnosis according to the Valve Academic Research Consortium (VARC)-2 definitions) from the start of the current intervention (including perioperative vascular complications and excluding cerebrovascular accident).
Arrhythmia	All forms of de novo rhythm problems require treatment during the index hospital admission (such as cardio-pulmonary resuscitation due to asystole, new-onset atrial fibrillation/flutter requiring specific intervention). This does not include a spontaneously transient period of atrial fibrillation without any consequence to the patient.
Re-thoracotomy within 30 d	Re-thoracotomy within 30 d due to a complication of the current intervention. This includes re-thoracotomies performed after the patient was discharged from the respective hospital. This refers to the first re-thoracotomy after the initial closure of the thorax. This applies to all

(Continued)

TABLE E1. Continued

Variable	Definition
	causes, except for opening the sternum in connection with mediastinitis re-fixation of the sternum.
Re-thoracotomy for bleeding/tamponade	Bleeding/tamponade: Re-thoracotomy due to bleeding, tamponade (this includes subxiphoid drainage of a tamponade by a thoracic surgeon). Pericardiocentesis is not included.
Re-thoracotomy for cardiac reason	Cardiac problems require surgery with or without the use of extracorporeal circulation. This includes revision of anastomosis, reperfusion, or similar. Also, performing a new surgery during the same admission (for example, a patient undergoing coronary artery bypass grafting who, after a few days, still receives a valve replacement or new coronary artery bypass grafting).
Re-thoracotomy for other reasons	All other causes of re-thoracotomy, except re-fixation of the sternum in connection with a mediastinitis.
Deep sternal wound infection within 30 d	First re-fixation of the sternum within 30 d after index surgery. This includes re-fixations performed after the patient was discharged from the hospital.
Mortality at follow-up	Mortality status of the patient, as determined after verification with Personal Records Database (Basisregistratie Personen) or date of the last contact.

TABLE E2. Baseline characteristics of hospital survivors. Patients groups are defined based on survival status 12 months after discharge

	Overall patients in the follow-up (N = 179)	12-mo deaths (n = 63)	12-mo survivors (n = 116)	*P* value
Age (y)	64.0 (53.0-71.0)	64.0 (49.0-71.0)	64.0 (54.0-71.0)	.566
Sex				.868
Female	58 (32.4)	21 (33.3)	37 (31.9)	
Male	121 (37.6)	42 (66.7)	79 (68.1)	
BMI	25.7 (23.6-1-28.4)	25.9 (22.8-27.9)	25.7 (24.2-28.4)	.257
Body surface area (m^2)	2.0 (1.8-2.1)	2.0 (1.8-2.1)	2.0 (1.8-2.1)	.195
Obesity defined as BMI >29.9	27 (16.5)	8 (14.0)	19 (17.8)	.660
Diabetes mellitus				.558
None	141 (84.9)	46 (79.3)	95 (88.0)	
Insulin-dependent	12 (7.2)	5 (8.6)	7 (6.5)	
Non–insulin-dependent	10 (6.0)	6 (10.3)	4 (3.7)	
Treatment unknown	3 (1.8)	1 (1.7)	2 (1.9)	
Chronic lung disease	15 (8.4)	6 (9.5)	9 (7.8)	.779
Extracardiac arterial vascular pathology	18 (10.1)	8 (12.7)	10 (8.6)	.439
Neurological dysfunction	5 (3.1)	1 (1.7)	4 (4.0)	.652
Previous cardiac surgery	53 (29.6)	22 (34.9)	31 (26.7)	.304
Active endocarditis	20 (11.2)	8 (12.7)	12 (10.3)	.628
Critical preoperative condition	58 (32.4)	20 (31.7)	38 (32.8)	1.00
Unstable angina pectoris	12 (6.7)	4 (6.3)	8 (6.9)	1.00
Recent myocardial infarction	42 (23.5)	12 (19.0)	30 (25.9)	.358
Postinfarct VSR	5 (2.8)	0 (0)	5 (4.3)	.163
Dialysis	0 (0)	0 (0)	0 (0)	NS
Poor mobility	11 (8.0)	1 (1.9)	10 (11.8)	.051
NYHA functional class				.003
I	19 (25.8)	7 (14.6)	12 (16.7)	
II	25 (20.8)	16 (33.3)	9 (12.5)	
III	38 (31.7)	18 (37.5)	20 (27.8)	
IV	38 (31.7)	7 (14.6)	31 (43.1)	
CCS class IV angina	21 (14.8)	5 (9.3)	16 (18.2)	.223
Urgency of the procedure				.410
Elective	72 (42.1)	28 (45.9)	44 (40)	
Urgent	36 (21.1)	15 (24.6)	21 (19.1)	
Emergency	40 (23.4)	10 (16.4)	30 (27.3)	
Salvage	23 (13.5)	8 (13.1)	15 (13.6)	
Weight of intervention				.060
Isolated CABG	22 (12.9)	7 (11.7)	15 (13.6)	
1 procedure other than CABG	45 (26.5)	10 (16.7)	35 (31.8)	
2 procedures other than CABG	70 (41.2)	26 (43.3)	44 (40.0)	
3 procedures other than CABG	33 (19.4)	17 (28.3)	16 (14.5)	
EuroSCORE II	9.2 (3.7-23.9)	10.5 (3.6-22.4)	8.5 (4.2-27.4)	.672
Left ventricular ejection fraction (%)	40.0 (25.0-55.0)	40.0 (25.0-55.0)	40.0 (25.0-55.0)	.575

Values are presented as n (% as a valid percentage, excluding missing values) or median (interquartile range). *BMI*, Body mass index; *VSR*, ventricular septal rupture; *NS*, not significance; *NYHA*, New York Heart Association; *CCS*, Canadian Cardiovascular Society; *CABG*, coronary artery bypass graft; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation score.

TABLE E3. Procedure-related characteristics of hospital survivors. Patients groups are defined based on survival status 12 months after discharge

Characteristic	Overall patients in the follow-up (N = 179)	12-mo deaths (n = 63)	12-mo survivors (n = 116)	*P* value
CABG	78 (43.6)	26 (41.3)	52 (44.8)	.752
No. of arterial grafts	0 (0-0)	1 (0-1)	1 (0-1)	.186
No. of venous anastomoses	0 (0-0)	2 (1-3)	2 (1-3)	.747
LITA	39 (21.8)	8 (30.8)	31 (59.6)	.030
OPCABG	4 (5.3)	3 (12.0)	1 (2.0)	.105
Valve surgery	112 (62.6)	39 (61.9)	73 (62.9)	1.00
Aortic valve surgery	71 (39.7)	23 (36.5)	48 (41.4)	.632
Mitral valve surgery	57 (31.8)	23 (36.5)	34 (29.3)	.401
Tricuspid valve surgery	17 (9.5)	9 (14.3)	8 (6.9)	.117
Pulmonary valve surgery	1 (0.6)	1 (1.6)	0 (0)	.352
Aortic surgery	44 (24.6)	17 (27.0)	27 (23.3)	.590
Ascending aorta surgery	43 (24.0)	17 (27.0)	26 (22.4)	.583
Aortic arch surgery	11 (6.1)	4 (6.3)	7 (6.0)	1.000
Descending aorta procedure	4 (2.3)	2 (3.2)	2 (1.8)	.396
Other cardiac procedures	135 (75.4)	48 (76.2)	87 (75.0)	1.00
Heart transplant	6 (3.4)	0 (0)	6 (5.2)	.092
Rhythm surgery	14 (7.8)	5 (7.9)	9 (7.8)	1.000
Correction of a cardiac aneurysm	5 (2.8)	3 (4.8)	2 (1.7)	.346
Cardiac rupture*	5 (2.8)	1 (1.6)	4 (3.4)	.133
Myectomy	2 (1.1)	0 (0)	2 (1.7)	.541
Congenital cardiac surgery	4 (2.2)	4 (6.3)	0 (0)	.014
Pericardiectomy	0 (0)	0 (0)	0 (0)	NA
Pulmonary embolectomy	3 (1.7)	2 (3.2)	1 (0.9)	.283
Extracorporeal circulation				.696
Off-pump	12 (3.7)	6 (9.7)	6 (5.2)	
Conventional ECC	159 (89.3)	54 (87.1)	105 (90.5)	
Miniaturized ECC	3 (1.7)	1 (1.6)	2 (1.7)	
ECC type unknown	4 (2.2)	1 (1.6)	3 (2.6)	
ECC time (min)	219.0 (138.0-324.0)	241 (131-382)	218 (147-305)	.465
Crossclamp time (min)	99.0 (57.0-146.0)	97 (48-173)	103 (58-140)	.819
Circulatory arrest	18 (10.1)	8 (12.9)	10 (8.6)	.436

Values are presented as n (% as a valid percentage, excluding missing values) or median (interquartile range). *CABG*, Coronary artery bypass grafting; *LITA*, left internal thoracic artery; *OPCABG*, off-pump coronary artery bypass grafting; *NA*, not applicable; *ECC*, Extracorporeal circulation. *Includes ventricular septal rupture and/or free wall rupture.

TABLE E4. Postoperative outcomes of hospital survivors. Patient groups are defined based on survival status 12 months after discharge

Outcome	Overall patients in the follow-up (N = 179)	12-mo deaths (n = 63)	12-mo survivors (n = 116)	*P* value
Perioperative myocardial infarction	22 (14.0)	8 (15.4)	14 (13.3)	.808
Lung infection during admission	26 (14.8)	12 (19.7)	14 (12.2)	.189
Respiratory failure during admission	25 (14.2)	16 (26.2)	9 (7.8)	.001
Re-admission to ICU/PACU	19 (11.0)	10 (16.7)	9 (8.0)	.123
CVA during admission				
CVA with residual damage	3 (1.7)	1 (1.6)	2 (1.7)	1.000
CVA without residual damage	1 (0.6)	0 (0)	1 (0.9)	1.000
Renal failure during admission	51 (29)	27 (44.3)	24 (20.9)	.002
Gastrointestinal complications during admission	14 (8.0)	6 (9.8)	8 (7.0)	.563
Vascular complications during admission	9 (5.8)	2 (3.6)	7 (7.1)	.490
Arrhythmia during admission	51 (29.0)	15 (24.6)	36 (31.3)	.387
Re-thoracotomy within 30 d				.108
Bleeding/tamponade	48 (31.4)	12 (26.1)	36 (33.6)	
Cardiac reason	27 (17.6)	13 (28.3)	14 (13.1)	
Other	10 (6.5)	4 (8.7)	6 (5.6)	
Length of stay (d)	29 (17-51)	39 (21-62)	26 (16-47)	.505
Postdischarge survival (d)	626 (94.3-1440)	77 (7-113)	1298 (651-1631)	<.001

Values are presented as n (% as a valid percentage, excluding missing values) or median (interquartile range). *ICU*, Intensive care unit; *PACU*, postanesthesia care unit; *CVA*, cerebrovascular accident.

TABLE E5. Univariate associations between patient characteristics and in-hospital mortality using logistic regression analysis

	Unadjusted odds ratio (lower 95% CI-upper 95% CI)	*P* value
Age (y)	1.024 (1.007-1.041)	.005
Sex		
Female	1.009 (0.667-1.528)	.965
Male	Ref	
BMI	1.090 (1.035-1.148)	.001
BSA (m^2)	3.078 (1.164-8.141)	.024
Obesity defined as BMI >29.9	1.744 (1.014-3.000)	.045
Diabetes mellitus*	1.455 (0.852-2.488)	.170
Chronic lung disease	1.755 (0.935-3.295)	.080
Extracardiac arterial vascular pathology	1.135 (0.606-2.128)	.692
Neurological dysfunction	1.296 (0.424-3.966)	.634
Previous cardiac surgery	0.803 (0.517-1.246)	.327
Active endocarditis	1.189 (0.638-2.218)	.586
Critical preoperative condition	1.230 (0.813-1.859)	.328
Unstable angina pectoris	1.293 (0.630-2.656)	.484
Recent myocardial infarction	0.968 (0.608-1.540)	.889
Dialysis	1.773 (0.393-8.002)	.412
Poor mobility	0.864 (0.329-2.270)	.746
NYHA functional class		
I-II	Ref	
III-IV	1.083 (0.645-1.817)	.756
CCS class IV angina	1.093 (0.517-2.309)	.805
Urgency of the procedure		
Elective	Ref	
Nonelective*	1.165 (0.780-1.741)	.454
Weight of intervention		
Isolated CABG	Ref	
1 procedure other than CABG	1.073 (0.543-1.646)	.840
≥2 procedures other than CAB	0.892 (0.483-1.646)	.714
EuroSCORE II	1.000 (0.989-1.010)	.947
Left ventricular ejection fraction (%)	1.008 (0.993-1.022)	.290
CABG	1.219 (0.823-1.805)	.324
Valve surgery	1.191 (0.799-1.777)	.391
Aortic valve surgery	1.267 (0.850-1.888)	.245
Mitral valve surgery	1.062 (0.698-1.616)	.779
Tricuspid valve surgery	0.464 (0.042-5.159)	.532
Pulmonary valve surgery	0.871 (0.435-1.743)	.696
Aortic surgery	1.280 (0.817-2.008)	.281
Other cardiac procedures	0.800 (0.510-1.256)	.332
Heart transplant	0.152 (0.018-1.270)	.082
Rhythm surgery	1.063 (0.516-2.191)	.869
Correction of a cardiac aneurysm	0.554 (0.131-2.348)	.422
Congenital cardiac surgery	0.462 (0.084-2.548)	.375
Pulmonary embolectomy	1.412 (0.392-5.080)	.598
Extracorporeal circulation		
Off-pump	Ref	
ECC	1.496 (0.615-3.637)	.374

(Continued)

TABLE E5. Continued

	Unadjusted odds ratio (lower 95% CI-upper 95% CI)	*P* value
MECC	2.333 (0.52-10.479)	.269
ECC time (min)	1.001 (0.999-1.002)	.269
Crossclamp time (min)	1.003 (1.000-1.005)	.049
Circulatory arrest	1.353 (0.737-2.484)	.329
Intraoperative ECMO implant	1.044 (0.695-1.567)	.863
Perioperative myocardial infarction	1.280 (698-2.347)	.422
Lung infection	0.345 (0.172-0.694)	.003
Respiratory failure	0.466 (0.240-0.903)	.024
CVA with residual damage	1.734 (0.376-7.991)	.453
CVA without residual damage	0.008 (0.000-/)	.999
Renal failure	0.991 (0.640-1.534)	.968
Gastrointestinal complications	0.872 (0.360-2.110)	.754
Vascular complications	1.445 (0.694-3.009)	.323
Arrhythmia	0.508 (0.313-0.823)	.006
Re-thoracotomy within 30 d		
Bleeding/tamponade	1.046 (0.626-1.747)	.863
Cardiac reason/other	1.014 (0.728-1.415)	.932

CI, Confidence limits; *BMI*, body mass index; *BSA*, body surface area; *NYHA*, New York Heart Association; *CCS*, Canadian Cardiovascular Society; *CABG*, coronary artery bypass; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation score; *ECC*, extracorporeal circulation; *MECC*, miniaturized extracorporeal circulation; *ECMO*, extracorporeal membrane oxygenation; *CVA*, cerebrovascular accident. *Differences in variable characterization; compared with the Netherlands Heart Registration Handbook: Diabetes mellitus (presence/absence); nonelective procedure (elective/nonelective where nonelective includes urgent, emergency, and salvage procedures).

TABLE E6. Univariate associations between patient characteristics and 12-month postdischarge mortality using logistic regression analysis*

Characteristic	Unadjusted odds ratio (lower 95% CI-upper 95% CI)	*P* value
Age (y)	1.015 (0.997-1.034)	.097
Sex		
Female	1.014 (0.635-1.619)	.954
Male	Ref	
BMI	1.063 (1.009-1.119)	.021
BSA (m^2)	1.569 (0.535-4.600)	.411
Obesity defined as BMI >29.9	1.654 (0.947-2.89)	.077
Diabetes mellitus	2.057 (1.067-3.967)	.031
Chronic lung disease	1.817 (0.843-3.915)	.127
Extracardiac arterial vascular pathology	1.462 (0.693-3.084)	.318
Neurological dysfunction	0.796 (0.309-2.048)	.631
Previous cardiac surgery	1.048 (0.641-1.714)	.852
Active endocarditis	1.153 (0.570-2.334)	.692
Critical preoperative condition	1.080 (0.679-1.716)	.746
Unstable angina pectoris	1.227 (0.530-2.844)	.633
Recent myocardial infarction	0.807 (0.486-1.341)	.408
Dialysis	1.940 (0.123-30.612)	.589
Poor mobility	0.546 (0.207-1.441)	.200
NYHA functional class		
I-II	Ref	
III-IV	0.849 (0.525-1.371)	.501
CCS class IV angina	0.826 (0.409-1.667)	.583
Urgency of the procedure		
Elective	Ref	
Nonelective	0.986 (0.629-1.546)	.952
Weight of intervention		
Isolated CABG	Ref	
1 procedure other than CABG	0.871 (0.416-1.821)	.713
≥2 procedures other than CABG	1.186 (0.603-2.332)	.621
EuroSCORE II	1.002 (0.990-1.014)	.755
Left ventricular ejection fraction (%)	1.005 (0.989-1.022)	.527
CABG	1.041 (0.672-1.615)	.856
Valve surgery	1.031 (0.656-1.621)	.895
Aortic valve surgery	0.996 (0.639-1.552)	.987
Mitral valve surgery	1.206 (0.750-1.938)	.440
Tricuspid valve surgery	1.475 (0.647-3.363)	.356
Aortic surgery	1.260 (0.758-2.094)	.373
Other cardiac procedures	0.906 (0.549-1.495)	.699
Heart transplant	0.070 (0.008-0.586)	.014
Rhythm surgery	1.081 (0.482-2.425)	.851
Correction of a cardiac aneurysm	1.326 (0.264-6.668)	.732
Pulmonary embolectomy	2.674 (0.318-22.468)	.365
Extracorporeal circulation		
Off-pump	Ref	
ECC	0.889 (0.336-2.353)	.813
MECC	1.6 (0.260-9.834)	.612

(Continued)

TABLE E6. Continued

Characteristic	Unadjusted odds ratio (lower 95% CI-upper 95% CI)	*P* value
ECC time (min)	1.001 (0.999-1.003)	.224
Crossclamp time (min)	1.002 (1.000-1.005)	.103
Circulatory arrest	1.627 (0.777-3.409)	.197
Intraoperative ECMO implant	0.877 (0.556-1.385)	.574
Perioperative myocardial infarction	1.175 (0.618-2.236)	.622
Lung infection	0.701 (0.347-1.414)	.321
Respiratory failure	1.624 (0.743-3.551)	.224
CVA with residual damage	2.880 (0.666-12.451)	.157
CVA without residual damage	0.680 (0.048-9.714)	.774
Renal failure	1.922 (1.148-3.216)	.013
Gastrointestinal complications	1.294 (0.565-2.966)	.542
Vascular complications	1.401 (0.590-3.326)	.442
Arrhythmia	0.507 (0.307-0.838)	.008
Re-thoracotomy within 30 d		
Bleeding/tamponade	1.038 (0.607-1.774)	.892
Cardiac reason/other	2.352 (1.378-4.014)	.02

CI, Confidence limits; *BMI*, body mass index; *BSA*, body surface area; *NYHA*, New York Heart Association; *CCS*, Canadian Cardiovascular Society; *CABG*, coronary artery bypass; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation score; *ECC*, extracorporeal circulation; *MECC*, miniaturized extracorporeal circulation; *ECMO*, extracorporeal membrane oxygenation; *CVA*, cerebrovascular accident. *Differences in variable characterization compared to the Netherlands Heart Registration Handbook: Diabetes mellitus (presence/absence); nonelective procedure (elective/nonelective).

TABLE E7. Details of missing data for each variable of interest

Variable	Overall population (N = 406)
Age	0 (0)
Sex	0 (0)
Body mass index	58 (14.3)
Body surface area	58 (14.3)
Diabetes mellitus	38 (9.4)
Chronic lung disease	0 (0)
Extracardiac arterial vascular pathology	0 (0)
Neurological dysfunction	51 (12.6)
Previous cardiac surgery	0 (0)
Active endocarditis	0 (0)
Critical preoperative condition	0 (0)
Unstable angina pectoris	0 (0)
Recent myocardial infarction	0 (0)
Postinfarct VSR	0 (0)
Dialysis	87 (21.4)
Poor mobility	115 (28.3)
NYHA functional class	152 (37.4)
CCS class IV angina	106 (26.1)
Urgency of the procedure	23 (5.7)
Weight of intervention	27 (6.7)
EuroSCORE II	110 (27.1)
Left ventricular ejection fraction	37 (9.1)
CABG (n,%)	0 (0)
No. of arterial grafts	0 (0)
No. of venous grafts	0 (0)
OPCABG	0 (0)
Valve surgery	0 (0)
Aortic surgery	0 (0)
Heart transplant	0 (0)
Rhythm surgery	0 (0)
Correction of a cardiac aneurysm	0 (0)
Cardiac rupture*	0 (0)
Myectomy	0 (0)
Congenital cardiac surgery	0 (0)
Pericardiectomy	0 (0)
Pulmonary embolectomy	0 (0)
Extracorporeal circulation	9 (2.2)
ECC time	160 (39.4)
Crossclamp time	156 (38.4)
Circulatory arrest	9 (2.2)
Perioperative myocardial infarction	66 (16.3)
Lung infection	14 (3.4)
Respiratory failure	16 (3.9)
Ventilation >24 h during admission	14 (3.4)
Re-admission to ICU/PACU	22 (5.4)
CVA with residual damage	15 (3.7)
CVA without residual damage	15 (3.7)
Renal failure	11 (2.7)
Gastrointestinal complications	15 (3.7)
Vascular complications	68 (16.7)
Arrhythmia	12 (3.0)
Re-thoracotomy within 30 d	81 (20)
Deep sternal wound infection within 30 d	114 (28.1)
In-hospital mortality	0 (0)
Length of stay	23 (5.7)
Mortality at follow-up	38 (9.4)

(Continued)

TABLE E7. Continued

Values are presented as n (%). *VSR*, Ventricular septal rupture; *NYHA*, New York Heart Association; *CCS*, Canadian Cardiovascular Society; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation score; *CABG*, coronary artery bypass graft; *OPCABG*, off-pump coronary artery bypass; *ECC*, extracorporeal circulation; *ICU*, intensive care unit; *PACU*, postanesthesia care unit; *CVA*, cerebrovascular accident. *VSR and/or free wall rupture.