The importance of timing in postcardiotomy venoarterial extracorporeal membrane oxygenation: A descriptive multicenter observational study

Silvia Mariani, MD,[a] I-wen Wang, MD, PhD,[b] Bas C. T. van Bussel, MD, PhD,[c] Samuel Heuts, MD, PhD,[a] Dominik Wiedemann, MD, PhD,[d] Diyar Saeed, MD, PhD,[e] Iwan C. C. van der Horst, MD, PhD,[c] Matteo Pozzi, MD, PhD,[f] Antonio Loforte, MD, PhD,[g] Udo Boeken, MD, PhD,[h] Robertas Samalavicius, MD, PhD,[i] Karl Bounader, MD,[j] Xiaotong Hou, MD, PhD,[k] Jeroen J. H. Bunge, MD,[l] Hergen Buscher, MD,[m] Leonardo Salazar, MD,[n] Bart Meyns, MD, PhD,[o] Daniel Herr, MD, PhD,[p] Sacha Matteucci, MD,[q] Sandro Sponga, MD, PhD,[r] Kollengode Ramanathan, MD,[s] Claudio Russo, MD,[t] Francesco Formica, MD,[u] Pranya Sakiyalak, MD,[v] Antonio Fiore, MD,[w] Daniele Camboni, MD, PhD,[x] Giuseppe Maria Raffa, MD, PhD,[y] Rodrigo Diaz, MD,[z] Jae-Seung Jung, MD, PhD,[aa] Jan Belohlavek, MD, PhD,[bb] Vin Pellegrino, MD. PhD,[cc] Giacomo Bianchi, MD, PhD,[dd] Matteo Pettinari, MD,[ee] Alessandro Barbone, MD, PhD,[ff] José P. Garcia, MD,[gg] Kiran Shekar, MD, PhD,[hh] Glenn Whitman, MD, PhD,[ii] and Roberto Lorusso, MD, PhD,[a] on behalf of the PELS-1 (PELS-1, Post-Cardiotomy Extracorporeal Life Support Study) Investigators*

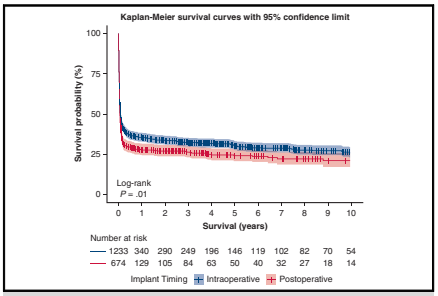
ABSTRACT

Objectives: Postcardiotomy extracorporeal membrane oxygenation (ECMO) can be initiated intraoperatively or postoperatively based on indications, settings, patient profile, and conditions. The topic of implantation timing only recently gained attention from the clinical community. We compare patient characteristics as well as in-hospital and long-term survival between intraoperative and postoperative ECMO.

Methods: The retrospective, multicenter, observational Postcardiotomy Extracorporeal Life Support (PELS-1) study includes adults who required ECMO due to postcardiotomy shock between 2000 and 2020. We compared patients who received ECMO in the operating theater (intraoperative) with those in the intensive care unit (postoperative) on in-hospital and postdischarge outcomes.

Results: We studied 2003 patients (women: 41.1%; median age: 65 years; interquartile range [IQR], 55.0-72.0). Intraoperative ECMO patients (n = 1287) compared with postoperative ECMO patients (n = 716) had worse preoperative risk profiles. Cardiogenic shock (45.3%), right ventricular failure (15.9%), and cardiac arrest (14.3%) were the main indications for postoperative ECMO initiation, with cannulation occurring after (median) 1 day (IQR, 1-3 days). Compared with intraoperative application, patients who received postoperative ECMO showed more complications, cardiac reoperations (intraoperative: 19.7%; postoperative: 24.8%, $P = .011$), percutaneous coronary interventions (intraoperative: 1.8%; postoperative: 3.6%, $P = .026$), and had greater in-hospital mortality (intraoperative: 57.5%; postoperative: 64.5%, $P = .002$). Among hospital survivors, ECMO duration was shorter after intraoperative ECMO (median, 104; IQR, 67.8-164.2 hours) compared with postoperative ECMO (median, 139.7; IQR, 95.8-192 hours, $P < .001$), whereas postdischarge long-term survival was similar between the 2 groups ($P = .86$).

Conclusions: Intraoperative and postoperative ECMO implantations are associated with different patient characteristics and outcomes, with greater complications and in-hospital mortality after postoperative ECMO. Strategies to identify the optimal location and timing of postcardiotomy ECMO in relation to specific patient characteristics are warranted to optimize in-hospital outcomes. (J Thorac Cardiovasc Surg 2023; ■:1-13)



Differences between intraoperative and postoperative postcardiotomy venoarterial ECMO.

CENTRAL MESSAGE

Patients' risk profiles and indications differ between intraoperative and postoperative postcardiotomy ECMO. Survival is more likely with intraoperative ECMO compared with rescue postoperative ECMO.

PERSPECTIVE

This study shows how postcardiotomy (PC) ECMO is differently used in operating theatre and intensive care unit. It supports the development of strategies to identify the optimal location and timing of PC ECMO, in relation to specific patient's characteristics. Finally, it introduces the implantation timing as an essential variable in future studies on PC ECMO patients.

See Commentary on page XXX.

MCS

Abbreviations and Acronyms

CPB = cardiopulmonary bypass
ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
IQR = interquartile range
IRB = institutional review board
MCS = mechanical circulatory support
PELS-1 = Postcardiotomy Extracorporeal Life Support Study
VA = venoarterial

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

MCS

In past decades, technical improvements have changed cardiac surgery radically, with less-invasive techniques and transcatheter approaches, whereas patient age and complexity have increased. In parallel, mechanical circulatory support (MCS) is used more often to manage patients who undergo cardiac surgery, particularly those suffering from postcardiotomy refractory cardiac compromise.[1,2] Although the use of venoarterial (VA) extracorporeal membrane oxygenation (ECMO) in cardiac surgery is common, universal guidelines regarding its indications and management need to be defined, leaving the current application to expert consensus, surgeon, and a center's experience.[3-5] Ideally, ECMO should be initiated before the onset of prolonged anaerobic metabolism and irreversible end-organ damage, particularly in patients at high risk for such events.[3,6] However, to identify the adequate timing in patients who required cardiac surgery is difficult due to different impact and interaction of preoperative high-risk factors, metabolic alterations induced by cardiopulmonary bypass (CPB), surgical stress, underlying disease or perioperative complications, and pharmacologic hemodynamic support. Usually, postcardiotomy VA ECMO is either implanted intraoperatively due to CPB weaning failure or postoperatively for cardiogenic shock and cardiac arrest occurring in the intensive care unit (ICU), although prophylactic support in high-risk patients is gaining popularity and attention.[3,4,7] However, specific drivers for patient selection during or after surgery, timing, indications, and prophylactic or rescue approaches have not been studied in detail yet. Some evidence suggests that ECMO implanted in an early phase of refractory cardiogenic shock leads to better clinical outcomes.[8] Nonetheless, since VA ECMO is invasive and resource-intensive, too-early implantation (eg, in patients who would recover without ECMO) increases risks and resource consumption. So, considering ECMO implantation by surgeons and intensivists in everyday clinical practice is challenging but becoming more and more common.

From the [a]Cardio-Thoracic Surgery Department, Maastricht University Medical Center, and Cardiovascular Research Institute Maastricht (CAIRM), Maastricht, The Netherlands; [b]Division of Cardiac Surgery, Memorial Healthcare System, Hollywood, Calif; [c]Department of Intensive Care Medicine, Maastricht University Medical Center, and Cardiovascular Research Institute Maastricht (CARIM), Maastricht, The Netherlands; [d]Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria; [e]Department of Cardiac Surgery, Leipzig Heart Center, Leipzig, Germany; [f]Department of Cardiac Surgery, Louis Pradel Cardiologic Hospital, Lyon, France; [g]Division of Cardiac Surgery, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [h]Department of Cardiac Surgery, Medical Faculty, Heinrich Heine University, Duesseldorf, Germany; [i]II Department of Anesthesiology, Centre of Anesthesia, Intensive Care and Pain management, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania; [j]Division of Cardiothoracic and Vascular Surgery, Pontchaillou University Hospital, Rennes, France; [k]Center for Cardiac Intensive Care, Beijing Institute of Heart, Lung, and Blood Vessels Diseases, Beijing Anzhen Hospital, Beijing, China; [l]Department of Intensive Care Adults, Erasmus MC, Rotterdam, The Netherlands; [m]Department of Intensive Care Medicine, Center of Applied Medical Research, St Vincent's Hospital, Darlinghurst, Australia; [n]Department of Cardiology, Fundación Cardiovascular de Colombia, Bucaramanga, Colombia; [o]Department of Cardiac Surgery, University Hospitals Leuven, and Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium; [p]Departments of Medicine and Surgery, University of Maryland, Baltimore, Md; [q]SOD Cardiochirurgia Ospedali Riuniti 'Umberto I–Lancisi–Salesi' Università Politecnica delle Marche, Ancona, Italy; [r]Division of Cardiac Surgery, Cardiothoracic Department, University Hospital of Udine, Udine, Italy; [s]Cardiothoracic Intensive Care Unit, National University Heart Centre, National University Hospital, Singapore, Singapore; [t]Cardiac Surgery Unit, Cardiac Thoracic and Vascular Department, Niguarda Hospital, Milan, Italy; [u]Department of Medicine and Surgery, Cardiac Surgery Clinic, San Gerardo Hospital, University of Milano-Bicocca, Monza, Italy, and Department of Medicine and Surgery, University of Parma, Cardiac Surgery Unit, University Hospital of Parma, Parma, Italy; [v]Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand; [w]Department of Cardio-Thoracic Surgery, University Hospital Henri-Mondor, Créteil, Paris, France; [x]Department of Cardiothoracic Surgery, University Medical Center Regensburg, Regensburg, Germany; [y]Department for the Treatment and Study of Cardiothoracic Diseases and Cardiothoracic Transplantation, Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione, Palermo, Italy; [z]ECMO Unit, Departamento de Anestesia, Clínica Las Condes, Santiago, Chile; [aa]Department of Thoracic and Cardiovascular Surgery, Korea University Anam Hospital, Seoul, South Korea; [bb]2nd Department of Internal Medicine, Cardiovascular Medicine General Teaching Hospital and 1st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; [cc]Intensive Care Unit, The Alfred Hospital, Melbourne, Australia; [dd]Ospedale del Cuore Fondazione Toscana "G. Monasterio," Massa, Italy; [ee]Department of Cardiovascular Surgery, Ziekenhuis Oost-Limburg, Genk, Belgium; [ff]Cardiac Surgery Unit, IRCCS Humanitas Research Hospital, Rozzano, Italy; [gg]IU Health Advanced Heart & Lung Care, Indiana University Methodist Hospital, Indianapolis, Ind; [hh]Adult Intensive Care Services, The Prince Charles Hospital, Brisbane, Australia; and [ii]Cardiac Intensive Care Unit, Johns Hopkins Hospital, Baltimore, Md.

Read at the 36th EACTS Annual Meeting, Milan, Italy, October 5-8, 2022, and at the EuroELSO Congress, Lisbon, Portugal, April 26-29, 2023.

*Complete affiliations and list of all PELS-1 Investigators are included in Appendix E1.

Received for publication Feb 5, 2023; revisions received April 5, 2023; accepted for publication April 22, 2023.

Address for reprints: Silvia Mariani, MD, Cardio-Thoracic Surgery Department, Maastricht University Medical Centre+, P. Debyelaan 25, 6202AZ Maastricht, The Netherlands (E-mail: s.mariani1985@gmail.com).

0022-5223

https://doi.org/10.1016/j.jtcvs.2023.04.042

Therefore, we aim to describe patient characteristics, in-hospital outcomes, and long-term survival of cardiac surgery patients receiving intraoperative versus postoperative VA ECMO. We conducted a multicenter, international, observational study and hypothesized that intraoperative compared with postoperative ECMO support are 2 different entities, marked by different patient characteristics, indications, and outcomes.

METHODS

The multicenter, retrospective observational Post-Cardiotomy Extracorporeal Life Support Study (PELS-1) enrolled consecutive patients supported with ECMO in the postoperative phase (ClinicalTrials.gov: NCT03857217) in 34 centers from 16 countries (Figure E1). Adults (≥18 year old) were included if they underwent ECMO implantation during or after cardiac surgery between January 2000 and December 2020. For the present analysis, characteristics and outcomes of patients receiving an intraoperative VA ECMO implantation in the operating theater or postoperatively in the ICU after cardiac surgery were compared (Figure E2). Exclusion criteria were ECMO support initiated outside the operating theater or ICU, ECMO support after noncardiac surgical procedures, and ECMO implantation not strictly related to cardiac surgery hospitalization.

The current study was conducted in accordance with the Declaration of Helsinki. Institutional review board (IRB) approval was acquired for all centers, of which the protocol was based on the IRB approval of the coordinating center (MUMC+, IRB approval number: METC-2018-0788, December 19, 2018). Data were collected centrally according to data-sharing agreements between participating centers. The need for informed consent was waived due to the observational character of the registry, the emergency of the performed procedure, and the de-identification of shared data.

Data Collection and Outcomes

Demographics, preoperative clinical and laboratory variables, procedural characteristics, ECMO details, in-hospital morbidity and mortality, and long-term survival were collected from each participating hospital and included in a dedicated electronic case report form (data.castoredc.com), according to the predefined protocol (Appendix E2). The primary outcome of interest was all-cause in-hospital mortality. Secondary outcomes included in-hospital complications and long-term mortality in in-hospital survivors.

Statistical Analysis

Demographic and clinical variables are expressed as numbers (valid percent on available data, excluding missing values) for categorical variables and median (interquartile range [IQR]) or mean (standard deviation) for continuous variables after evaluation for normality. All descriptive statistics were performed on original data, and pairwise deletion was applied after missing value analysis (Table E1). Kernel density estimation was applied to estimate the probability density function of continuous variables, and histograms were used to represent their observed frequencies. Stacked bar plots were produced to represent the distributions of levels within each categorical variable comparing study groups.

Categorical data were compared with the χ^2 test. As appropriate, continuous variables were analyzed using the Student *t* test or Mann–Whitney *U* test. Survival analysis was performed using the Kaplan–Meier curves, and differences in survival were assessed with the log-rank test. A subgroup analysis was performed to investigate long-term survival in in-hospital survivors. Hospital survivors' loss to follow-up after discharge was considered censored at the time of their last clinical control. Comparisons were performed between patients who received an intraoperative VA ECMO or a postoperative VA ECMO implantation. A further subgroup analysis was performed to compare survivors with nonsurvivors within each study group.

Finally, to test robustness of our results, we performed 2 sensitivity analyses[9]: we stratified results by implanting decade (2000-2010 and 2011-2020), and we excluded patients who received a postcardiotomy ECMO with the indication "failure to wean from cardiopulmonary bypass."

All data were extracted from the electronic case report form and merged from separate deidentified files for statistical analyses in SPSS 26.0 (IBM Corp) and R 4.1.2 (R Foundation for Statistical Computing).

RESULTS

Baseline, Surgical, and ECMO Characteristics

Among the 2163 patients whose data were collected in the PELS-1, 160 patients (7.4%) were excluded (Figure E2) due to missing data on primary outcome (n = 72), venovenous ECMO support (n = 33), or cannulation outside the operating theater or ICU (n = 55). Thus, 2003 patients were studied and included in this analysis.

Use of both intraoperative and postoperative ECMO remained stable over years (P = .344, Figure E3). Median age was 65.0 years (IQR, 55.0-72.0) with female patients accounting for 41.1% (n = 823; Table 1). Patients who received intraoperative compared with postoperative VA ECMO were younger but had a greater preoperative risk profile in terms of greater creatinine values, lower left ventricular ejection fraction, previous cardiac surgery, greater European System for Cardiac Operative Risk Evaluation II, preoperative cardiac failure, and pulmonary edema; suffered more often from ventricular septal rupture following acute myocardial infarction or endocarditis; and had more often an emergency or urgent surgical indication (Table 1). Patients who required postoperative ECMO, compared with intraoperative, more often underwent isolated coronary artery bypass surgery and off-pump surgery and shorter CPB and crossclamp times (Table 2 and Figure E4). A subgroup analysis showed that nonsurvivors compared with survivors had a greater risk profile in both study groups (Tables E2-E5).

The indication to start VA ECMO differed between patients receiving intraoperative versus postoperative ECMO (P < .001, Figure E5): failure to wean from CPB was the most common reason for intraoperative ECMO implantation (n = 764, 61.1%) followed by cardiogenic shock (n = 165, 13.2%), whereas postoperative ECMO implantation was mainly performed for cardiogenic shock (n = 320, 45.3%), acute right ventricular failure (n = 112, 15.9%), or cardiac arrest (n = 101, 14.3%). Peripheral cannulation was seen more commonly in cases of postoperative implantation, whereas central cannulation was more frequent in intraoperative implantation (P < .001, Table 3). Postoperative implantations occurred (median) 1 day (IQR, 1-3) after surgery (Figure 1). ECMO duration of nonsurvivors was similar in both study groups (intraoperative ECMO: 120 hours [IQR, 48-216]; postoperative ECMO: 120 hours [IQR, 43.4-205.2]; P = .685). It was significantly

MCS

TABLE 1. Venoarterial extracorporeal membrane oxygenation (VA ECMO) population, and according to implantation timing

Variable	Overall population (n = 2003)	Intraoperative VA ECMO (n = 1287)	Postoperative VA ECMO (n = 716)	*P* value
Age, y	65.0 (55-72)	64.4 (55-72)	65.8 (56.2-72)	<.001
Sex				.064
Female	823 (41.1%)	549 (42.7%)	274 (38.3%)	
Male	1179 (58.9%)	738 (57.3%)	441 (61.7%)	
Race				<.001
Asian	137 (6.8%)	82 (6.4%)	55 (7.7%)	
Black	11 (0.5%)	5 (0.4%)	6 (0.8%)	
Hispanic	53 (2.6%)	29 (2.3%)	24 (3.4%)	
White	1218 (60.8%)	851 (66.1%)	367 (51.3%)	
Other	50 (2.5%)	40 (3.1%)	10 (1.4%)	
Unknown	534 (26.7%)	280 (21.8%)	254 (35.5%)	
BMI, kg/m^2	27.1 ± 0.1	26.9 ± 0.1	27.5 ± 0.2	.007
BSA, m^2	1.9 ± 0.3	1.9 ± 0.2	1.9 ± 0.3	.964
Comorbidities				
Hypertension	1267 (65.6%)	786 (63.4%)	481 (69.6%)	.006
Dialysis	168 (8.7%)	110 (9%)	58 (8.2%)	.615
Previous myocardial infarction	539 (26.9%)	350 (27.2%)	189 (26.4%)	.713
Myocardial infarction (<30 d)	226 (11.7%)	155 (12.5%)	71 (10.3%)	.161
Previous endocarditis	156 (7.8%)	109 (8.5%)	47 (6.6%)	.139
Smoking	460 (27.2%)	288 (27.6%)	172 (26.5%)	.613
Previous stroke	278 (13.9%)	175 (13.6%)	103 (14.4%)	.637
Atrial fibrillation	534 (26.7%)	308 (24%)	226 (31.6%)	<.001
Previous pulmonary embolism	32 (1.8%)	21 (1.8%)	11 (1.6%)	.854
Diabetes mellitus	498 (24.9%)	310 (24.1%)	188 (26.3%)	.281
Previous TIA	40 (2.3%)	25 (2.3%)	15 (2.2%)	1.000
Implanted pacemaker	135 (7.4%)	88 (7.6%)	47 (7%)	.644
Implanted ICD	180 (9.8%)	123 (10.6%)	57 (8.5%)	.166
Previous PCI	343 (17.3%)	226 (17.8%)	117 (16.4%)	.458
COPD	202 (10.5%)	132 (10.9%)	70 (9.9%)	.538
Peripheral artery disease	291 (14.5%)	178 (13.8%)	113 (15.8%)	.235
Pulmonary hypertension (>50 mm Hg)	421 (21.2%)	285 (22.4%)	136 (19%)	.086
Previous cardiac surgery	532 (26.6%)	378 (29.4%)	154 (21.5%)	<.001
Implanted LVAD	72 (3.7%)	54 (4.4%)	18 (2.6%)	.060
Preoperative creatinine, μmol/L	101.7 (79.6-140)	104.0 (81.3-142)	97.3 (78.6-132.6)	.013
LVEF, %	45.0 (30-60)	45.0 (28-60)	50.0 (30-60)	<.001
EuroSCORE II	7.6 (3-18.6)	9.48 (3.7-22.1)	4.60 (2.1-12.4)	.006
Preoperative condition				
NYHA class				<.001
Class I	141 (7.4%)	87 (7.2%)	54 (7.9%)	
Class II	406 (21.4%)	247 (20.3%)	159 (23.2%)	
Class III	743 (39.1%)	437 (35.9%)	306 (44.7%)	
Class IV	610 (32.1%)	445 (36.6%)	165 (24.1%)	
Preoperative cardiogenic shock	423 (21.4%)	287 (22.7%)	136 (19.1%)	.067
Preoperative intubation	227 (11.3%)	167 (13%)	60 (8.4%)	.002
Preoperative cardiac arrest	183 (9.2%)	126 (9.9%)	57 (8%)	.170
Preoperative septic shock	50 (2.6%)	30 (2.4%)	20 (2.9%)	.553
Preoperative vasopressors	308 (15.5%)	232 (18.2%)	76 (10.7%)	<.001
Preoperative acute pulmonary edema	138 (7.2%)	106 (8.6%)	32 (4.6%)	.001
Preoperative IABP	190 (9.5%)	134 (10.4%)	56 (7.8%)	.067

(Continued)

TABLE 1. Continued

Variable	Overall population (n = 2003)	Intraoperative VA ECMO (n = 1287)	Postoperative VA ECMO (n = 716)	*P* value
Preoperative right ventricular failure	180 (10.3%)	126 (11.6%)	54 (8.1%)	.019
Preoperative biventricular failure	120 (7.6%)	83 (8.8%)	37 (5.8%)	.033
Emergency surgery	516 (26.1%)	353 (27.9%)	163 (22.8%)	.014
Urgent surgery	438 (22.1%)	321 (25.3%)	117 (16.4%)	<.001
Diagnosis				
Coronary artery disease	961 (48%)	593 (46.1%)	368 (51.4%)	.025
Aortic vessel disease	328 (16.4%)	220 (17.1%)	108 (15.1%)	.257
Aortic valve disease	680 (33.9%)	446 (34.7%)	234 (32.7%)	.376
Mitral valve disease	685 (34.2%)	431 (33.5%)	254 (35.5%)	.377
Tricuspid valve disease	317 (15.8%)	183 (14.2%)	134 (18.7%)	.009
Pulmonary valve disease	17 (0.8%)	12 (0.9%)	5 (0.7%)	.800
Post-AMI ventricular septal rupture	58 (2.9%)	48 (3.7%)	10 (1.4%)	.002
Free wall/papillary muscle rupture	38 (1.9%)	29 (2.3%)	9 (1.3%)	.127
Active endocarditis	142 (7.1%)	104 (8.1%)	38 (5.3%)	.023
Atrial septal defect	33 (1.6%)	21 (1.6%)	12 (1.7%)	1.000
Post-LVAD right ventricular failure	19 (0.9%)	16 (1.2%)	3 (0.4%)	.091
Other diagnosis	255 (12.7%)	155 (12%)	100 (14%)	.234

Data are reported as n (% as a valid percentage excluding missing values), mean ± standard deviation, or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. *VA ECMO*, venoarterial extracorporeal membrane oxygenation; *BMI*, Body mass index; *BSA*, body surface area; *TIA*, transient ischemic attack; *ICD*, implantable cardioverter defibrillator; *PCI*, percutaneous coronary intervention; *COPD*, chronic obstructive pulmonary disease; *LVAD*, left ventricular assist device; *LVEF*, left ventricular ejection fraction; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *IABP*, intra-aortic balloon pump; *AMI*, acute myocardial infarction.

shorter in survivors who received intraoperative ECMO (median, 104 hours; IQR, 67.8-164.2) compared with those who received postoperative ECMO (median, 139.7 hours; IQR, 95.8-192, $P < .001$, Table E4 and Figure E4).

In-Hospital Outcomes and Follow-up Survival

Patients who underwent postoperative compared to intraoperative ECMO experienced a greater number of complications and required more procedures, including cardiac operations and percutaneous coronary interventions (Table 4). Overall, most complications were experienced by nonsurvivors (Table E5). In-hospital mortality was 60%, with a greater percentage dying after postoperative ECMO implantation (n = 462, 64.5%) compared with intraoperative (n = 740, 57.5%, $P = .002$, Figures 2 and E6, Table 4). After excluding patients who underwent heart transplant (n = 205), the gap in in-hospital mortality between groups narrowed but remained statistically significant (intraoperative ECMO: n = 688/1133, 60.7%; postoperative ECMO: n = 439/664, 66.1%, $P = .023$). The overall survival probability was greater in patients who received intraoperative ECMO implantation, mainly due to lower in-hospital deaths ($P = .01$, Figure 3, *A*). Among hospital survivors, no differences were observed in long-term survival between the 2 study groups ($P = .86$, Figure 3, *B*).

Sensitivity Analyses

Of 2003 included patients, 442 (22.1%) had ECMO support between 2000 and 2010 and 1561 (77.9%) had ECMO support between 2011 and 2020 (Tables E6-E9 and Figures E7-E10). The population characteristics over the whole study period were similar to those over the 2011 to 2020 decade. Differences between intraoperative and postoperative implantation in terms of complications rates were less evident in the 2011 to 2020 decade for postoperative bleedings ($P = .135$), bowel ischemia ($P = .165$), acute respiratory distress syndrome ($P = .186$), and postoperative procedures (percutaneous coronary interventions: $P = .101$; cardiac surgery: $P = .140$). In-hospital mortality in the 2011 to 2020 cohort was 59.2% (n = 924; intraoperative ECMO implantation: n = 564, 57%; postoperative ECMO implantation: n = 360, 63.2%; $P = .019$), whereas the in-hospital mortality in the 2000 to 2010 cohort was 62.9% (n = 278; intraoperative ECMO implantation: n = 176, 59.3%; postoperative ECMO implantation: n = 102, 70.3%; $P = .028$). The lower in-hospital mortality in the

TABLE 2. Procedural characteristics

Variable	Overall population (n = 2003)	Intraoperative VA ECMO (n = 1287)	Postoperative VA ECMO (n = 716)	*P* value
Weight of surgery				<.001
Unknown	13 (0.6%)	7 (0.5%)	6 (0.8%)	
Isolated CABG	351 (17.5%)	183 (14.2%)	168 (23.5%)	
Isolated non-CABG	1121 (56%)	717 (55.7%)	404 (56.4%)	
Two procedures	147 (7.3%)	123 (9.6%)	24 (3.4%)	
Three or more procedures	371 (18.5%)	257 (20%)	114 (15.9%)	
CABG	885 (44.2%)	558 (43.4%)	327 (45.7%)	.325
Aortic valve surgery	693 (34.6%)	459 (35.7%)	234 (32.7%)	.186
Mitral valve surgery	635 (31.7%)	409 (31.8%)	226 (31.6%)	.920
Tricuspid valve surgery	270 (13.5%)	164 (12.7%)	106 (14.8%)	.195
Aortic surgery	373 (18.6%)	260 (20.2%)	113 (15.8%)	.017
Pulmonary valve surgery	12 (0.6%)	8 (0.6%)	4 (0.6%)	1.000
LVAD	23 (1.1%)	17 (1.3%)	6 (0.8%)	.388
RVAD	6 (0.3%)	5 (0.4%)	1 (0.1%)	.430
ASD repair	38 (1.9%)	23 (1.8%)	15 (2.1%)	.613
VSD repair	68 (3.4%)	54 (4.2%)	14 (2%)	.007
Ventricular surgery	74 (3.7%)	45 (3.5%)	29 (4.1%)	.538
Rhythm surgery	66 (3.3%)	41 (3.2%)	25 (3.5%)	.698
Pulmonary embolectomy	23 (1.1%)	15 (1.2%)	8 (1.1%)	1.000
Pulmonary endarterectomy	47 (2.3%)	36 (2.8%)	11 (1.5%)	.09
Heart transplantation	205 (10.2%)	154 (12%)	51 (7.1%)	<.001
Off-pump surgery	79 (4%)	33 (2.6%)	46 (6.5%)	<.001
Conversion to CPB	24 (29.3%)	14 (42.4%)	10 (20.4%)	.047
CPB time, min	205 (142-290)	234 (168-323)	159 (108-222)	.027
Crossclamp time, min	100 (64-148)	104 (68-155)	89 (59-132)	.007
Intraoperative lactate,* mmol/L	5.3 (2.8-8.7)	6.0 (3.7-10)	3.3 (1.9-6.5)	<.001
Intraoperative transfusions*	746 (92.2%)	497 (92.2%)	249 (92.2%)	1.000

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. *VA ECMO*, Venoarterial extracorporeal membrane oxygenation; *CABG*, coronary artery bypass graft; *LVAD*, left ventricular assist device; *RVAD*, right ventricular assist device; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass. *Variable with >50% missing data.

2011-2020 cohort is reflected by the Kaplan–Meier curves, where survival differences were not statistically significant in recent years ($P = .055$).

A sensitivity analysis excluding patients who received postcardiotomy ECMO after failure to wean from CPB (Tables E10-E13 and Figures E11-E13), showed an intraoperative ECMO group with a reduced percentage of patients with mitral valve diseases (n = 131, 27%) undergoing mitral valve surgery (n = 123, 25.4%) and an increased percentage of patients undergoing off-pump operations (n = 23, 4.8%) or left ventricular assist device implantation (n = 13, 2.7%) and receiving intraoperative transfusions (n = 245, 96.5%). Despite these different characteristics, survival outcomes reflected those identified in the overall population and the gap in in-hospital mortality between groups was even larger (overall: n = 711, 60.9%; postoperative ECMO implantation: n = 441, 64.7%; intraoperative ECMO implantation: n = 270, 55.6%, $P = .002$). Nevertheless, the intraoperative group showed a lower incidence of postoperative acute kidney injury (n = 227, 49.3%) and greater requirements of postoperative cardiac operations (n = 106, 22.9%) or percutaneous coronary interventions (n = 13, 2.9%).

DISCUSSION

This study demonstrates that pre-ECMO etiology and indications, characteristics of the ECMO support, and complications are different in cardiac surgery patients receiving intraoperative versus postoperative VA ECMO. The study has 5 main findings. First, intraoperative patients compared with postoperative patients who received VA ECMO showed greater risk profiles before surgery. Second,

TABLE 3. Details on ECMO

Variable	Overall population (n = 2003)	Intraoperative VA ECMO (n = 1287)	Postoperative VA ECMO (n = 716)	*P* value
ECMO indication				<.001
Failure to wean	788 (40.3%)	764 (61.1%)	24 (3.4%)	
Acute pulmonary embolism	3 (0.2%)	1 (0.1%)	2 (0.3%)	
Arrhythmia	40 (2%)	13 (1%)	27 (3.8%)	
Cardiac arrest	150 (7.7%)	49 (3.9%)	101 (14.3%)	
Cardiogenic shock	485 (24.8%)	165 (13.2%)	320 (45.3%)	
Pulmonary hemorrhage	9 (0.5%)	7 (0.6%)	2 (0.3%)	
Right ventricular failure	235 (12%)	123 (9.8%)	112 (15.9%)	
Respiratory failure	70 (3.6%)	23 (1.8%)	47 (6.7%)	
Biventricular failure	146 (7.5%)	89 (7.1%)	57 (8.1%)	
Other	30 (1.5%)	16 (1.3%)	14 (2%)	
Cannulation approach				<.001
Only central cannulation	333 (16.6%)	238 (18.5%)	95 (13.3%)	
Only peripheral cannulation	930 (46.4%)	549 (42.7%)	381 (53.2%)	
Mixed/switch cannulation	699 (34.9%)	478 (37.1%)	221 (30.9%)	
Unknown	41 (2%)	22 (1.7%)	19 (2.7%)	
ECMO duration, h	118 (60-192)	112 (60-192)	122 (60-197)	<.001

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. *VA ECMO*, venoarterial extracorporeal membrane oxygenation.

postoperative patients who received VA ECMO experienced more postoperative cardiogenic shock, cardiac arrest, or acute right ventricular failure 24 to 48 hours after surgery. Third, patients who received an intraoperative ECMO implantation experienced shorter ECMO runs as well as fewer complications and reinterventions. Fourth, patients who received ECMO intraoperatively had a greater in-hospital survival than patients who received VA ECMO postoperatively. The gap in in-hospital mortality between groups narrowed in the 2011 to 2020 decade and after exclusion of transplant patients and increased after exclusion of patients cannulated after failure to wean from CPB. Fifth, long-term

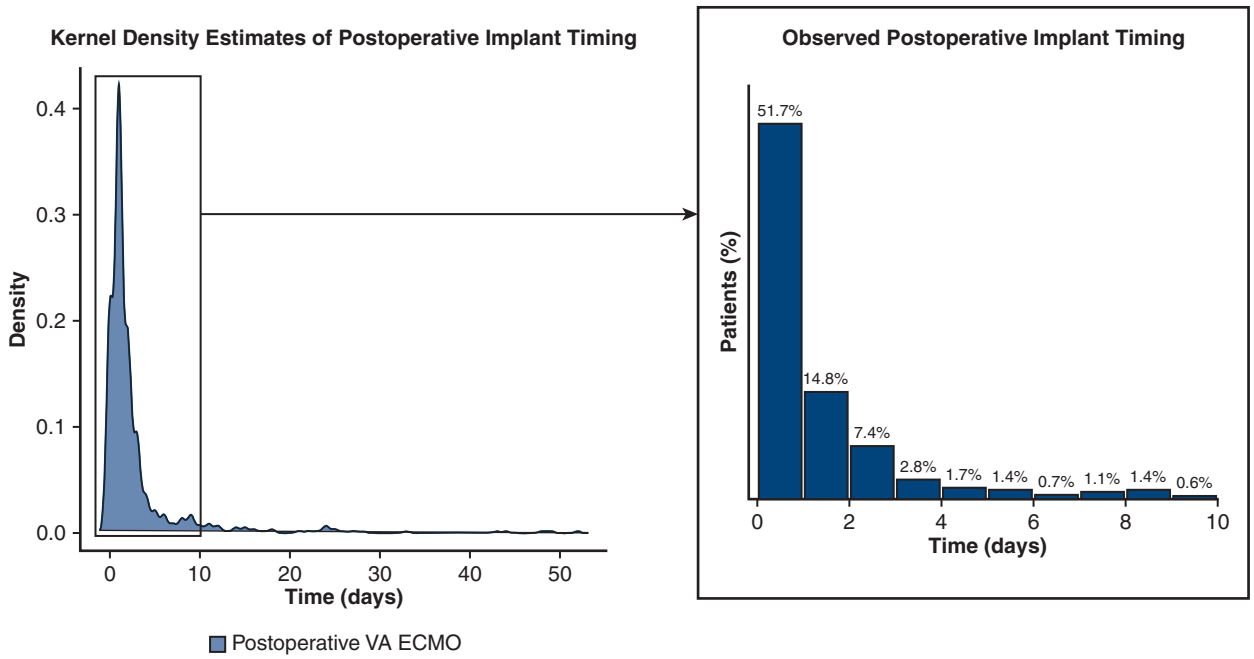


FIGURE 1. Postoperative venoarterial extracorporeal membrane oxygenation (*VA ECMO*) implantation timing.

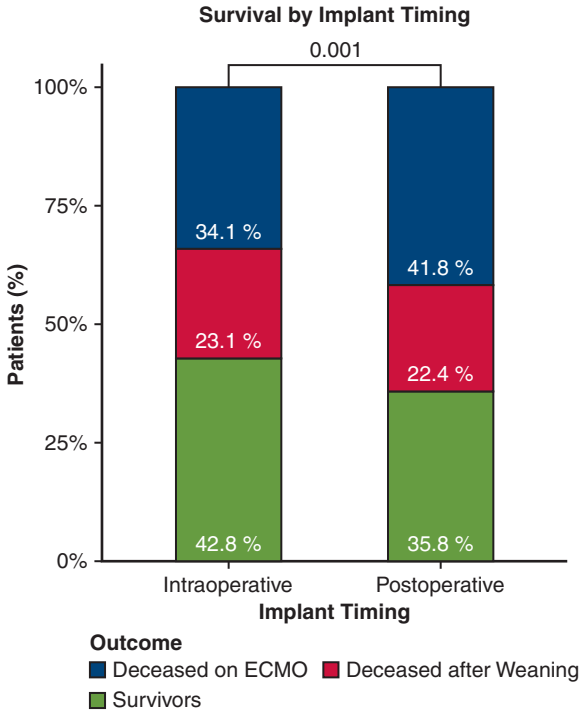


FIGURE 2. In-hospital survival based on implantation timing. *ECMO*, Extracorporeal membrane oxygenation.

survival after hospital discharge was comparable in the 2 study groups. Although intraoperative and postoperative postcardiotomy ECMO are 2 different entities both associated with high mortality, survival appears more likely with intraoperative ECMO.

Evidence shows that most ECMO implantations in cardiac surgery occur for postcardiotomy cardiogenic shock, affecting 0.3% to 3.6% of patients who undergo cardiac surgery either due to failure to wean from CPB or complications after surgery.[3,4,7,10] The escalation to postcardiotomy ECMO generally follows a period of increasing demand for vasoactive support and resuscitation. Notwithstanding, institutional protocols differ significantly with respect to the acceptable duration of this phase. Furthermore, there is an institutional variability in the logistics for MCS, in the multidisciplinary approach, and in the ECMO expertise.[11] Finally, geographic variations, cultural aspects, different health care systems, and lack of evidence may impact the overall ECMO policies and application.[12] Most previous studies report on intraoperative and postoperative ECMO as one group. The present evidence suggests that these are 2 distinct entities, characterized by different populations, indications, and outcomes. In most series investigating postcardiotomy ECMOs, 30% to 60% of patients are cannulated in the ICU,[13-18] highlighting the importance of this distinction. We observed that intraoperative ECMO tends to be used in those patients who arrive at surgery in a more unstable situation (eg, greater creatinine concentrations, lower left ventricular ejection fraction, previous cardiac surgery, greater European System for Cardiac Operative Risk Evaluation II, preoperative cardiac failure, pulmonary edema, and emergency or urgent surgical indication), undergo more complex surgeries requiring longer CPB times, and have greater intraoperative lactates. Indeed, many of these variables have been previously identified as variables associated with ECMO mortality, which might have supported surgeons' choice toward a direct intraoperative ECMO implantation.[19-25] Surgeons might have perceived ECMO implantation performed under controlled conditions as part of an operation as inherently safer in these complex cases. Surprisingly, these patients experienced 7% lower in-hospital mortality compared with the postoperative implantation group, despite the latter group's more favorable preoperative and intraoperative profile. Furthermore, survivors who received intraoperative ECMO required a shorter ECMO run compared with survivors who underwent postoperative ECMO support. Despite the mortality remaining important, these observations support the intraoperative use of ECMO even in very high-risk patients. Moreover, knowing the characteristics of patients who likely will receive an intraoperative ECMO could be useful in the preoperative planning and patient information process, especially within those teams familiar with the practice of prophylactic intraoperative ECMO.[3,7] We can only speculate that this approach could be advantageous in those patients who receive an intraoperative ECMO for reasons other than failure to wean from CPB. Indeed, in this specific group, mortality dropped to 55.6% when an intraoperative ECMO has been used.

In contrast, the strategy of delaying the ECMO use to ICU might allow a significant number of patients avoiding the use of ECMO at all. This is true, for example, when ECMO might have become necessary for unexpected conditions in patients with theoretical low preoperative risk. Accordingly, this is the case of early coronary artery bypass graft occlusion, sudden onset of ventricular arrhythmia, right ventricular failure, or massive pericardial effusion. These patients are unlikely to be a candidate of intraoperative ECMO cannulation but it is important to underline, based on our findings, that they experience worse outcomes than patients who just need a period of ECMO support for recovery of heart function after a complicated cardiac operation. This is confirmed by our results that show how most postoperative ECMO cannulations occur in the first 24 to 48 hours after surgery, when surgical complications are more frequent, the myocardial stunning and the systemic inflammation are important, and the oxygen delivery might be compromised by anemia, hemodilution, arrhythmias, and pulmonary problems. Ideally, ECMO should be considered in refractory cardiogenic shock within 6 hours and before severe or refractory end-organ injury or onset of

TABLE 4. Postoperative outcomes

Variable	Overall population (n = 2003)	Intraoperative VA ECMO (n = 1287)	Postoperative VA ECMO (n = 716)	*P* value
ICU stay, d	14 (6-26)	13 (6-25)	14 (6-28)	<.001
Hospital stay, d	20 (8-40)	21 (8-40)	20 (9-39)	<.001
Postoperative bleeding	1125 (57.2%)	696 (55.3%)	429 (60.7%)	.023
Requiring rethoracotomy	749 (40.1%)	477 (40.4%)	272 (39.5%)	.732
Cannulation site bleeding	237 (12.1%)	143 (11.3%)	94 (13.3%)	.220
Diffuse nonsurgical bleeding	459 (25.5%)	255 (22.5%)	204 (30.4%)	<.001
Neurologic complications				
Brain edema	81 (4.3%)	54 (4.4%)	27 (4%)	.723
Cerebral hemorrhage	62 (3.3%)	34 (2.8%)	28 (4.1%)	.139
Seizure	38 (2%)	25 (2.1%)	13 (1.9%)	.866
Stroke	212 (10.7%)	138 (10.8%)	74 (10.5%)	.879
Vasospasm	2 (0.1%)	1 (0.1%)	1 (0.2%)	1.000
Arrhythmia	597 (32.5%)	343 (29.4%)	254 (38%)	<.001
Leg ischemia	189 (10%)	116 (9.6%)	73 (10.7%)	.473
Cardiac arrest	283 (15.4%)	130 (11.2%)	153 (22.8%)	<.001
Pacemaker implantation	56 (3.1%)	37 (3.2%)	19 (2.8%)	.779
Bowel ischemia	105 (5.7%)	56 (4.8%)	49 (7.3%)	.028
Right ventricular failure	380 (21.1%)	211 (18.7%)	169 (25.4%)	<.001
Acute kidney injury	1037 (56.7%)	655 (56.6%)	382 (56.8%)	.922
Pneumonia	405 (22.6%)	247 (21.8%)	158 (23.8%)	.350
Septic shock	296 (16.5%)	161 (14.2%)	135 (20.3%)	<.001
Distributive shock	172 (9.6%)	104 (9.2%)	68 (10.2%)	.507
ARDS	100 (5.4%)	53 (4.5%)	47 (7%)	.032
MOF	679 (34.4%)	405 (32%)	274 (38.6%)	.004
Embolism	112 (6.2%)	70 (6.2%)	42 (6.3%)	.920
Postoperative procedures				
PCI	44 (2.5%)	20 (1.8%)	24 (3.6%)	.026
Cardiac surgery	396 (21.6%)	230 (19.7%)	166 (24.8%)	.011
Abdominal surgery	79 (4.5%)	37 (3.4%)	42 (6.4%)	.004
Vascular surgery	200 (11.4%)	116 (10.5%)	84 (12.7%)	.163
In-hospital mortality	1202 (60%)	740 (57.5%)	462 (64.5%)	.002

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. *VA ECMO*, Venoarterial extracorporeal membrane oxygenation; *ICU*, intensive care unit; *ARDS*, acute respiratory distress syndrome; *MOF*, multiorgan failure; *PCI*, percutaneous coronary intervention.

anaerobic metabolism (lactate <4 mmol/L) in the absence of uncontrollable bleeding.[3] Nevertheless, our data show that cardiac arrest still represents the indication for ECMO cannulation in ICU in 14.3% of patients while complicating the postoperative course of a much greater rate of nonsurvivors. It can be speculated that at least some of these patients experienced a cardiac arrest because of waiting too long before deploying ECMO. Therefore, even in potentially low-risk patients, when signs of severe complications or progressive shock appear,[26] rapid action should be taken to implement an accurate hemodynamic evaluation,[27] and MCS should promptly be considered in the context of a multidisciplinary heart team approach[28] before the occurrence of a cardiac arrest or conditions known for immediately preceding it. The same concept can be applied to patients experiencing postoperative acute right ventricular failure, which represents almost 16% of postoperative ECMO indications. Although intraoperative right ventricular failure is treated with immediate drug escalation, perioperatively, these patients risk a delayed or progressive refractory cardiac compromise early in the ICU with ominous prognosis in most cases.[29] Furthermore in many circumstances, perioperative right ventricular failure could be predicted by preoperative or intraoperative

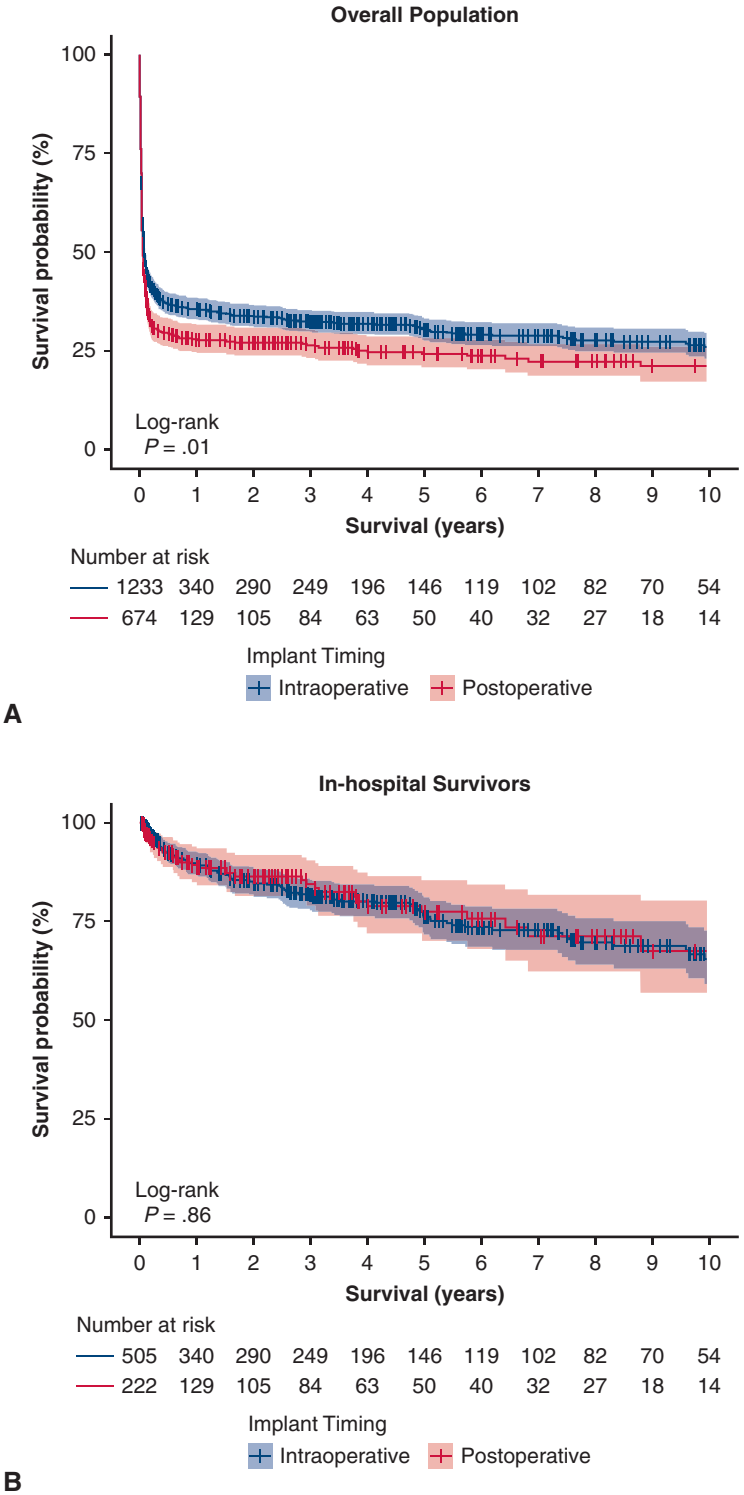


FIGURE 3. Overall (A) and postdischarge (B) Kaplan–Meier survival curves with 95% confidence limit. Groups are defined according to venoarterial extracorporeal membrane oxygenation implantation timing.

conditions, calling for a temporary prophylactic support which, unfortunately, is often applied too late in nonsurvivors.[30] Overall, the first 48 hours after surgery are those considered at greater risk of new complications or deterioration of pre-existing situations requiring postoperative ECMO. In this period, it is crucial to implement preventive

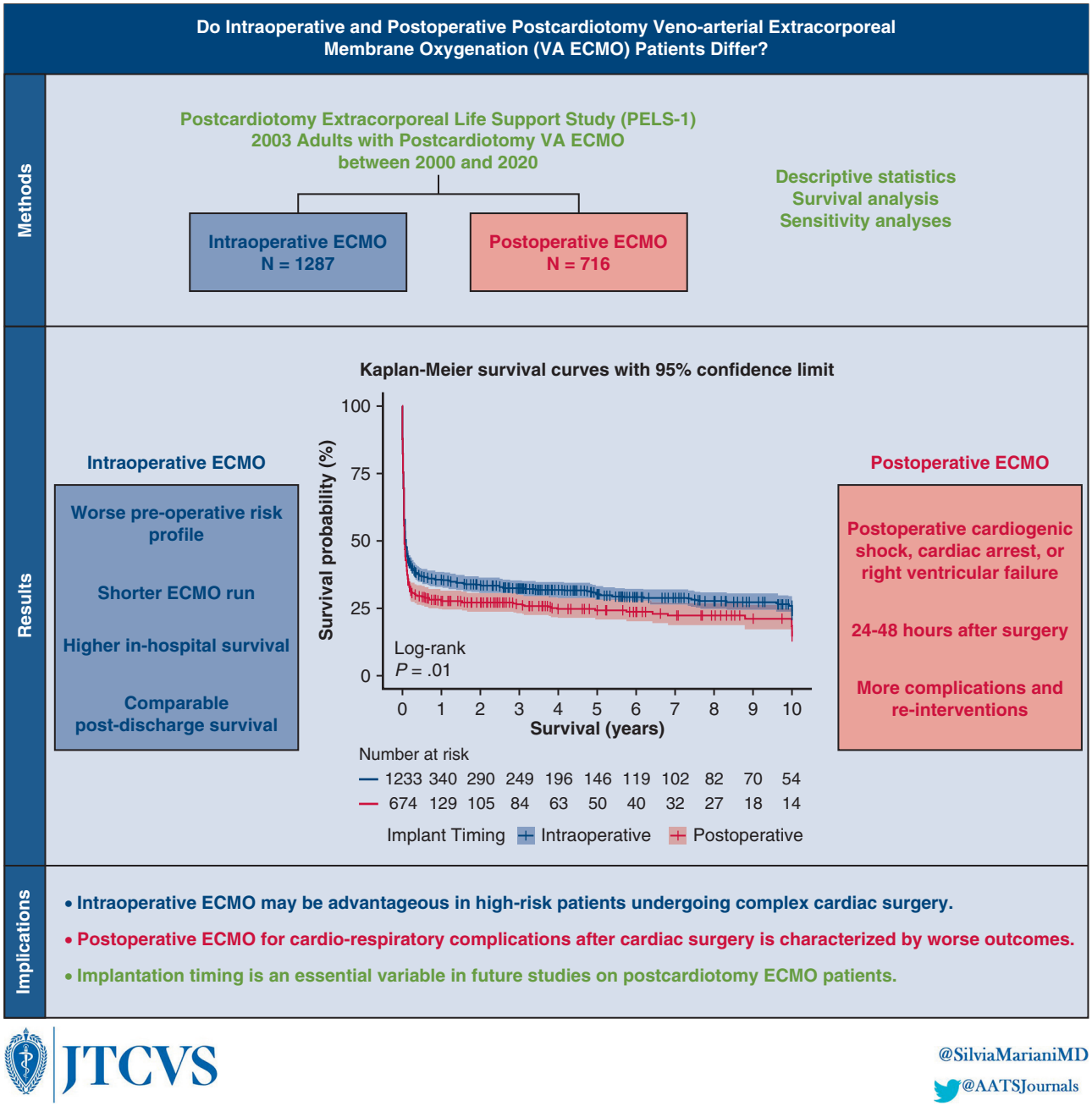


FIGURE 4. This analysis of the Postcardiotomy Extracorporeal Life Support Study (*PELS-1*) included 2003 patients and showed that intraoperative and postoperative ECMO implantation are associated with different patient characteristics and survival, with greater in-hospital mortality and complications after postoperative cannulation. *ECMO*, Extracorporeal membrane oxygenation.

strategies or implant an ECMO before severe or refractory end-organ injury. Our study suggests that these aspects of postcardiotomy ECMO management could significantly affect the in-hospital course of patients who undergo cardiac surgery. At the same time, they seem to have little effect on postdischarge survival.

As further implication of our study, we can suggest more attention to the description and consideration of ECMO implantation timing in future studies addressing patients after cardiac surgery. Indeed, based on our findings, we can speculate that this underestimated variable might significantly influence postcardiotomy ECMO outcomes to the point that it might play an essential role in predictive models and risk scores as well as ultimate outcomes. Finally, patients and relatives approaching cardiac surgery should be adequately informed about the risks associated with an intraoperative or postoperative postcardiotomy ECMO implantation.[31]

Strengths and Limitations

The structured data collection performed in the PELS-1, the participation of 34 centers from 16 countries, and the large sample size enhance data robustness and statistical power. Nevertheless, our study is observational by nature, preventing causal inferences.[32] Moreover, postcardiotomy ECMO retrospective observational studies, by design, suffer from confounding by indication,[33] preventing any prediction modeling. Further prospective and/or interventional studies are required to test the hypotheses that intraoperative VA ECMO implantation is advantageous in selected cases. Prospective and randomized designs are needed to investigate the role of favorable patient selection, ECMO timing, and clinical management to reduce on-ECMO mortality and the role of complication prevention or prompt treatment to decrease postweaning deaths. The study period extended more than 20 years, which guarantees a complete overview of postcardiotomy ECMO. In contrast, differences in ECMO care over the study period might be confounding factors. A sensitivity analysis was performed to control for these factors, but further studies are required to investigate the association between calendar time and postcardiotomy ECMO care itself. Participation in the PELS-1 was on a voluntary basis, and centers received no funding during the whole study period. Thus, we cannot exclude that some centers did not provide all eligible consecutive cases due to lack of resources in the most recent years, despite the actions taken to support a comprehensive and granular data collection (Figure E1). A partial overlapping with previously reported series cannot be excluded. In particular, we estimate an overlap of 478 patients between this study and the study by Schaefer and colleagues.[34] Data on how many adult patients received cardiac surgery at each center during the study period were not available since the analysis of ECMO implantation rates in cardiac surgery was beyond the aim of this study. The database does not capture specific variables, such as interinstitutional clinical management variations, device changes over time, or serial arterial lactate concentrations before and during ECMO support. Furthermore, an in-depth analysis of intraoperative and postoperative hemodynamic parameters, quality of life and rehospitalization after discharge were not possible. Patients who received a postcardiotomy ECMO in the catheter laboratory or normal ward were excluded from the current analysis, and further studies are required to describe these populations. Finally, we cannot exclude the influence of an immortal bias based on the fact that those patients who died perioperatively before receiving an ECMO support could introduced selection.[35]

CONCLUSIONS

Intraoperative and postoperative ECMO are 2 different clinical entities, marked by different patient characteristics, indications, and outcomes. In-hospital mortality of both remains high, with even worse in-hospital outcomes after postoperative ICU-based ECMO implantation (Figure 4). An intraoperative ECMO initiation should be considered in high-risk patients undergoing complex cardiac surgery, even beyond the classic "failure-to-wean" indication. Much work is required to improve outcomes of postoperative VA ECMO implantation in patients experiencing postcardiotomy cardiogenic shock, cardiac arrest, acute right ventricular failure, or other cardiorespiratory complications in the first 24 to 48 hours after cardiac surgery. Further studies are warranted to investigate the patient selection process for intraoperative (prophylactic or not) ECMO implantation and establish criteria for postoperative ECMO initiation. Finally, it is advisable to consider the implantation timing as an essential variable in future studies on postcardiotomy ECMO patients.

Conflict of Interest Statement

D.W. reports consultant/proctor for Abbott and scientific advisor for Xenios. R.L. reports consultant for Medtronic, Getinge, Abiomed, and LivaNova; and Advisory Board Member of Eurosets, Xenios, and Hemocure (honoraria paid as research funding). K.R. received honoraria from Baxter and Fresenius, Ltd, for educational lectures. 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. Whitman GJ. Extracorporeal membrane oxygenation for the treatment of postcardiotomy shock. *J Thorac Cardiovasc Surg*. 2017;153:95-101.
2. Vallabhajosyula S, Arora S, Sakhuja A, Lahewala S, Kumar V, Shantha GPS, et al. Trends, predictors, and outcomes of temporary mechanical circulatory support for postcardiac surgery cardiogenic shock. *Am J Cardiol*. 2019;123:489-97.
3. Lorusso R, Whitman G, Milojevic M, Raffa G, McMullan DM, Boeken U, et al. 2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients. *J Thorac Cardiovasc Surg*. 2021;161:1287-331.
4. Kowalewski M, Zielinski K, Brodie D, MacLaren G, Whitman G, Raffa GM, et al. Venoarterial extracorporeal membrane oxygenation for postcardiotomy shock-analysis of the extracorporeal life support organization registry. *Crit Care Med*. 2021;49:1107-17.
5. Kowalewski M, Raffa GM, Zielinski K, Alanazi M, Gilbers M, Heuts S, et al. The impact of Centre's heart transplant status and volume on in-hospital outcomes following extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock: a meta-analysis. *BMC Cardiovasc Disord*. 2020;20:10.
6. Lorusso R, Shekar K, MacLaren G, Schmidt M, Pellegrino V, Meyns B, et al. ELSO Interim Guidelines for venoarterial extracorporeal membrane oxygenation in adult cardiac patients. *ASAIO J*. 2021;67:827-44.
7. Lorusso R, Raffa GM, Alenizy K, Sluijpers N, Makhoul M, Brodie D, et al. Structured review of post-cardiotomy extracorporeal membrane oxygenation: part 1—adult patients. *J Heart Lung Transplant*. 2019;38:1125-43.
8. Lee HH, Kim HC, Ahn CM, Lee SJ, Hong SJ, Yang JH, et al. Association between timing of extracorporeal membrane oxygenation and clinical outcomes in refractory cardiogenic shock. *JACC Cardiovasc Interv*. 2021;14:1109-19.

9. Thabane L, Mbuagbaw L, Zhang S, Samaan Z, Marcucci M, Ye C, et al. A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. *BMC Med Res Methodol*. 2013;13:92.
10. Lomivorotov VV, Efremov SM, Kirov MY, Fominskiy EV, Karaskov AM. Low-cardiac-output syndrome after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2017;31:291-308.
11. Biancari F, Dalen M, Fiore A, Ruggieri VG, Saeed D, Jonsson K, et al. Multicenter study on postcardiotomy venoarterial extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*. 2020;159:1844-54.e6.
12. Mariani S, van Bussel BCT, Ravaux JM, Roefs MM, De Piero ME, Di Mauro M, et al. Variables associated with in-hospital and postdischarge outcomes after postcardiotomy extracorporeal membrane oxygenation: Netherlands Heart Registration Cohort. *J Thorac Cardiovasc Surg*. 2023;165:1127-37. https://doi.org/10.1016/j.jtcvs.2022.08.024
13. Pozzi M, Alvau F, Armoiry X, Grinberg D, Hugon-Vallet E, Koffel C, et al. Outcomes after extracorporeal life support for postcardiotomy cardiogenic shock. *J Card Surg*. 2019;34:74-81.
14. Saxena P, Neal J, Joyce LD, Greason KL, Schaff HV, Guru P, et al. Extracorporeal membrane oxygenation support in postcardiotomy elderly patients: the Mayo clinic experience. *Ann Thorac Surg*. 2015;99:2053-60.
15. Unosawa S, Sezai A, Hata M, Nakata K, Yoshitake I, Wakui S, et al. Long-term outcomes of patients undergoing extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *Surg Today*. 2013;43:264-70.
16. Slottosch I, Liakopoulos O, Kuhn E, Deppe AC, Scherner M, Madershahian N, et al. Outcomes after peripheral extracorporeal membrane oxygenation therapy for postcardiotomy cardiogenic shock: a single-center experience. *J Surg Res*. 2013;181:e47-55.
17. Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T, et al. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg*. 2010;139:302-11. 311.e1.
18. Ko WJ, Lin CY, Chen RJ, Wang SS, Lin FY, Chen YS. Extracorporeal membrane oxygenation support for adult postcardiotomy cardiogenic shock. *Ann Thorac Surg*. 2002;73:538-45.
19. Fux T, Holm M, Corbascio M, Lund LH, van der Linden J. Venoarterial extracorporeal membrane oxygenation for postcardiotomy shock: risk factors for mortality. *J Thorac Cardiovasc Surg*. 2018;156:1894-902.e3.
20. Fux T, Holm M, van der Linden J. Arterial lactate before initiation of venoarterial extracorporeal membrane oxygenation for postcardiotomy shock improves postimplant outcome prediction. *J Thorac Cardiovasc Surg*. 2019;157:e266-7.
21. Biancari F, Fiore A, Jonsson K, Gatti G, Zipfel S, Ruggieri VG, et al. Prognostic significance of arterial lactate levels at weaning from postcardiotomy venoarterial extracorporeal membrane oxygenation. *J Clin Med*. 2019;8:2218.
22. Hu RTC, Broad JD, Osawa EA, Ancona P, Iguchi Y, Miles LF, et al. 30-day outcomes post veno-arterial extra corporeal membrane oxygenation (VA-ECMO) after cardiac surgery and predictors of survival. *Heart Lung Circ*. 2020;29:1217-25.
23. Li CL, Wang H, Jia M, Ma N, Meng X, Hou XT. The early dynamic behavior of lactate is linked to mortality in postcardiotomy patients with extracorporeal membrane oxygenation support: a retrospective observational study. *J Thorac Cardiovasc Surg*. 2015;149:1445-50.
24. Mashiko Y, Abe T, Tokuda Y, Oshima H, Usui A. Extracorporeal membrane oxygenation support for postcardiotomy cardiogenic shock in adult patients: predictors of in-hospital mortality and failure to be weaned from extracorporeal membrane oxygenation. *J Artif Organs*. 2020;23:225-32.
25. Xie H, Yang F, Hou D, Wang X, Wang L, Wang H, et al. Risk factors of in-hospital mortality in adult postcardiotomy cardiogenic shock patients successfully weaned from venoarterial extracorporeal membrane oxygenation. *Perfusion*. 2020;35:417-26.
26. Naidu SS, Baran DA, Jentzer JC, Hollenberg SM, van Diepen S, Basir MB, et al. SCAI SHOCK stage classification expert consensus update: a review and incorporation of validation studies: this statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. *J Am Coll Cardiol*. 2022;79:933-46.
27. Stawiarski K, Ramakrishna H. The pulmonary artery catheter in cardiogenic and post-cardiotomy shock-analysis of recent data. *J Cardiothorac Vasc Anesth*. 2021;36:2780-2.
28. Masud F, Gheewala G, Giesecke M, Suarez EE, Ratnani I. Cardiogenic shock in perioperative and intraoperative settings: a team approach. *Methodist Debakey Cardiovasc J*. 2020;16:e1-7.
29. Kapur NK, Esposito ML, Bader Y, Morine KJ, Kiernan MS, Pham DT, et al. Mechanical circulatory support devices for acute right ventricular failure. *Circulation*. 2017;136:314-26.
30. Anderson M, Morris DL, Tang D, Batsides G, Kirtane A, Hanson I, et al. Outcomes of patients with right ventricular failure requiring short-term hemodynamic support with the Impella RP device. *J Heart Lung Transplant*. 2018;37:1448-58.
31. Simons J, Suverein M, van Mook W, Caliskan K, Soliman O, van de Poll M, et al. Do-(not-)mechanical-circulatory-support orders: should we ask all cardiac surgery patients for informed consent for post-cardiotomy extracorporeal life circulatory support? *J Clin Med*. 2021;10:383.
32. Altman N, Krzywinski M. Association, correlation and causation. *Nat Methods*. 2015;12:899-900.
33. Bosco JL, Silliman RA, Thwin SS, Geiger AM, Buist DS, Prout MN, et al. A most stubborn bias: no adjustment method fully resolves confounding by indication in observational studies. *J Clin Epidemiol*. 2010;63:64-74.
34. Schaefer AK, Riebandt J, Bernardi MH, Distelmaier K, Goliasch G, Zimpfer D, et al. Fate of patients weaned from post-cardiotomy extracorporeal life support. *Eur J Cardiothorac Surg*. 2022;61:1178-85.
35. Lévesque LE, Hanley JA, Kezouh A, Suissa S. Problem of immortal time bias in cohort studies: example using statins for preventing progression of diabetes. *BMJ*. 2010;340:b5087.

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

APPENDIX E1

Complete Affiliations and List of PELS-1 Investigators

Justine Ravaux,[jj] Ann-Kristin Schaefer,[kk] Luca Conci,[kk] Philipp Szalkiewicz,[kk] Jawad Khalil,[ll] Sven Lehmann,[ll] Jean-Francois Obadia,[mm] Nikolaos Kalampokas,[nn] Erwan Flecher,[oo] Dinis Dos Reis Miranda,[pp] Kogulan Sriranjan,[qq] Michael A. Mazzeffi,[rr] Nazli Vedadi,[rr] Marco Di Eusanio,[ss] Graeme MacLaren,[tt] Vitaly Sorokin,[tt] Alessandro Costetti,[uu] Chistof Schmid,[vv] Roberto Castillo,[ww] Vladimir Mikulenka,[xx] and Marco Solinas[yy]

[jj]Cardio-Thoracic Surgery Department, and Cardiovascular Research Institute Maastricht, Maastricht, the Netherlands

[kk]Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria

[ll]Department of Cardiac Surgery, Leipzig Heart Center, Leipzig, Germany

[mm]Department of Cardiac Surgery, Louis Pradel Cardiologic Hospital, Lyon, France

[nn]Department of Cardiac Surgery, Medical Faculty, Heinrich Heine University, Duesseldorf, Germany

[oo]Division of Cardiothoracic and Vascular Surgery, Pontchaillou University Hospital, Rennes, France

[pp]Department of Intensive Care Adults, and Department of cardiology, Erasmus MC, Rotterdam, the Netherlands

[qq]Department of Intensive Care Medicine, Center of Applied Medical Research, St Vincent's Hospital, Darlinghurst, New South Wales, Australia

[rr]Departments of Medicine and Surgery, University of Maryland, Baltimore, Md

[ss]SOD Cardiochirurgia Ospedali Riuniti 'Umberto I - Lancisi - Salesi' Università Politecnica delle Marche, Ancona, Italy

[tt]Cardiothoracic Intensive Care Unit, National University Heart Centre, National University Hospital, Singapore, Singapore

[uu]Cardiac Surgery Unit, Cardiac Thoracic and Vascular Department, Niguarda Hospital, Milan, Italy

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

[ww]ECMO Unit, Departamento de Anestesia, Clínica Las Condes, Las Condes, Santiago, Chile

[xx]2nd Department of Internal Medicine, Cardiovascular Medicine General Teaching Hospital and 1st Faculty of Medicine, Charles University in Prague, Prague, Czech Republic

[yy]Ospedale del Cuore Fondazione Toscana "G. Monasterio," Massa, Italy

APPENDIX E2

Data Collection

The following predefined variables were collected:

—Demographic data: age, sex, race

—Patient characteristics: European System for Cardiac Operative Risk Evaluation, length, weight, serum creatinine level, left ventricular ejection fraction, comorbidities (hypertension, chronic kidney disease requiring dialysis, previous myocardial infarction, previous endocarditis, smoking, previous stroke, atrial fibrillation, previous pulmonary embolism, diabetes mellitus, previous transient ischemic attack, implanted pacemaker, implanted implantable cardioverter defibrillator, previous percutaneous coronary intervention, chronic obstructive pulmonary disease, peripheral artery disease, chronic pulmonary embolism, asthma, pulmonary hypertension, previous cardiac surgery, implanted left ventricular assist device, New York Heart Association class)

—Preoperative status: urgency of the procedure, weight of intervention, planned intervention, preoperative cardiogenic shock, preoperative intubation, preoperative cardiac arrest, preoperative septic shock, preoperative vasopressors, preoperative acute pulmonary oedema, preoperative intra-aortic balloon pump, preoperative right ventricular failure, preoperative biventricular failure

—Diagnosis: coronary artery disease, aortic vessel disease, aortic valve disease, mitral valve disease, tricuspid valve disease, pulmonary valve disease, post-acute myocardial infarction ventricular septal rupture, free wall/papillary muscle rupture, graft failure, active endocarditis, atrial septal defect, post-left ventricular assist device right ventricular failure, other diagnoses

—Coronary surgery: arterial graft, number of distal arterial anastomoses, left internal mammary artery, right internal mammary artery, radial artery, gastroepiploic artery, other arterial graft, venous graft, number of distal venous anastomoses, other coronary surgery

—Valve surgery: valve surgery, aortic valve surgery, aortic valve procedure, mitral valve surgery, mitral valve procedure, pulmonary valve surgery, pulmonary valve procedure, pulmonary valve implant, tricuspid valve surgery, tricuspid valve procedure.

—Aortic surgery: approach to aortic surgery, aortic ascending surgery, aortic arch surgery, descending aortic procedure

—Other cardiac surgeries: cardiac assist device, heart transplantation, rhythm surgery, ventricular septal defect closure, atrial septal defect closure, ventricular surgery, pericardiectomy, pulmonary embolectomy/endarterectomy, other cardiac surgery, other cardiac surgery description.

—Preoperative, intraoperative and postoperative measures: lactates, hemoglobin, hematocrit, platelets, oxygen tension, carbon dioxide tension, bilirubin,

aspartate aminotransferase, alanine aminotransferase, creatinine, urea, creatine kinase, creatine kinase-MB, fluid balance, bleeding in the first 24 hours after surgery, transfusions.

—Extracorporeal circulation: extracorporeal circulation duration, crossclamp duration, circulation arrest, cardioplegia characteristics, off-pump conversion.

—Extracorporeal membrane oxygenation (ECMO) variables: ECMO indication, chest status, cannulation approach, use of left ventricular vent, ECMO duration (hours), configuration change, ECMO monitoring.

—In-hospital outcomes: deceased in hospital, deceased timing, intensive care unit stay (days), hospital stay (days), in-hospital mortality, death timing, postoperative bleeding (requiring rethoracotomy, cannulation site bleeding, diffuse nonsurgical related bleeding), neurologic complications (brain edema, cerebral hemorrhage, seizure, stroke, vasospasm), arrhythmia, leg ischemia, cardiac arrest, pacemaker implant, bowel ischemia, right ventricular failure, acute kidney injury, pneumonia, septic shock, distributive syndrome, acute respiratory distress syndrome, multiorgan failure, embolism

—Postoperative procedures: percutaneous coronary intervention, new cardiac surgery, abdominal surgery, vascular surgery

—Outcomes at follow-up: mortality status, follow-up time

Methods: Variable and outcomes definitions

Variable	Definition
Baseline characteristics	
Hypertension	Systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg,[E1] or use of antihypertensive agents to maintain normal blood pressure
Impaired immunity	Use of immunosuppressant drugs or history of immunosuppressive disorders, including HIV and hematologic malignancies.
Smoking	Active (smoking during the past 30 days) and more than 100 cigarettes during lifetime[E2]
COPD	Diagnosis of chronic obstructive pulmonary disease, any Gold classification[E3]
Peripheral arterial disease	Claudication, carotid occlusion or >50% stenosis, amputation for arterial disease or previous or planned intervention on the abdominal aorta, limb arteries or carotids[E4]
Asthma	Reversible obstructive airway disease for which bronchodilators are currently or intermittently used with or without exacerbations or reduction in FEV1.[E5]
Pulmonary hypertension	Systolic pulmonary artery pressure >50 mm Hg
EuroSCORE II	European System for Cardiac Operative Risk Evaluation II proposing a risk assessment of cardiac surgical procedures which incorporates patient age, sex, diabetic status, pulmonary disease, neurologic function, renal function, presence of active endocarditis, preoperative state, procedural urgency, and procedure type[E4]
NYHA class	Functional class of dyspnea according to the classification as proposed by the New York Heart Association
Preoperative cardiogenic shock	Preoperative state with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, with worsening acidosis and/or lactate levels[E6]
Preoperative cardiac arrest	Preoperative cardiopulmonary resuscitation in the 24 hours before surgery
Preoperative septic shock	Septic patients with vasopressor requirement to maintain MAP >65 mm Hg and serum lactate levels greater than 2 mmol/L in the absence of hypovolemia[E7]
Preoperative right ventricular failure	Evidence of right-sided structural and/or functional abnormalities in combination with clinical symptoms and signs of RV failure[E8]
Preoperative biventricular failure	Biventricular dysfunction accompanied by both signs and symptoms of right-sided and left-sided heart failure[E9]
Emergency surgery	Surgery before the beginning of the next working day after the decision to operate is made[E4]
Urgent surgery	Patients not electively admitted for operation but requiring surgery during the current admission without a possibility to be discharged before undergoing the definite procedure[E4]
Aortic vessel disease	Any disease of the ascending aorta, aortic arch, or proximal descending aorta warranting surgical correction during the current procedure
Aortic valve disease	Any aortic valve disease, including (prosthetic) aortic valve stenosis, regurgitation, and endocarditis
Mitral valve disease	Any mitral valve disease, including (prosthetic) mitral valve stenosis, regurgitation, and endocarditis
Tricuspid valve disease	Any tricuspid valve disease, including (prosthetic) tricuspid valve stenosis, regurgitation, and endocarditis
Pulmonary valve disease	Any pulmonary valve disease, including (prosthetic) pulmonary valve stenosis, regurgitation, and endocarditis

(Continued)

MCS

Continued

Methods: Variable and outcomes definitions	
Variable	**Definition**
Graft failure	Severe ventricular dysfunction of the donor graft, which fails to meet the circulatory requirements of the recipient in the immediate posttransplant period[E10]
Active endocarditis	Patients still on antibiotic treatment for endocarditis at the time of surgery[E4]
Post-LVAD right ventricular failure	RV failure, as described previously in the presence of LVAD
Procedural characteristics	
Ventricular surgery	Surgery performed to restore structural ventricular function, especially in case of ventricular aneurysm formation or rupture
Rhythm surgery	Surgical (either epicardial or endo-epicardial) ablation performed for atrial or ventricular arrhythmia
Details on ECMO	
Failure to wean	Failure to wean from CPB despite preload optimization and completeness of surgery
Arrhythmia	Refractory ventricular arrhythmia with uncontrollable hemodynamic consequences
Cardiac arrest	Abrupt loss of heart function despite acute and simple interventions such as pacing and defibrillation
Cardiogenic shock	State of life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, with worsening acidosis and/or lactate levels[E6]
Right ventricular failure	Evidence of right-sided structural and/or functional abnormalities in combination with clinical symptoms and signs of RV failure[E8]
Respiratory failure	Reversible pulmonary disease which cannot anymore be managed by conventional mechanical ventilation, despite optimization of pharmacological interventions with or without prone positioning
Biventricular failure	Biventricular dysfunction accompanied by both signs and symptoms of right-sided and left-sided heart failure[E9]
Chest closed	Any cannulation condition in which the sternum is closed, irrespective location of cannulas
Chest open	Any cannulation condition in which the sternum is left open irrespective of skin closure
Postoperative outcomes	
Stroke	Neurologic dysfunction caused by focal brain or retinal ischemia with clinical symptoms lasting less more than 24 hours, with or without permanent disability
TIA	A brief episode of neurologic dysfunction caused by focal brain or retinal ischemia with clinical symptoms lasting less than 1 hour, without evidence of acute brain infarction[E11]
Arrhythmia	Any atrial or ventricular arrhythmia lasting more than 30 seconds
Leg ischemia	Clinical signs of lower-extremity ischemia requiring intervention (either by vascular surgery or cannula removal)
Bowel ischemia	Intestinal ischemia with elevated lactate levels requiring abdominal surgical intervention
Acute kidney injury	Postoperative requirement for dialysis while not on dialysis before or duplication of preoperative creatinine levels (and absolute creatinine level >177 μmol/L)
Pneumonia	Any (suspected) pulmonary infection treated with antibiotics
Septic shock	Sepsis with vasopressor requirement to maintain MAP >65 mm Hg and serum lactate levels greater than 2 mmol/L in the absence of hypovolemia[E7]
Distributive shock syndrome	MAP <50 mm Hg with cardiac index >2.5 L/min/m^2, right atrial pressure <5 mm Hg, left atrial pressure <10 mm Hg a low systemic vascular resistance (<800 dyne/s/cm^{-5}) during intravenous norepinephrine infusion (>0.5 μg/kg/min)[E12]
ARDS	Acute diffuse inflammatory lung injury requiring invasive mechanical ventilation of extracorporeal membrane oxygenation
Multiorgan failure	Hypometabolic state with involvement of more than one organ as established by biochemical and/or radiologic analysis

COPD, Chronic obstructive pulmonary disease; *FEV1*, forced expiratory volume in 1 second; *EuroSCORE II*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *MAP*, mean arterial pressure; *LVAD*, left ventricular assist device; *RV*, right ventricle; *ECMO*, extracorporeal membrane oxygenation; *CPB*, cardiopulmonary bypass; *TIA*, transient ischemic attack; *ARDS*, acute respiratory distress syndrome.

E-References

E1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39:3021-104.

E2. Centers for Disease Control and Prevention. Glossary. Accessed February 2, 2022. https://www.cdc.gov/nchs/nhis/tobacco/tobacco_glossary.htm

E3. Global initiative for chronic obstructive lung disease (gold). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2022 Report. Accessed May 23, 2023. https://goldcopd.org/

E4. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734-44; discussion 744-5.

E5. Bousquet J, Mantzouranis E, Cruz AA, Aït-Khaled N, Baena-Cagnani CE, Bleecker ER, et al. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol*. 2010;126:926-38.

E6. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42:3599-726.

E7. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315:801-10.

E8. Gorter TM, van Veldhuisen DJ, Bauersachs J, Borlaug BA, Celutkiene J, Coats AJS, et al. Right heart dysfunction and failure in heart failure with preserved ejection fraction: mechanisms and management. Position statement on behalf of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2018;20:16-37.

E9. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *Eur J Heart Fail*. 2021;23:352-80.

E10. Singh SSA, Dalzell JR, Berry C, Al-Attar N. Primary graft dysfunction after heart transplantation: a thorn amongst the roses. *Heart Fail Rev*. 2019;24:805-20.

E11. Easton JD, Saver JL, Albers GW, Alberts MJ, Chaturvedi S, Feldmann E, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke*. 2009;40:2276-93.

E12. Shanmugam G. Vasoplegic syndrome—the role of methylene blue. *Eur J Cardiothorac Surg*. 2005;28:705-10.

FIGURE E1. Scatter plot representing the yearly contribution of patients from each center taking part in the PELS-1 study. The size of each point represents the number of patients added to the PELS-1 database in that year. *PELS-1*, Postcardiotomy Extracorporeal Life Support Study.

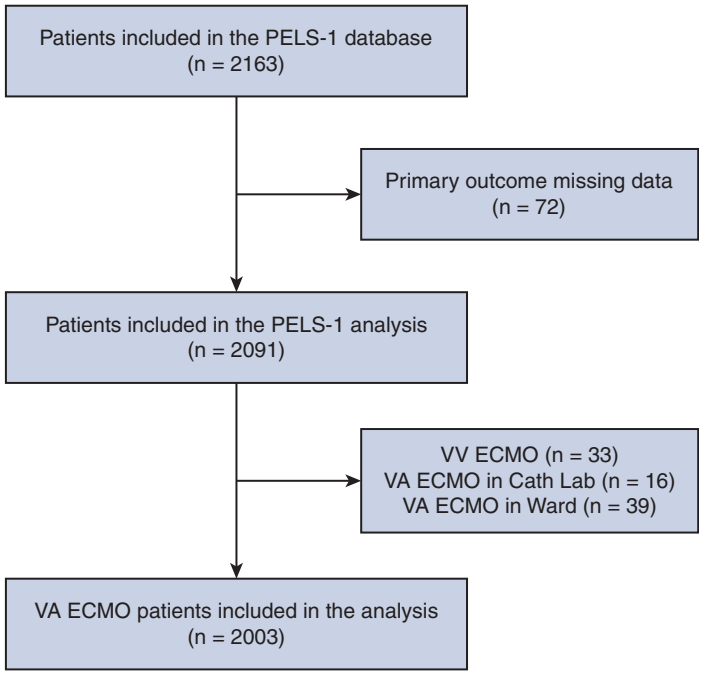


FIGURE E2. Flowchart describing the PELS-1 study database and patients included in the present analysis. *PELS-1*, Postcardiotomy Extracorporeal Life Support Study; *VV ECMO*, Venovenous extracorporeal membrane oxygenation; *VA ECMO*, venoarterial extracorporeal membrane oxygenation.

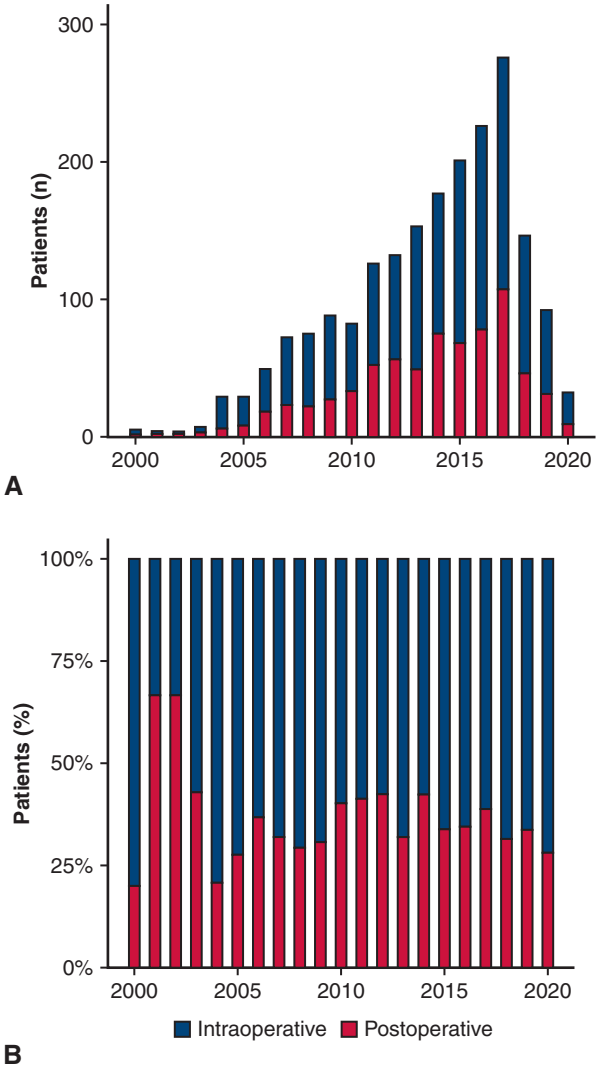


FIGURE E3. Bar chart representing the yearly variations of intraoperative and postoperative use of extracorporeal membrane oxygenation (*ECMO*) reported as absolute numbers (A) and percentages (B).

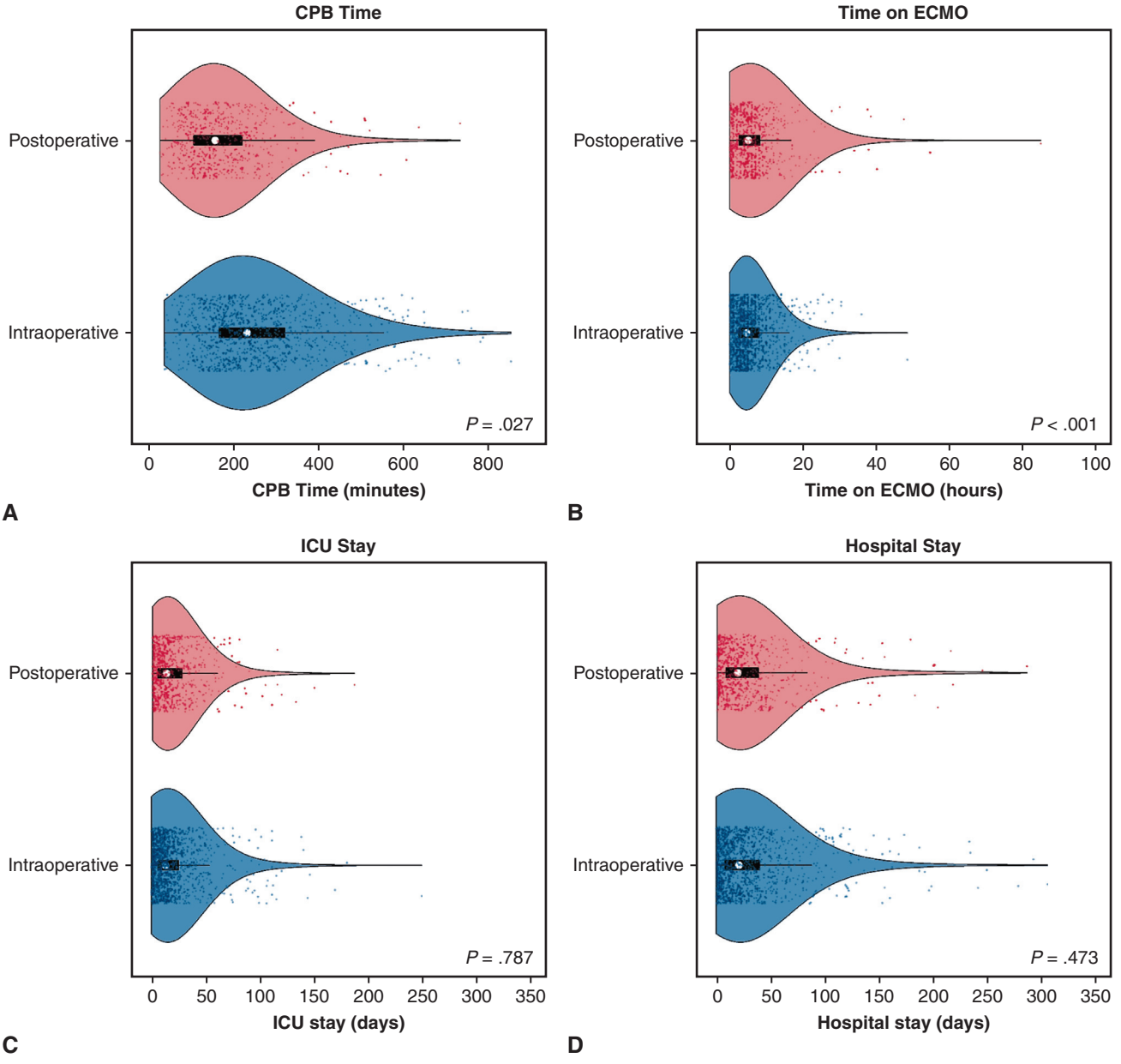
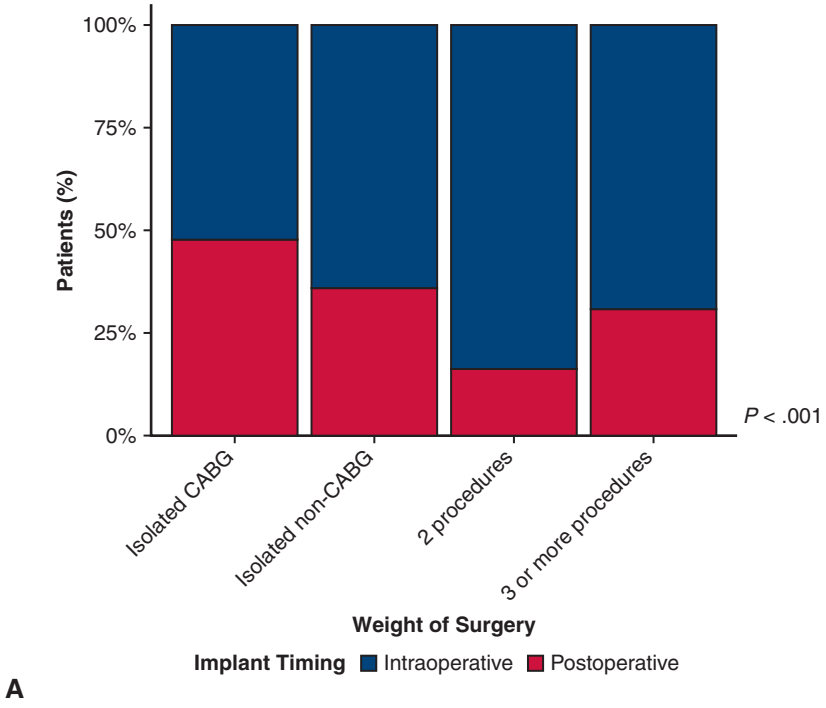
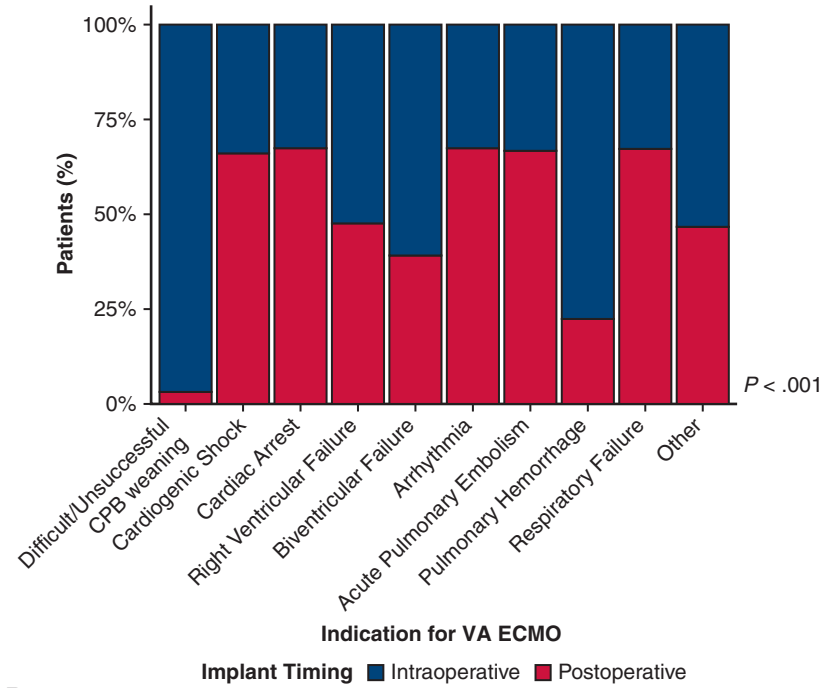


FIGURE E4. Violin plots representing the duration of cardiopulmonary bypass (*CPB*) during surgery (A), the duration of extracorporeal membrane oxygenation (*ECMO*) support (B), the length of stay in intensive care unit (*ICU*, C), and the overall hospital stay (D) of patients who received intraoperative venoarterial extracorporeal membrane oxygenation (*VA ECMO*) implant versus patients who received postoperative VA ECMO implant.



A



B

FIGURE E5. Implantation timing by surgery weight (A) and indication (B). *CABG*, Coronary artery bypass grafting; *CPB*, cardiopulmonary bypass.

MCS

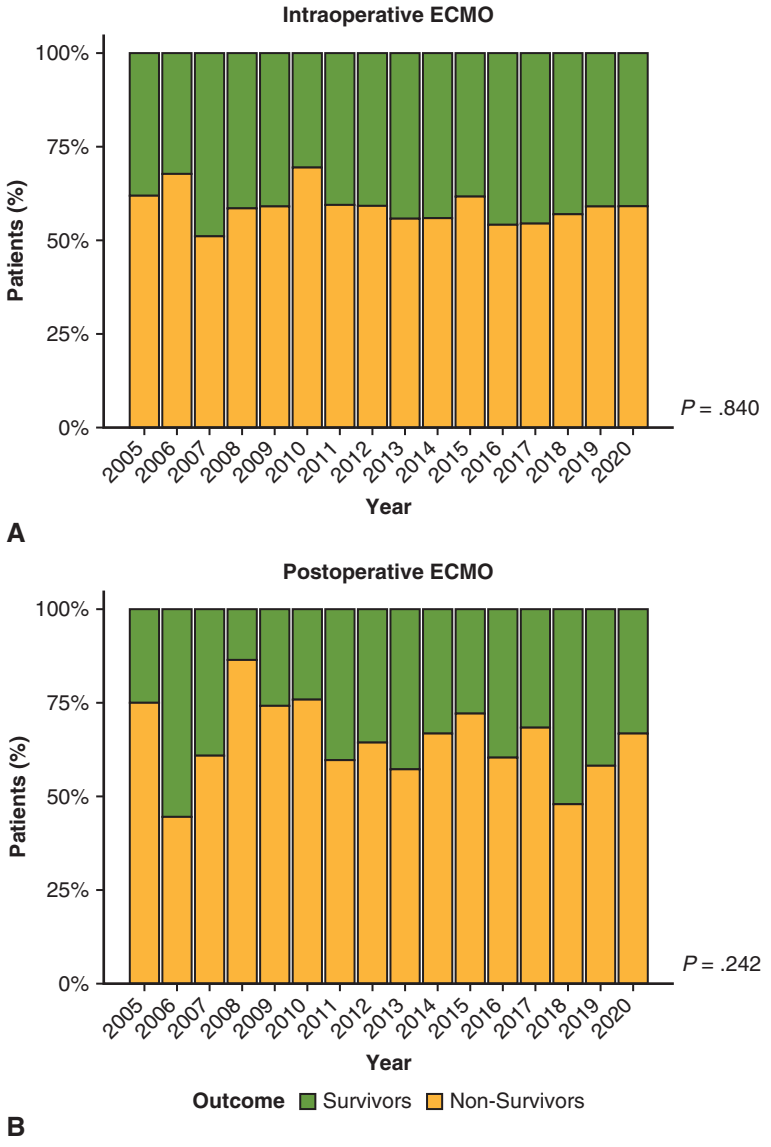


FIGURE E6. In-hospital survival over years in patients who received intraoperative extracorporeal membrane oxygenation (*ECMO*) cannulation (A) and postoperative ECMO cannulation (B).

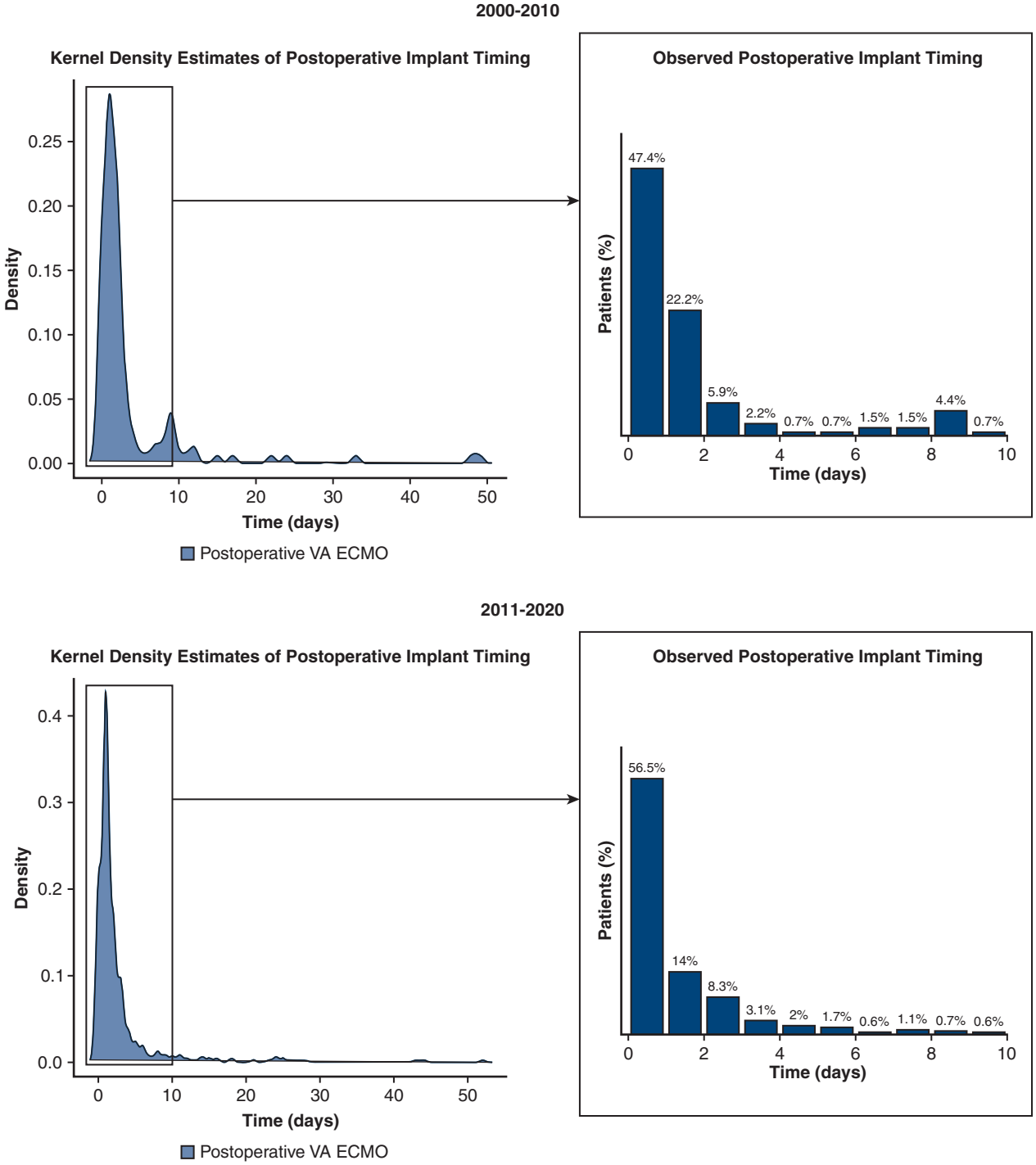


FIGURE E7. Postoperative venoarterial extracorporeal membrane oxygenation (*VA ECMO*) implantation timing stratified by implantation decade (2000-2010 vs 2011-2020).

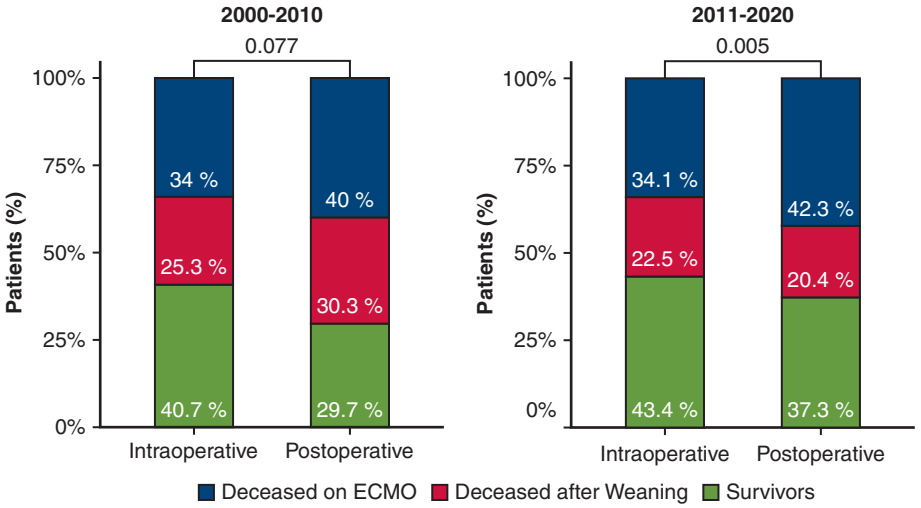


FIGURE E8. Implantation timing survival and death stratified by implantation decade (2000-2010 vs 2011-2020). *ECMO*, Extracorporeal membrane oxygenation.

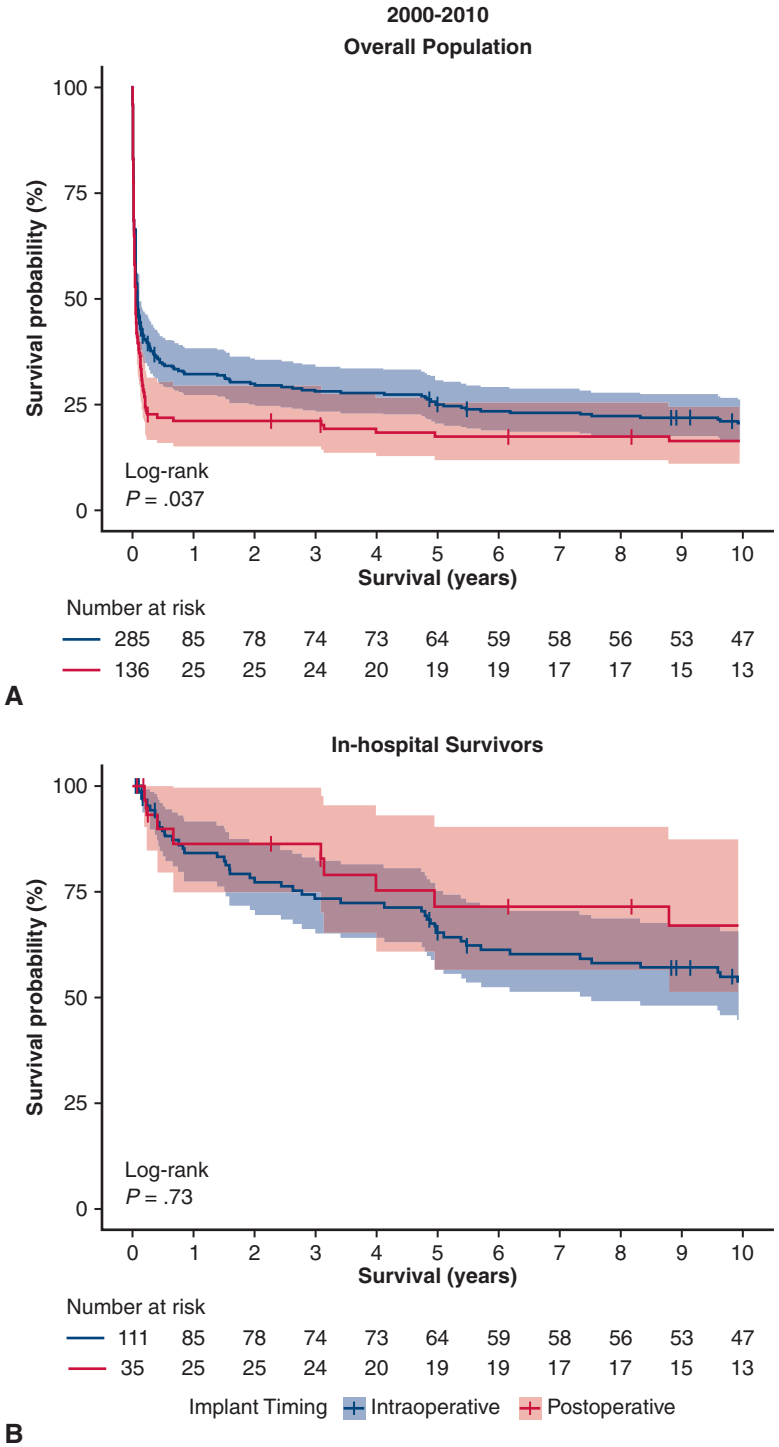
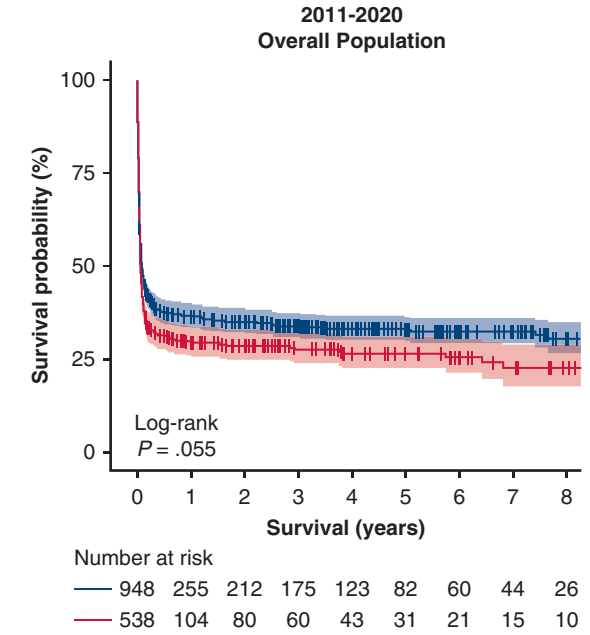


FIGURE E9. Overall (A) and postdischarge (B) Kaplan–Meier survival curves with 95% confidence limit of patients who had venoarterial extracorporeal membrane oxygenation for postcardiotomy support between 2000 and 2010. Groups are defined according to venoarterial extracorporeal membrane oxygenation implantation timing.



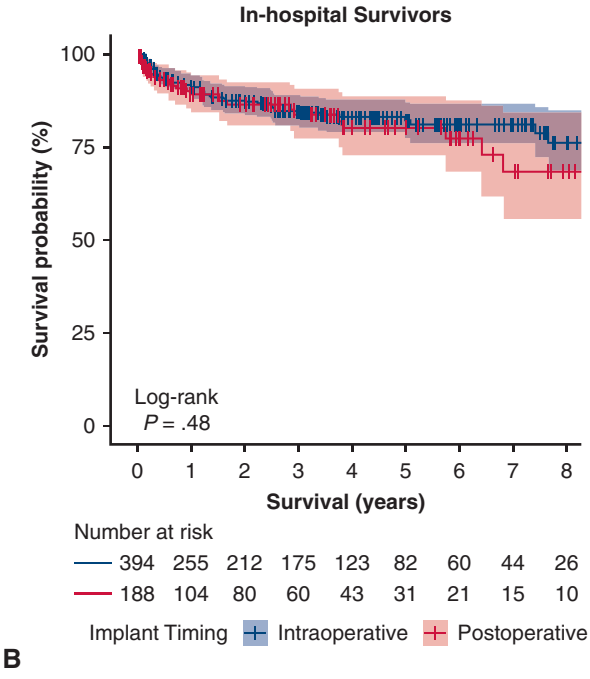


FIGURE E10. Overall (A) and postdischarge (B) Kaplan–Meier survival curves with 95% confidence limit of patients who had venoarterial extracorporeal membrane oxygenation for postcardiotomy support between 2011 and 2020. Groups are defined according to venoarterial extracorporeal membrane oxygenation implantation timing.

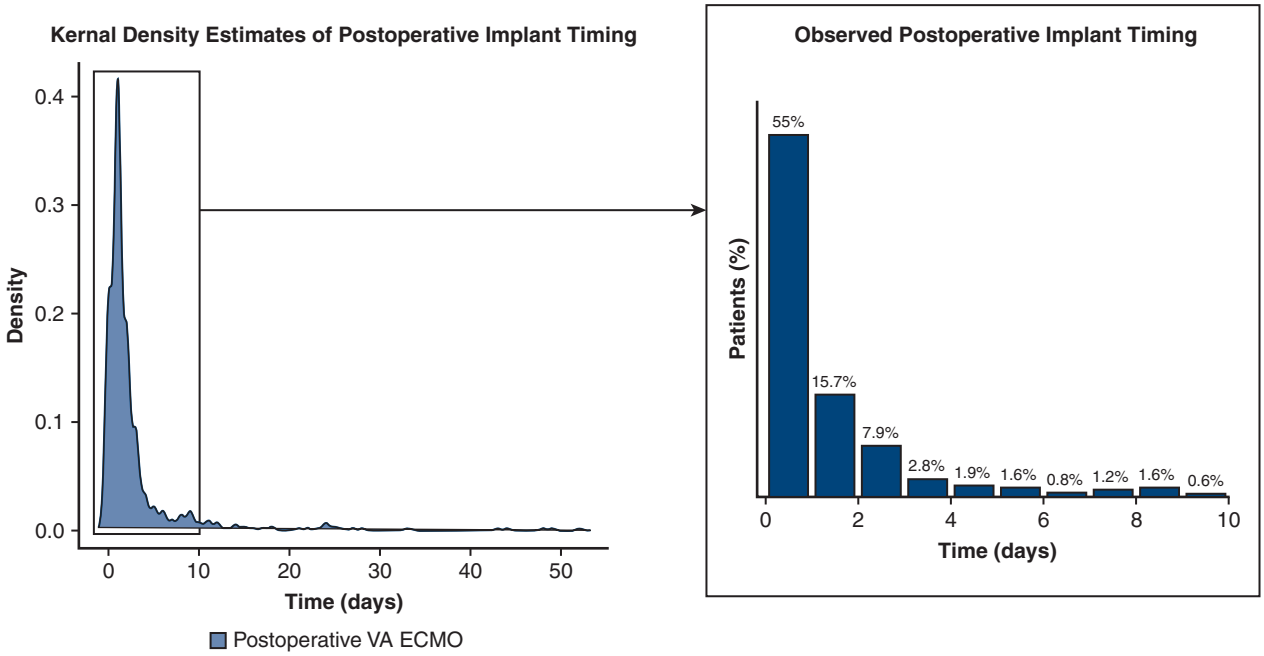


FIGURE E11. Postoperative venoarterial extracorporeal membrane oxygenation (*VA ECMO*) implantation timing after excluding patients who received VA ECMO with indication "failure to wean."

MCS

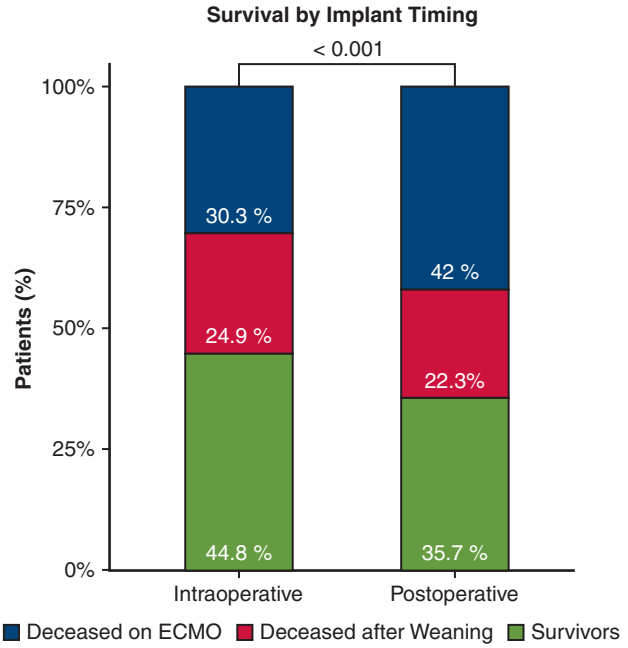


FIGURE E12. Implantation timing survival and death after excluding patients who received a venoarterial extracorporeal membrane oxygenation with indication "failure to wean." *ECMO*, Extracorporeal membrane oxygenation.

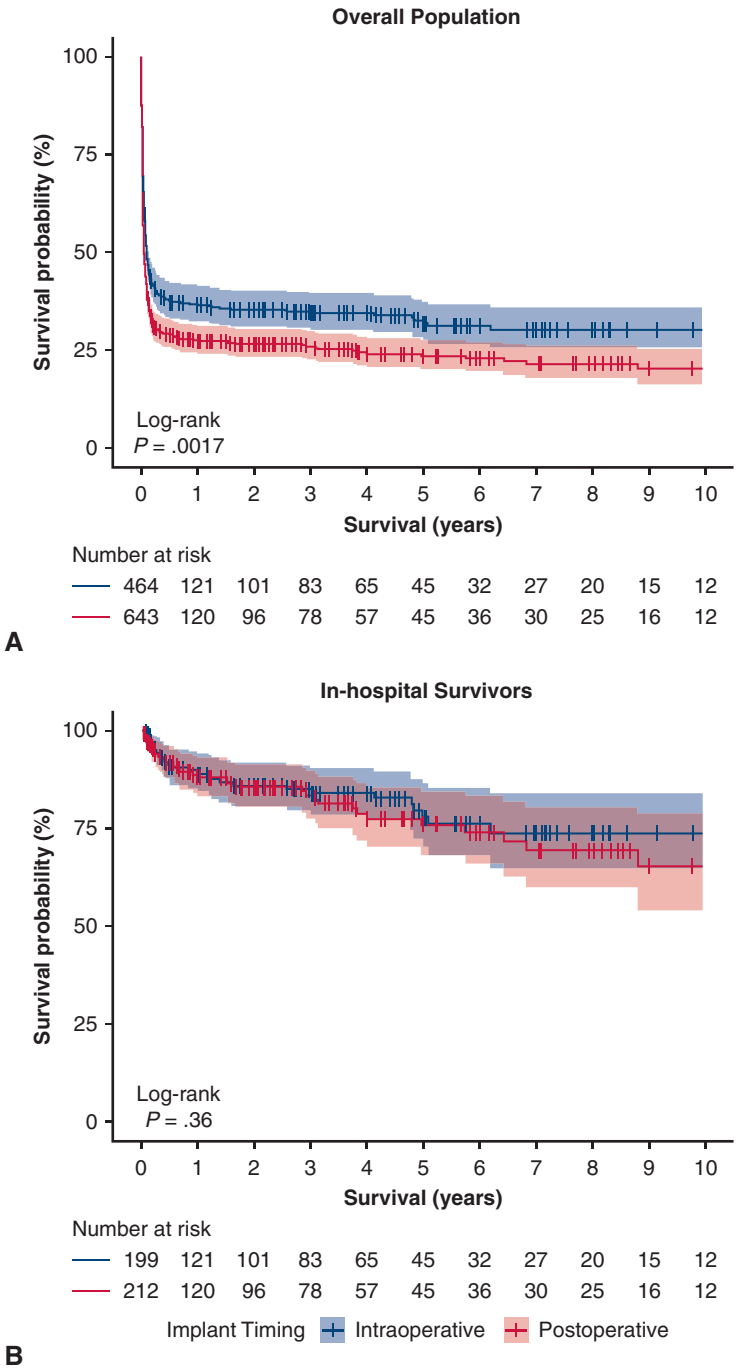


FIGURE E13. Overall (A) and postdischarge (B) Kaplan–Meier survival curves with 95% confidence limit of the study population after excluding patients who received a venoarterial extracorporeal membrane oxygenation with indication "failure to wean."

TABLE E1. Complete and missing cases for each study variable

Variable	Complete cases	Missing cases
Age, y	2002 (99.9%)	1 (0%)
Sex	2002 (99.9%)	1 (0%)
Race	2003 (100%)	0 (0%)
Body mass index, kg/m^2	1992 (99.5%)	11 (0.5%)
Body surface area, m^2	1992 (99.5%)	11 (0.5%)
Comorbidities		
Hypertension	1931 (96.4%)	72 (3.6%)
Dialysis	1936 (96.7%)	67 (3.3%)
Previous myocardial infarction	2003 (100%)	0 (0%)
Myocardial infarction (last 30 d)	1932 (96.5%)	71 (3.5%)
Previous endocarditis	2003 (100%)	0 (0%)
Smoking	1692 (84.5%)	311 (15.5%)
Previous stroke	2003 (100%)	0 (0%)
Atrial fibrillation	2002 (99.9%)	1 (0%)
Previous pulmonary embolism	1815 (90.6%)	188 (9.4%)
Diabetes mellitus	2003 (100%)	0 (0%)
Previous transient ischemic attack	1777 (88.7%)	226 (11.3%)
Implanted pacemaker	1830 (91.4%)	173 (8.6%)
Implanted cardioverter–defibrillator	1837 (91.7%)	166 (8.3%)
Previous percutaneous coronary intervention	1986 (99.2%)	17 (0.8%)
Chronic obstructive pulmonary disease	1919 (95.8%)	84 (4.2%)
Peripheral artery disease	2003 (100%)	0 (0%)
Previous transplant	1932 (96.5%)	71 (3.5%)
Chronic pulmonary embolism	1914 (95.6%)	89 (4.4%)
Asthma	1588 (79.3%)	415 (20.7%)
Pulmonary hypertension (>50 mm Hg)	1989 (99.3%)	14 (0.7%)
Previous cardiac surgery	2003 (100%)	0 (0%)
Implanted left ventricular assist device	1931 (96.4%)	72 (3.6%)
Preoperative creatinine, μmol/L	1860 (92.9%)	143 (7.1%)
Left ventricular ejection fraction (%)	1910 (95.4%)	93 (4.6%)
EuroSCORE II	1412 (70.5%)	591 (29.5%)
Preoperative condition		
NYHA class	1900 (94.9%)	103 (5.1%)
Preoperative cardiogenic shock	1974 (98.6%)	29 (1.4%)
Preoperative intubation	2002 (99.9%)	1 (0%)
Preoperative cardiac arrest	1981 (98.9%)	22 (1.1%)
Preoperative septic shock	1918 (95.8%)	85 (4.2%)
Preoperative vasopressors	1986 (99.8%)	17 (0.8%)
Preoperative acute pulmonary edema	1915 (95.6%)	88 (4.4%)
Preoperative intra-aortic balloon pump	1999 (99.8%)	4 (0.2%)
Preoperative right ventricular failure	1749 (87.3%)	254 (12.7%)
Preoperative biventricular failure	1573 (78.5%)	430 (21.5%)
Emergency surgery	1980 (98.9%)	23 (1.1%)
Urgent surgery	1983 (99.0%)	20 (1.0%)
Diagnosis		
Coronary artery disease	2003 (100%)	0 (0%)
Aortic vessel disease	2003 (100%)	0 (0%)
Aortic valve disease	2003 (100%)	0 (0%)
Mitral valve disease	2003 (100%)	0 (0%)
Tricuspid valve disease	2003 (100%)	0 (0%)
Pulmonary valve disease	2003 (100%)	0 (0%)
Post-AMI ventricular septal rupture	2003 (100%)	0 (0%)

(Continued)

TABLE E1. Continued

Variable	Complete cases	Missing cases
Free wall/papillary muscle rupture	2003 (100%)	0 (0%)
Graft failure	2003 (100%)	0 (0%)
Active endocarditis	2003 (100%)	0 (0%)
Atrial septal defect	2003 (100%)	0 (0%)
Post-left ventricular assist device right ventricular failure	2003 (100%)	0 (0%)
Other diagnosis	2003 (100%)	0 (0%)
Weight of surgery	2003 (100%)	0 (0%)
Coronary artery bypass graft	2003 (100%)	0 (0%)
Aortic valve surgery	2003 (100%)	0 (0%)
Mitral valve surgery	2002 (99.9%)	1 (0%)
Tricuspid valve surgery	2003 (100%)	0 (0%)
Aortic surgery	2003 (100%)	0 (0%)
Pulmonary valve surgery	2003 (100%)	0 (0%)
Left ventricular assist device	2003 (100%)	0 (0%)
Right ventricular assist device	2003 (100%)	0 (0%)
Atrial septal defect repair	2003 (100%)	0 (0%)
Ventricular septal defect repair	2003 (100%)	0 (0%)
Ventricular surgery	2003 (100%)	0 (0%)
Rhythm surgery	2003 (100%)	0 (0%)
Pulmonary embolectomy	2003 (100%)	0 (0%)
Pulmonary endarterectomy	2003 (100%)	0 (0%)
Heart transplantation	2003 (100%)	0 (0%)
Off-pump surgery	1969 (98.3%)	34 (1.7%)
Cardiopulmonary bypass time, min	1825 (91.1%)	178 (8.9%)
Crossclamp time, min	1812 (90.5%)	191 (9.5%)
Intraoperative lactate, mmol/L	753 (37.6%)	1250 (62.4%)
Intraoperative transfusions	809 (40.4%)	1194 (59.6%)
Extracorporeal membrane oxygenation indication	1956 (97.7%)	47 (2.3%)
Cannulation approach	2003 (100%)	0 (0%)
Extracorporeal membrane oxygenation duration, h	1825 (91.1%)	178 (8.9%)
Intensive care unit stay, d	1920 (95.9%)	83 (4.1%)
Hospital stay, d	1932 (96.5%)	71 (3.5%)
Postoperative bleeding	1966 (98.2%)	37 (1.8%)
Requiring rethoracotomy	1870 (93.4%)	133 (6.6%)
Cannulation site bleeding	1966 (98.2%)	37 (1.8%)
Diffuse—no surgical-related bleeding	1803 (90.0%)	200 (10%)
Neurologic complications		
Brain edema	1898 (94.8%)	105 (5.2%)
Cerebral hemorrhage	1895 (94.6%)	108 (4.5%)
Seizure	1897 (94.7%)	106 (5.3%)
Stroke	1990 (99.4%)	13 (0.6%)
Vasospasm	1580 (78.9%)	423 (21.1%)
Arrhythmia	1836 (91.7%)	167 (8.3%)
Leg ischemia	1892 (94.5%)	111 (5.5%)
Cardiac arrest	1836 (91.7%)	167 (8.3%)

(Continued)

TABLE E1. Continued

Variable	Complete cases	Missing cases
Pacemaker implant	1836 (91.7%)	167 (8.3%)
Bowel ischemia	1837 (91.7%)	166 (8.3%)
Right ventricular failure	1797 (89.7%)	206 (10.3%)
Acute kidney injury	1830 (91.4%)	173 (8.6%)
Pneumonia	1796 (89.7%)	207 (10.3%)
Septic shock	1794 (89.6%)	209 (10.4%)
Distributive syndrome	1793 (89.5%)	210 (10.5%)
Acute respiratory distress syndrome	1836 (91.7%)	167 (8.3%)
Multiorgan failure	1976 (98.7%)	27 (1.3%)
Embolism	1797 (89.7%)	206 (10.3%)
Postoperative procedures		
Percutaneous coronary intervention	1758 (87.8%)	245 (12.2%)
Cardiac surgery	1837 (91.7%)	166 (8.3%)
Abdominal surgery	1758 (87.8%)	245 (12.2%)
Vascular surgery	1762 (88.0%)	241 (12%)
In-hospital mortality	2003 (100%)	0 (0%)
In-hospital mortality - timing	1989 (99.3%)	14 (0.7%)

EuroSCORE II, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *AMI*, acute myocardial infarction.

TABLE E2. Baseline characteristics of the overall population stratified according to venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing groups and survivors and nonsurvivors

Variable	Intraoperative VA ECMO (n = 1287)			Postoperative VA ECMO (n = 716)		
	Survivors (n = 547)	Nonsurvivors (n = 740)	*P* value	Survivors (n = 254)	Nonsurvivors (n = 462)	*P* value
Age, y	61.00 (52-69)	67.00 (58-73)	<.001	64.00 (54-71.2)	66.19 (58-73)	.009
Sex			.776			.064
Female	236 (43.1%)	313 (42.3%)		85 (33.6%)	189 (40.9%)	
Male	311 (56.9%)	427 (57.7%)		168 (66.4%)	273 (59.1%)	
Race			<.001			.173
Asian	20 (4.2%)	62 (10.3%)		15 (8.7%)	40 (13%)	
Black	2 (0.4%)	3 (0.5%)		3 (1.7%)	3 (1%)	
Hispanic	18 (3.8%)	11 (1.8%)		5 (2.9%)	19 (6.2%)	
White	376 (79%)	475 (78.6%)		136 (78.6%)	231 (75%)	
Other	24 (5%)	16 (2.6%)		6 (3.5%)	4 (1.3%)	
Unknown	36 (7.6%)	37 (6.1%)		8 (4.6%)	11 (3.6%)	
BMI, kg/m^2	26.6 ± 0.2	27.0 ± 0.2	<.001	27.1 ± 0.3	27.7 ± 0.3	.861
BSA, m^2	1.9 ± 0.01	1.9 ± 0.01	.343	1.9 ± 0.02	1.9 ± 0.01	.603
Comorbidities						
Hypertension	318 (60.2%)	468 (65.7%)	.049	159 (65.4%)	322 (71.9%)	.084
Dialysis	47 (8.9%)	63 (9%)	1.000	17 (6.8%)	41 (8.9%)	.390
Previous myocardial infarction	158 (28.9%)	192 (25.9%)	.254	78 (30.7%)	111 (24%)	.063
Myocardial infarction (last 30 d)	70 (13.2%)	85 (11.9%)	.543	24 (9.9%)	47 (10.5%)	.896
Previous endocarditis	48 (8.8%)	61 (8.2%)	.762	15 (5.9%)	32 (6.9%)	.640
Smoking	125 (28.7%)	163 (26.9%)	.528	74 (33.2%)	98 (23%)	.007
Previous stroke	68 (12.4%)	107 (14.5%)	.324	34 (13.4%)	69 (14.9%)	.656
Atrial fibrillation	117 (21.4%)	191 (25.8%)	.065	81 (31.9%)	145 (31.4%)	.933
Previous pulmonary embolism	4 (0.8%)	17 (2.6%)	.042	2 (0.9%)	9 (2.1%)	.345
Diabetes mellitus	112 (20.5%)	198 (26.8%)	.010	60 (23.6%)	128 (27.7%)	.249
Previous TIA	11 (2.4%)	14 (2.2%)	.841	7 (3%)	8 (1.8%)	.415
Implanted pacemaker	36 (7.4%)	52 (7.7%)	.911	12 (5.1%)	35 (8%)	.204
Implanted ICD	71 (14.5%)	52 (7.7%)	<.001	25 (10.6%)	32 (7.3%)	.150
Previous PCI	103 (19%)	123 (16.8%)	.335	44 (17.3%)	73 (15.9%)	.673
COPD	46 (9%)	86 (12.2%)	.092	21 (8.5%)	49 (10.7%)	.360
Peripheral artery disease	65 (11.9%)	113 (15.3%)	.087	32 (12.6%)	81 (17.5%)	.087
Previous transplant	13 (2.5%)	22 (3.1%)	.604	9 (3.7%)	27 (6%)	.213
Chronic pulmonary embolism	10 (1.9%)	19 (2.7%)	.449	6 (2.5%)	6 (1.3%)	.360
Asthma	7 (1.8%)	5 (0.9%)	.247	4 (1.9%)	7 (1.7%)	1.000
Pulmonary hypertension (>50 mm Hg)	111 (20.6%)	174 (23.6%)	.221	45 (17.7%)	91 (19.8%)	.551
Previous cardiac surgery	157 (28.7%)	221 (29.9%)	.665	51 (20.1%)	103 (22.3%)	.507
Implanted LVAD	35 (6.6%)	19 (2.7%)	.001	10 (4.1%)	8 (1.8%)	.081
Preoperative creatinine, μmol/L	100.40 (80.4-132)	106.10 (82.2-152.1)	.010	95.47 (75.1-123.2)	100.89 (79.6-139.7)	.047
LVEF, %	40.00 (25-60)	46.00 (30-60)	.005	45.00 (30-60)	50.00 (35-60)	.013
EuroSCORE II	7.55 (3.2-18.3)	11.26 (4-25.2)	<.001	3.92 (1.9-10.7)	5.19 (2.2-13.5)	.089
Preoperative condition			.010			
NYHA class			.073			.729
Class I	47 (9.1%)	40 (5.7%)		21 (8.6%)	33 (7.5%)	
Class II	105 (20.3%)	142 (20.3%)		59 (24.3%)	100 (22.7%)	

(Continued)

TABLE E2. Continued

Variable	Intraoperative VA ECMO (n = 1287)			Postoperative VA ECMO (n = 716)		
	Survivors (n = 547)	Nonsurvivors (n = 740)	*P* value	Survivors (n = 254)	Nonsurvivors (n = 462)	*P* value
Class III	171 (33.1%)	266 (38.1%)		110 (45.3%)	196 (44.4%)	
Class IV	194 (37.5%)	251 (35.9%)		53 (21.8%)	112 (25.4%)	
Preoperative cardiogenic shock	103 (19.4%)	184 (25.2%)	.017	38 (15.1%)	98 (21.4%)	.046
Preoperative intubation	57 (10.4%)	110 (14.9%)	.023	17 (6.7%)	43 (9.3%)	.261
Preoperative cardiac arrest	46 (8.5%)	80 (11%)	.155	19 (7.6%)	38 (8.3%)	.775
Preoperative septic shock	4 (0.8%)	26 (3.7%)	.001	6 (2.5%)	14 (3.1%)	.813
Preoperative vasopressors	87 (16.1%)	145 (19.8%)	.106	21 (8.3%)	55 (12%)	.163
Preoperative acute pulmonary oedema	42 (8.1%)	64 (9.1%)	.607	9 (3.7%)	23 (5.1%)	.453
Preoperative IABP	51 (9.4%)	83 (11.2%)	.310	18 (7.1%)	38 (8.2%)	.664
Preoperative right ventricular failure	44 (9.6%)	82 (13.1%)	.085	18 (7.8%)	36 (8.3%)	.882
Preoperative biventricular failure	39 (10.2%)	44 (7.9%)	.243	10 (4.7%)	27 (6.4%)	.474
Emergency surgery	136 (25.4%)	217 (29.7%)	.099	54 (21.4%)	109 (23.6%)	.576
Urgent surgery	143 (26.6%)	178 (24.3%)	.361	43 (17.1%)	74 (16%)	.751
Diagnosis						
Coronary artery disease	247 (45.2%)	346 (46.8%)	.572	136 (53.5%)	232 (50.2%)	.435
Aortic vessel disease	78 (14.3%)	142 (19.2%)	.020	29 (11.4%)	79 (17.1%)	.049
Aortic valve disease	158 (28.9%)	288 (38.9%)	<.001	62 (24.4%)	172 (37.2%)	<.001
Mitral valve disease	161 (29.4%)	270 (36.5%)	.009	80 (31.5%)	174 (37.7%)	.103
Tricuspid valve disease	62 (11.3%)	121 (16.4%)	.012	46 (18.1%)	88 (19%)	.841
Pulmonary valve disease	5 (0.9%)	7 (0.9%)	1.000	3 (1.2%)	2 (0.4%)	.353
Post-AMI ventricular septal rupture	20 (3.7%)	28 (3.8%)	1.000	5 (2%)	5 (1.1%)	.338
Free wall/Papillary muscle rupture	10 (1.8%)	19 (2.6%)	.450	3 (1.2%)	6 (1.3%)	1.000
Graft failure	51 (9.3%)	27 (3.6%)	<.001	11 (4.3%)	4 (0.9%)	.004
Active endocarditis	41 (7.5%)	63 (8.5%)	.536	10 (3.9%)	28 (6.1%)	.296
Atrial septal defect	11 (2%)	10 (1.4%)	.380	4 (1.6%)	8 (1.7%)	1.000
Post-LVAD right ventricular failure	10 (1.8%)	6 (0.8%)	.128	1 (0.4%)	2 (0.4%)	1.000
Other diagnosis	76 (13.9%)	79 (10.7%)	.084	41 (16.1%)	59 (12.8%)	.217

Data are reported as n (% as valid percentage excluding missing values), mean ± standard deviation, or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between survivors and nonsurvivor groups. *BMI*, Body mass index; *BSA*, body surface area; *TIA*, transient ischemic attack; *ICD*, implantable cardioverter defibrillator; *PCI*, percutaneous coronary intervention; *COPD*, chronic obstructive pulmonary disease; *LVAD*, left ventricular assist device; *LVEF*, left ventricular ejection fraction; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *IABP*, intra-aortic balloon pump; *AMI*, acute myocardial infarction.

TABLE E3. Procedural characteristics stratified according to venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing groups and survivors and nonsurvivors

Variable	Intraoperative VA ECMO (n = 1287)			Postoperative VA ECMO (n = 716)		
	Survivors (n = 547)	Nonsurvivors (n = 740)	*P* value	Survivors (n = 254)	Nonsurvivors (n = 462)	*P* value
Weight of surgery			<.001			.121
Unknown	5 (0.9%)	2 (0.3%)		1 (0.4%)	5 (1.1%)	
Isolated CABG	91 (16.6%)	92 (12.4%)		72 (28.3%)	96 (20.8%)	
Isolated non-CABG	321 (58.7%)	396 (53.5%)		139 (54.7%)	265 (57.4%)	
Two procedures	52 (9.5%)	71 (9.6%)		9 (3.5%)	15 (3.2%)	
Three or more procedures	78 (14.3%)	179 (24.2%)		33 (13%)	81 (17.5%)	
CABG	225 (41.1%)	333 (45%)	.172	120 (47.2%)	207 (44.8%)	.532
Aortic valve surgery	165 (30.2%)	294 (39.7%)	<.001	59 (23.2%)	175 (37.9%)	<.001
Mitral valve surgery	149 (27.3%)	260 (35.1%)	.003	71 (28%)	155 (33.5%)	.131
Tricuspid valve surgery	51 (9.3%)	113 (15.3%)	.002	31 (12.2%)	75 (16.2%)	.153
Aortic surgery	92 (16.8%)	168 (22.7%)	.009	29 (11.4%)	84 (18.2%)	.018
Pulmonary valve surgery	3 (0.5%)	5 (0.7%)	1.000	3 (1.2%)	1 (0.2%)	.130
LVAD	7 (1.3%)	10 (1.4%)	1.000	1 (0.4%)	5 (1.1%)	.431
RVAD	2 (0.4%)	3 (0.4%)	1.000	0 (0%)	1 (0.2%)	1.000
ASD repair	11 (2%)	12 (1.6%)	.672	4 (1.6%)	11 (2.4%)	.591
VSD repair	21 (3.8%)	33 (4.5%)	.674	7 (2.8%)	7 (1.5%)	.268
Ventricular surgery	10 (1.8%)	35 (4.7%)	.005	10 (3.9%)	19 (4.1%)	1.000
Rhythm surgery	15 (2.7%)	26 (3.5%)	.522	10 (3.9%)	15 (3.2%)	.673
Pulmonary embolectomy	6 (1.1%)	9 (1.2%)	1.000	4 (1.6%)	4 (0.9%)	.464
Pulmonary endarterectomy	11 (2%)	25 (3.4%)	.172	4 (1.6%)	7 (1.5%)	1.000
Heart transplantation	102 (18.6%)	52 (7%)	<.001	28 (11%)	23 (5%)	.004
Off-pump surgery	17 (3.2%)	16 (2.2%)	.286	17 (6.8%)	29 (6.3%)	.873
Conversion to CPB	5 (29.4%)	9 (56.3%)	.166	2 (10.5%)	8 (26.7%)	.278
CPB time (min)	216.00 (164-299)	249.00 (173-339)	<.001	152.00 (107-211)	162.00 (109-229)	.146
Crossclamp time, min	97.00 (65-137)	114.00 (70-168)	<.001	89.00 (54-128)	90.00 (62-138)	.216
Intraoperative lactate, mmol/L*	5.45 (3.4-8.1)	6.40 (4.3-11)	.001	3.00 (1.8-5.9)	4.00 (1.9-7.3)	.060
Intraoperative transfusions*	196 (89.9%)	301 (93.8%)	.105	76 (92.7%)	173 (92%)	1.000

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between survivor and nonsurvivor groups. *CABG*, Coronary artery bypass graft; *LVAD*, left ventricular assist device; *RVAD*, right ventricular assist device; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass. *Variable with >50% missing data.

TABLE E4. Details on extracorporeal membrane oxygenation (ECMO) stratified according to venoarterial ECMO implantation timing groups and survivors and nonsurvivors

Variable	Intraoperative VA ECMO (n = 1287)		*P* value	Postoperative VA ECMO (n = 716)		*P* value
	Survivors (n = 547)	Nonsurvivors (n = 740)		Survivors (n = 254)	Nonsurvivors (n = 462)	
ECMO indication			.092			.481
Failure to wean	309 (58.9%)	455 (62.8%)		9 (3.6%)	15 (3.3%)	
Acute pulmonary embolism	0 (0%)	1 (0.1%)		1 (0.4%)	1 (0.2%)	
Arrhythmia	9 (1.7%)	4 (0.6%)		15 (6%)	12 (2.6%)	
Cardiac arrest	22 (4.2%)	27 (3.7%)		35 (14%)	66 (14.5%)	
Cardiogenic shock	65 (12.4%)	100 (13.8%)		104 (41.6%)	216 (47.4%)	
Pulmonary hemorrhage	5 (1%)	2 (0.3%)		1 (0.4%)	1 (0.2%)	
Right ventricular failure	56 (10.7%)	67 (9.2%)		43 (17.2%)	69 (15.1%)	
Respiratory failure	12 (2.3%)	11 (1.5%)		17 (6.8%)	30 (6.6%)	
Biventricular failure	36 (6.9%)	53 (7.3%)		18 (7.2%)	39 (8.6%)	
Other	11 (2.1%)	5 (0.7%)		7 (2.8%)	7 (1.5%)	
Cannulation approach			.014			.086
Only central cannulation	81 (14.8%)	157 (21.2%)		25 (9.8%)	70 (15.2%)	
Only peripheral cannulation	242 (44.2%)	307 (41.5%)		149 (58.7%)	232 (50.2%)	
Mixed/switch cannulation	211 (38.6%)	267 (36.1%)		75 (29.5%)	146 (31.6%)	
Unknown	13 (2.4%)	9 (1.2%)		5 (2%)	14 (3%)	
ECMO duration, h	104.00 (67.8-164.2)	120.00 (48-216)	.371	139.67 (95.8-192)	120.00 (43.4-205.2)	.013

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between the survivor and nonsurvivor groups. *VA*, Venoarterial.

TABLE E5. Postoperative outcomes stratified according to venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing groups and survivors and nonsurvivors

Variable	Intraoperative VA ECMO (n = 1287)			Postoperative VA ECMO (n = 716)		
	Survivors (n = 547)	Nonsurvivors (n = 740)	*P* value	Survivors (n = 254)	Nonsurvivors (n = 462)	*P* value
ICU stay, d	20.00 (13-35)	8.00 (3-18)	<.001	24.00 (15-37)	9.00 (4-18)	<.001
Hospital stay, d	37.00 (26-60)	10.00 (4-21.5)	<.001	39.00 (26-61)	12.00 (5-23)	<.001
Postoperative bleeding	237 (44.7%)	459 (63%)	<.001	141 (56.4%)	288 (63%)	.091
Requiring rethoracotomy	155 (31.9%)	322 (46.3%)	<.001	97 (40.2%)	175 (39.1%)	.807
Cannulation site bleeding	44 (8.3%)	99 (13.6%)	.003	29 (11.6%)	65 (14.3%)	.355
Diffuse nonsurgical-related bleeding	73 (15%)	182 (28.3%)	<.001	62 (26.4%)	142 (32.5%)	.113
Neurologic complications						
Brain edema	9 (1.7%)	45 (6.4%)	<.001	6 (2.5%)	21 (4.8%)	.157
Cerebral hemorrhage	13 (2.5%)	21 (3%)	.726	9 (3.7%)	19 (4.3%)	.841
Seizure	11 (2.1%)	14 (2%)	1.000	4 (1.7%)	9 (2.1%)	1.000
Stroke	61 (11.2%)	77 (10.4%)	.716	33 (13%)	41 (9.1%)	.124
Vasospasm	0 (0%)	1 (0.2%)	1.000	0 (0%)	1 (0.2%)	1.000
Arrhythmia	166 (33.8%)	177 (26.2%)	.005	104 (44.3%)	150 (34.6%)	.016
Leg ischemia	37 (7.2%)	79 (11.4%)	.014	18 (7.4%)	55 (12.4%)	.052
Cardiac arrest	30 (6.1%)	100 (14.8%)	<.001	36 (15.2%)	117 (27%)	<.001
Pacemaker implant	30 (6.1%)	7 (1%)	<.001	10 (4.3%)	9 (2.1%)	.142
Bowel ischemia	7 (1.4%)	49 (7.2%)	<.001	6 (2.6%)	43 (9.9%)	<.001
Right ventricular failure	49 (10.4%)	162 (24.6%)	<.001	37 (15.9%)	132 (30.5%)	<.001
Acute kidney injury	241 (49.8%)	414 (61.4%)	<.001	117 (49.8%)	265 (60.6%)	.007
Pneumonia	128 (27.1%)	119 (18.1%)	<.001	66 (28.4%)	92 (21.2%)	.045
Septic shock	36 (7.6%)	125 (19%)	<.001	34 (14.7%)	101 (23.3%)	.009
Distributive syndrome	21 (4.5%)	83 (12.6%)	<.001	9 (3.9%)	59 (13.7%)	<.001
ARDS	16 (3.3%)	37 (5.5%)	.087	15 (6.4%)	32 (7.4%)	.752
MOF	26 (4.9%)	379 (51.9%)	<.001	18 (7.1%)	256 (55.9%)	<.001
Embolism	24 (5.1%)	46 (7%)	.212	15 (6.5%)	27 (6.2%)	1.000
Postoperative procedures						
PCI	9 (2%)	11 (1.7%)	.820	12 (5.2%)	12 (2.8%)	.128
Cardiac surgery	87 (17.7%)	143 (21.2%)	.157	55 (23.4%)	111 (25.6%)	.574
Abdominal surgery	13 (2.9%)	24 (3.7%)	.499	14 (6.1%)	28 (6.5%)	1.000
Vascular surgery	57 (12.5%)	59 (9.1%)	.074	35 (15.2%)	49 (11.4%)	.178

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between survivor and nonsurvivor groups. *ICU*, Intensive care unit; *ARDS*, acute respiratory distress syndrome; *MOF*, multiorgan failure; *PCI*, percutaneous coronary intervention.

TABLE E6. Baseline characteristics of the overall population stratified according to implantation decade (2000-2010 vs 2011-2020) and venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing

Variable	2000-2010 (n = 442)			2011-2020 (n = 1561)		
	Intraoperative (n = 297)	Postoperative (n = 145)	*P* value	Intraoperative (n = 990)	Postoperative (n = 571)	*P* value
Age, y	**64.00 (55-70.6)**	**65.44 (56.5-71)**	**.290**	**65.00 (55-72)**	**66.00 (56.2-72.2)**	**.090**
Sex			.189			.196
Female	149 (50.2%)	63 (43.4%)		400 (40.4%)	211 (37%)	
Male	148 (49.8%)	82 (56.6%)		590 (59.6%)	359 (63%)	
Race			**.107**			.004
Asian	**4 (1.6%)**	**4 (5.2%)**		78 (9.3%)	51 (12.6%)	
Black	**0 (0%)**	**0 (0%)**		5 (0.6%)	6 (1.5%)	
Hispanic	**2 (0.8%)**	**0 (0%)**		27 (3.2%)	24 (5.9%)	
White	**220 (89.8%)**	**70 (90.9%)**		631 (75.6%)	297 (73.5%)	
Other	**12 (4.9%)**	**0 (0%)**		28 (3.4%)	10 (2.5%)	
Unknown	**7 (2.9%)**	**3 (3.9%)**		66 (7.9%)	16 (4%)	
BMI, kg/m^2	**26.83 (23.8-30.4)**	**25.95 (23.4-29.1)**	**.206**	26.04 (23.4-29.4)	26.99 (23.8-30.9)	.001
BSA, m^2	**1.89 (1.7-2)**	**1.83 (1.7-2)**	**.014**	1.89 (1.8-2)	1.90 (1.7-2.1)	.367
Comorbidities						
Hypertension	**177 (60.2%)**	**88 (62.4%)**	**.676**	609 (64.4%)	393 (71.5%)	.005
Dialysis	23 (8.6%)	5 (3.5%)	.063	87 (9.1%)	53 (9.4%)	.855
Previous myocardial infarction	88 (29.6%)	36 (24.8%)	.312	262 (26.5%)	153 (26.8%)	.905
Myocardial infarction (last 30 d)	**49 (16.7%)**	**9 (6.4%)**	**.003**	106 (11.2%)	62 (11.3%)	1.000
Previous endocarditis	16 (5.4%)	7 (4.8%)	1.000	93 (9.4%)	40 (7%)	.110
Smoking	67 (34.4%)	33 (26.6%)	.173	221 (26.1%)	139 (26.4%)	.900
Previous stroke	39 (13.1%)	27 (18.6%)	.155	136 (13.7%)	76 (13.3%)	.878
Atrial fibrillation	**73 (24.6%)**	**47 (32.4%)**	**.088**	235 (23.8%)	179 (31.3%)	.001
Previous pulmonary embolism	6 (2.2%)	2 (1.4%)	.724	15 (1.7%)	9 (1.7%)	1.000
Diabetes mellitus	82 (27.6%)	30 (20.7%)	.131	**228 (23%)**	**158 (27.7%)**	**.044**
Previous TIA	5 (2.7%)	1 (0.8%)	.407	20 (2.2%)	14 (2.6%)	.720
Implanted pacemaker	21 (7.6%)	8 (5.8%)	.683	67 (7.6%)	39 (7.3%)	.836
Implanted ICD	27 (9.7%)	16 (11.6%)	.609	96 (10.8%)	41 (7.7%)	.052
Previous PCI	44 (15.1%)	26 (18.1%)	.488	182 (18.6%)	91 (16%)	.213
COPD	46 (16.7%)	13 (9.2%)	.053	86 (9.2%)	57 (10.1%)	.586
Peripheral artery disease	51 (17.2%)	25 (17.2%)	1.000	127 (12.8%)	88 (15.4%)	.170
Pulmonary hypertension (>50 mm Hg)	80 (27.4%)	28 (19.3%)	.077	205 (20.9%)	108 (19%)	.394
Previous cardiac surgery	**95 (32%)**	**34 (23.4%)**	**.075**	283 (28.6%)	120 (21%)	<.001
Implanted LVAD	10 (3.4%)	3 (2.1%)	.561	44 (4.7%)	15 (2.7%)	.073
Preoperative creatinine, μmol/L	106.10 (88.4-165)	97.02 (79.6-123.8)	<.001	**101.68 (80-139)**	**99.00 (77.8-135.3)**	**.126**
LVEF, %	40.00 (22-60)	51.00 (30-60)	<.001	45.00 (30-60)	50.00 (30.5-60)	.042
EuroSCORE II	10.77 (3.5-28.7)	3.92 (2-10.4)	<.001	9.12 (3.8-20.7)	4.84 (2.1-13.1)	<.001
Preoperative condition						
NYHA class			.001			<.001
Class I	14 (4.9%)	8 (6%)		73 (7.8%)	46 (8.3%)	
Class II	50 (17.5%)	35 (26.3%)		197 (21.2%)	124 (22.5%)	
Class III	101 (35.3%)	60 (45.1%)		336 (36.1%)	246 (44.6%)	
Class IV	121 (42.3%)	30 (22.6%)		324 (34.8%)	135 (24.5%)	
Preoperative cardiogenic shock	63 (21.9%)	22 (15.4%)	.124	224 (23%)	114 (20.1%)	.202

(Continued)

TABLE E6. Continued

Variable	2000-2010 (n = 442) Intraoperative (n = 297)	2000-2010 (n = 442) Postoperative (n = 145)	*P* value	2011-2020 (n = 1561) Intraoperative (n = 990)	2011-2020 (n = 1561) Postoperative (n = 571)	*P* value
Preoperative intubation	**38 (12.8%)**	**10 (6.9%)**	**.073**	129 (13%)	50 (8.8%)	.011
Preoperative cardiac arrest	44 (15.1%)	21 (14.5%)	1.000	82 (8.4%)	36 (6.4%)	.164
Preoperative septic shock	3 (1.1%)	2 (1.4%)	.666	27 (2.9%)	18 (3.3%)	.641
Preoperative vasopressors	56 (19.4%)	15 (10.4%)	.019	176 (17.9%)	61 (10.7%)	<.001
Preoperative acute pulmonary edema	34 (12%)	2 (1.4%)	<.001	**72 (7.6%)**	**30 (5.5%)**	**.112**
Preoperative IABP	52 (17.5%)	16 (11.0%)	.092	82 (8.3%)	40 (7.0%)	.380
Preoperative right ventricular failure	**30 (14%)**	**15 (11.3%)**	**.514**	96 (11.1%)	39 (7.3%)	.020
Preoperative biventricular failure	**8 (6%)**	**7 (6%)**	**1.000**	75 (9.3%)	30 (5.8%)	.022
Emergency surgery	94 (31.8%)	32 (22.1%)	.043	**259 (26.7%)**	**131 (23%)**	**.115**
Urgent surgery	82 (27.7%)	19 (13.1%)	<.001	239 (24.6%)	98 (17.2%)	<.001
Diagnosis						
Coronary artery disease	**139 (46.8%)**	**64 (44.1%)**	**.613**	454 (45.9%)	304 (53.2%)	.005
Aortic vessel disease	35 (11.8%)	14 (9.7%)	.629	185 (18.7%)	94 (16.5%)	.274
Aortic valve disease	103 (34.7%)	51 (35.2%)	.916	343 (34.6%)	183 (32%)	.317
Mitral valve disease	94 (31.6%)	49 (33.8%)	.666	337 (34%)	205 (35.9%)	.473
Tricuspid valve disease	**32 (10.8%)**	**18 (12.4%)**	**.633**	151 (15.3%)	116 (20.3%)	.012
Pulmonary valve disease	1 (0.3%)	0 (0%)	1.000	11 (1.1%)	5 (0.9%)	.797
Post-AMI ventricular septal rupture	**12 (4%)**	**2 (1.4%)**	**.159**	36 (3.6%)	8 (1.4%)	.010
Free wall/Papillary muscle rupture	7 (2.4%)	4 (2.8%)	.756	22 (2.2%)	5 (0.9%)	1.000
Active endocarditis	**10 (3.4%)**	**8 (5.5%)**	**.310**	94 (9.5%)	30 (5.3%)	.003
Atrial septal defect	3 (1%)	2 (1.4%)	.665	18 (1.8%)	10 (1.8%)	1.000
Post-LVAD right ventricular failure	1 (0.3%)	0 (0%)	1.000	15 (1.5%)	3 (0.5%)	.088
Other diagnosis	23 (7.7%)	20 (13.8%)	.059	132 (13.3%)	80 (14%)	.702

Data are reported as n (% as valid percentage excluding missing values), mean ± standard deviation or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared with the overall population analysis. *BMI*, Body mass index; *BSA*, body surface area; *TIA*, transient ischemic attack; *ICD*, implantable cardioverter defibrillator; *PCI*, percutaneous coronary intervention; *COPD*, chronic obstructive pulmonary disease; *LVAD*, left ventricular assist device; *LVEF*, left ventricular ejection fraction; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *IABP*, intra-aortic balloon pump; *AMI*, acute myocardial infarction.

TABLE E7. Procedural characteristics stratified according to implantation decade (2000-2010 vs 2011-2020) and venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing

Variable	2000-2010 (n = 442)			2011-2020 (n = 1561)		
	Intraoperative (n = 297)	Postoperative (n = 145)	*P* value	Intraoperative (n = 990)	Postoperative (n = 571)	*P* value
Weight of surgery			.002			<.001
Unknown	1 (0.3%)	3 (2.1%)		6 (0.6%)	3 (0.5%)	
Isolated CABG	48 (16.2%)	27 (18.6%)		135 (13.6%)	141 (24.7%)	
Isolated non-CABG	152 (51.2%)	90 (62.1%)		565 (57.1%)	314 (55%)	
Two procedures	46 (15.5%)	6 (4.1%)		77 (7.8%)	18 (3.2%)	
Three or more procedures	50 (16.8%)	19 (13.1%)		207 (20.9%)	95 (16.6%)	
CABG	131 (44.1%)	56 (38.6%)	.306	427 (43.1%)	271 (47.5%)	.102
Aortic valve surgery	99 (33.3%)	48 (33.1%)	1	360 (36.4%)	186 (32.6%)	.137
Mitral valve surgery	87 (29.3%)	44 (30.3%)	.825	322 (32.6%)	182 (31.9%)	.822
Tricuspid valve surgery	31 (10.4%)	15 (10.3%)	1	133 (13.4%)	91 (15.9%)	.178
Aortic surgery	**40 (13.5%)**	**17 (11.7%)**	**.653**	220 (22.2%)	96 (16.8%)	.011
Pulmonary valve surgery	1 (0.3%)	0 (0%)	1	7 (0.7%)	4 (0.7%)	1.000
LVAD	2 (0.7%)	1 (0.7%)	1	15 (1.5%)	5 (0.9%)	.354
RVAD	2 (0.7%)	0 (0%)	1	3 (0.3%)	1 (0.2%)	1.000
ASD repair	4 (1.3%)	2 (1.4%)	1	19 (1.9%)	13 (2.3%)	.711
VSD repair	**13 (4.4%)**	**3 (2.1%)**	**.285**	41 (4.1%)	11 (1.9%)	.019
Ventricular surgery	5 (1.7%)	4 (2.8%)	.484	40 (4%)	25 (4.4%)	.793
Rhythm surgery	4 (1.3%)	5 (3.4%)	.161	37 (3.7%)	20 (3.5%)	.889
Pulmonary embolectomy	3 (1%)	3 (2.1%)	.399	12 (1.2%)	5 (0.9%)	.621
Pulmonary endarterectomy	13 (4.4%)	6 (4.1%)	1	**23 (2.3%)**	**5 (0.9%)**	**.046**
Heart transplantation	**51 (17.2%)**	**18 (12.4%)**	**.212**	103 (10.4%)	33 (5.8%)	.002
Off-pump surgery	**4 (1.4%)**	**5 (3.5%)**	**.167**	29 (3%)	41 (7.3%)	<.001
Conversion to CPB	2 (50%)	0 (0%)	.167	12 (41.4%)	10 (22.7%)	.119
CPB time, min	238.00 (173-332)	145.00 (103-207)	<.001	233.00 (167-322)	164.00 (110-227)	<.001
Crossclamp time, min	94.00 (62-150)	78.00 (51-121)	.005	108.00 (71-157)	93.00 (62-138)	<.001
Intraoperative lactate, mmol/L*	6.30 (4.2-10.2)	3.95 (1.7-7.4)	.066	5.95 (3.6-10)	3.30 (1.9-6.5)	<.001
Intraoperative transfusions*	59 (86.8%)	35 (89.7%)	.765	438 (93%)	214 (92.6%)	.877

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared to the overall population analysis. *CABG*, Coronary artery bypass graft; *LVAD*, left ventricular assist device; *RVAD*, right ventricular assist device; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass. *Variable with >50% missing data.

TABLE E8. Details on extracorporeal membrane oxygenation (ECMO) stratified according to implantation decade (2000-2010 vs 2011-2020) and venoarterial (VA) ECMO implantation timing

Variable	2000-2010 (n = 442)			2011-2020 (n = 1561)		
	Intraoperative (n = 297)	Postoperative (n = 145)	*P* value	Intraoperative (n = 990)	Postoperative (n = 571)	*P* value
ECMO indication			<.001			<.001
Failure to wean	220 (74.8%)	2 (1.4%)		544 (56.9%)	22 (3.9%)	
Acute pulmonary embolism	0 (0%)	0 (0%)		1 (0.1%)	2 (0.4%)	
Arrhythmia	1 (0.3%)	7 (5%)		12 (1.3%)	20 (3.5%)	
Cardiac arrest	12 (4.1%)	19 (13.6%)		37 (3.9%)	82 (14.5%)	
Cardiogenic shock	17 (5.8%)	60 (42.9%)		148 (15.5%)	260 (45.9%)	
Pulmonary hemorrhage	1 (0.3%)	1 (0.7%)		6 (0.6%)	1 (0.2%)	
Right ventricular failure	19 (6.5%)	21 (15%)		104 (10.9%)	91 (16.1%)	
Respiratory failure	6 (2%)	16 (11.4%)		17 (1.8%)	31 (5.5%)	
Biventricular failure	17 (5.8%)	11 (7.9%)		72 (7.5%)	46 (8.1%)	
Other	1 (0.3%)	3 (2.1%)		15 (1.6%)	11 (1.9%)	
Cannulation approach			**.176**			<.001
Only central cannulation	**68 (22.9%)**	**26 (17.9%)**		170 (17.2%)	69 (12.1%)	
Only peripheral cannulation	**153 (51.5%)**	**73 (50.3%)**		396 (40%)	308 (53.9%)	
Mixed/switch cannulation	**72 (24.2%)**	**40 (27.6%)**		406 (41%)	181 (31.7%)	
Unknown	**4 (1.3%)**	**6 (4.1%)**		18 (1.8%)	13 (2.3%)	
ECMO duration, h	**96.00 (52-164.2)**	**104.13 (48-168)**	**.981**	117.68 (61-192.1)	130.00 (68.8-206)	.043

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared with the overall population analysis.

TABLE E9. Postoperative outcomes stratified according to implantation decade (2000-2010 vs 2011-2020) and venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing

Variable	2000-2010 (n = 442) Intraoperative (n = 297)	2000-2010 (n = 442) Postoperative (n = 145)	*P* value	2011-2020 (n = 1561) Intraoperative (n = 990)	2011-2020 (n = 1561) Postoperative (n = 571)	*P* value
ICU stay, d	15.00 (7-27)	14.00 (6-28)	.735	13.00 (6-25)	14.00 (6-28)	.149
Hospital stay, d	22.00 (7-38)	18.00 (6-38)	.595	20.00 (8-41)	20.00 (9-39)	.551
Postoperative bleeding	173 (58.2%)	100 (69.4%)	.028	**523 (54.4%)**	**329 (58.4%)**	**.135**
Requiring rethoracotomy	127 (46%)	61 (43.6%)	.677	350 (38.6%)	211 (38.5%)	1.000
Cannulation site bleeding	**41 (13.8%)**	**13 (9.1%)**	**.167**	102 (10.6%)	81 (14.4%)	.034
Diffuse nonsurgical-related bleeding	71 (26.3%)	63 (45.3%)	<.001	184 (21.4%)	141 (26.5%)	.032
Neurological complications						
Brain edema	18 (6.4%)	9 (6.4%)	1	36 (3.9%)	18 (3.3%)	.667
Cerebral hemorrhage	8 (2.8%)	9 (6.5%)	.109	26 (2.8%)	19 (3.5%)	.531
Seizure	6 (2.1%)	6 (4.3%)	.221	19 (2%)	7 (1.3%)	.412
Stroke	29 (9.8%)	14 (9.7%)	1	109 (11%)	60 (10.7%)	.866
Vasospasm	0 (0%)	0 (0%)	n.a.	1 (0.1%)	1 (0.2%)	1.000
Arrhythmia	78 (29.4%)	63 (46.7%)	<.001	265 (29.4%)	191 (35.8%)	.014
Leg ischemia	40 (14.2%)	20 (14.5%)	1	76 (8.2%)	53 (9.7%)	.341
Cardiac arrest	28 (10.5%)	44 (32.6%)	<.001	102 (11.3%)	109 (20.3%)	<.001
Pacemaker implant	8 (3%)	3 (2.2%)	.757	29 (3.2%)	16 (3%)	.876
Bowel ischemia	**9 (3.4%)**	**11 (8.1%)**	**.051**	**47 (5.2%)**	**38 (7.1%)**	**.165**
Right ventricular failure	56 (21.1%)	44 (32.6%)	.015	155 (17.9%)	125 (23.5%)	.013
Acute kidney injury	179 (67%)	97 (71.9%)	.363	476 (53.4%)	285 (53.1%)	.913
Pneumonia	56 (21.1%)	35 (25.9%)	.313	191 (22.1%)	123 (23.2%)	.644
Septic shock	**39 (14.7%)**	**26 (19.3%)**	**.254**	122 (14.1%)	109 (20.6%)	.002
Distributive syndrome	15 (5.7%)	4 (3%)	.321	89 (10.3%)	64 (12.1%)	.331
ARDS	18 (6.8%)	18 (13.3%)	.041	**35 (3.9%)**	**29 (5.4%)**	**.186**
MOF	93 (33%)	64 (44.8%)	.019	312 (31.7%)	210 (37%)	.034
Embolism	19 (7.2%)	10 (7.4%)	1	51 (5.9%)	32 (6%)	.908
Postoperative procedures						
PCI	0 (0%)	3 (2.3%)	.045	**20 (2.3%)**	**21 (4%)**	**.101**
Cardiac surgery	27 (10.2%)	27 (19.9%)	.009	**203 (22.5%)**	**139 (26.1%)**	**.140**
Abdominal surgery	8 (3.3%)	11 (8.3%)	.049	29 (3.4%)	31 (5.9%)	.029
Vascular surgery	22 (9.1%)	13 (9.8%)	.854	94 (10.9%)	71 (13.5%)	.171
In-hospital mortality	176 (59.3%)	102 (70.3%)	.028	564 (57%)	360 (63.2%)	.019

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared with the overall population analysis. *ICU*, Intensive care unit; *n.a.*, not available; *ARDS*, acute respiratory distress syndrome; *MOF*, multiorgan failure; *PCI*, percutaneous coronary intervention.

TABLE E10. Venoarterial extracorporeal membrane oxygenation (VA ECMO) population, stratified according to implantation timing, after exclusion of patients who received a VA ECMO with indication "failure to wean from cardiopulmonary bypass"

Variable	Intraoperative VA ECMO (n = 486)	Postoperative VA ECMO (n = 682)	*P* value
Age, y	63.78 (54.5-71)	65.79 (56-72)	.017
Sex			.854
Female	182 (37.4%)	259 (38%)	
Male	304 (62.6%)	422 (62%)	
Race			.032
Asian	30 (7%)	53 (11.6%)	
Black	2 (0.5%)	6 (1.3%)	
Hispanic	17 (3.9%)	24 (5.2%)	
White	339 (78.7%)	347 (75.8%)	
Other	13 (3%)	10 (2.2%)	
Unknown	30 (7%)	18 (3.9%)	
BMI, kg/m^2	26.079 (23.4-29.4)	26.87 (23.8-30.8)	.041
BSA, m^2	1.90 (1.8-2)	1.90 (1.7-2.1)	.706
Comorbidities			
Hypertension	296 (61.8%)	463 (70%)	.004
Dialysis	40 (8.5%)	56 (8.3%)	.914
Previous myocardial infarction	152 (31.3%)	185 (27.1%)	.132
Myocardial infarction (last 30 d)	47 (9.8%)	70 (10.6%)	.693
Previous endocarditis	36 (7.4%)	45 (6.6%)	.641
Smoking	104 (23.6%)	163 (26%)	.389
Previous stroke	53 (10.9%)	94 (13.8%)	.153
Atrial fibrillation	118 (24.3%)	210 (30.8%)	.015
Previous pulmonary embolism	9 (2%)	10 (1.6%)	.644
Diabetes mellitus	112 (23%)	179 (26.2%)	.218
Previous TIA	13 (2.9%)	14 (2.2%)	.554
Implanted pacemaker	28 (6.1%)	44 (6.8%)	.711
Implanted ICD	49 (10.6%)	54 (8.4%)	.249
Previous PCI	86 (17.8%)	114 (16.8%)	.694
COPD	49 (10.4%)	67 (10%)	.842
Peripheral artery disease	56 (11.5%)	105 (15.4%)	.059
Pulmonary hypertension (>50 mm Hg)	80 (16.6%)	132 (19.4%)	.248
Previous cardiac surgery	**127 (26.1%)**	**146 (21.4%)**	**.068**
Implanted LVAD	23 (4.8%)	17 (2.6%)	.051
Preoperative creatinine, μmol/L	**99.35 (79.6-140)**	**97.26 (78.7-132.6)**	**.230**
LVEF (%)	**47.52 (30-60)**	**50.00 (30-60)**	**.160**
EuroSCORE II	7.98 (3.2-17.5)	4.64 (2.1-13.1)	<.001
Preoperative condition			
NYHA class			.029
Class I	36 (8%)	46 (7.1%)	
Class II	109 (24.1%)	146 (22.4%)	
Class III	167 (36.9%)	297 (45.6%)	
Class IV	140 (31%)	162 (24.9%)	
Preoperative cardiogenic shock	95 (19.8%)	132 (19.5%)	.940
Preoperative intubation	**50 (10.3%)**	**59 (8.7%)**	**.359**

(Continued)

TABLE E10. Continued

Variable	Intraoperative VA ECMO (n = 486)	Postoperative VA ECMO (n = 682)	*P* value
Preoperative cardiac arrest	49 (10.1%)	50 (7.4%)	.110
Preoperative septic shock	12 (2.5%)	20 (3%)	.717
Preoperative vasopressors	76 (15.7%)	72 (10.6%)	.012
Preoperative acute pulmonary edema	**26 (5.5%)**	**32 (4.9%)**	**.683**
Preoperative IABP	46 (9.5%)	54 (7.9%)	.396
Preoperative right ventricular failure	41 (9.2%)	54 (8.5%)	.744
Preoperative biventricular failure	**36 (8.6%)**	**37 (6.1%)**	**.138**
Emergency surgery	**124 (25.6%)**	**158 (23.2%)**	**.367**
Urgent surgery	112 (23.1%)	110 (16.2%)	.004
Diagnosis			
Coronary artery disease	**232 (47.7%)**	**354 (51.9%)**	**.172**
Aortic vessel disease	84 (17.3%)	102 (15%)	.292
Aortic valve disease	153 (31.5%)	220 (32.3%)	.799
Mitral valve disease	**131 (27%)**	**244 (35.8%)**	**.001**
Tricuspid valve disease	64 (13.2%)	129 (18.9%)	.010
Pulmonary valve disease	6 (1.2%)	5 (0.7%)	.541
Post-AMI ventricular septal rupture	16 (3.3%)	10 (1.5%)	.044
Free wall/Papillary muscle rupture	10 (2.1%)	9 (1.3%)	.354
Active endocarditis	**35 (7.2%)**	**37 (5.4%)**	**.219**
Atrial septal defect	5 (1%)	12 (1.8%)	.335
Post-LVAD right ventricular failure	**11 (2.3%)**	**3 (0.4%)**	**.006**
Other diagnosis	73 (15%)	94 (13.8%)	.554

Sensitivity analysis after exclusion of patients who received VA ECMO with indication "failure to wean." Data are reported as n (% as valid percentage excluding missing values), mean ± standard deviation, or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative V-A ECMO groups. Text in bold indicates differences compared with the overall population analysis. *BMI*, Body mass index; *BSA*, body surface area; *TIA*, transient ischemic attack; *ICD*, implantable cardioverter defibrillator; *PCI*, percutaneous coronary intervention; *COPD*, chronic obstructive pulmonary disease; *LVAD*, left ventricular assist device; *LVEF*, left ventricular ejection fraction; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *IABP*, intra-aortic balloon pump; *AMI*, acute myocardial infarction.

TABLE E11. Procedural characteristics stratified according to venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing, after exclusion of patients who received a VA ECMO with indication "failure to wean from cardiopulmonary bypass"

Variable	Intraoperative VA ECMO (n = 486)	Postoperative VA ECMO (n = 682)	*P* value
Weight of surgery			**.133**
Unknown	**6 (1.2%)**	**6 (0.9%)**	
Isolated CABG	**84 (17.3%)**	**160 (23.5%)**	
Isolated non-CABG	**291 (59.9%)**	**382 (56%)**	
Two procedures	**19 (3.9%)**	**21 (3.1%)**	
Three or more procedures	**86 (17.7%)**	**113 (16.6%)**	
CABG	210 (43.2%)	312 (45.7%)	.404
Aortic valve surgery	166 (34.2%)	219 (32.1%)	.487
Mitral valve surgery	**123 (25.4%)**	**216 (31.7%)**	**.022**
Tricuspid valve surgery	57 (11.7%)	105 (15.4%)	.086
Aortic surgery	101 (20.8%)	108 (15.8%)	.030
Pulmonary valve surgery	4 (0.8%)	4 (0.6%)	.725
LVAD	**13 (2.7%)**	**6 (0.9%)**	**.02**
RVAD	3 (0.6%)	1 (0.1%)	.314
ASD repair	9 (1.9%)	15 (2.2%)	.835
VSD repair	21 (4.3%)	14 (2.1%)	.035
Ventricular surgery	19 (3.9%)	29 (4.3%)	.881
Rhythm surgery	14 (2.9%)	25 (3.7%)	.512
Pulmonary embolectomy	6 (1.2%)	8 (1.2%)	1.000
Pulmonary endarterectomy	16 (3.3%)	11 (1.6%)	.075
Heart transplantation	55 (11.3%)	50 (7.3%)	.022
Off-pump surgery	**23 (4.8%)**	**45 (6.7%)**	**.205**
Conversion to CPB	**7 (30.4%)**	**10 (20.8%)**	**.389**
CPB time, min	226.00 (168-313)	158.00 (109-222)	<.001
Crossclamp time, min	107.00 (71-155)	89.00 (59-132)	<.001
Intraoperative lactate, mmol/L*	5.70 (3.5-8.8)	3.20 (1.8-6.3)	<.001
Intraoperative transfusions*	**245 (96.5%)**	**240 (92%)**	**.037**

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared to the overall population analysis. *CABG*, Coronary artery bypass graft; *LVAD*, left ventricular assist device; *RVAD*, right ventricular assist device; *ASD*, atrial septal defect; *VSD*, ventricular septal defect; *CPB*, cardiopulmonary bypass. *Variable with >50% missing data.

TABLE E12. Details on extracorporeal membrane oxygenation (ECMO) stratified according to venoarterial (VA ECMO) implantation timing, after exclusion of patients who received a VA ECMO with indication "failure to wean from cardiopulmonary bypass"

Variable	Intraoperative VA ECMO (n = 486)	Postoperative VA ECMO (n = 682)	*P* value
ECMO indication			<.001
Acute pulmonary embolism	1 (0.2%)	2 (0.3%)	
Arrhythmia	13 (2.7%)	27 (4%)	
Cardiac arrest	49 (10.1%)	101 (14.8%)	
Cardiogenic shock	165 (34%)	320 (46.9%)	
Pulmonary hemorrhage	7 (1.4%)	2 (0.3%)	
Right ventricular failure	123 (25.3%)	112 (16.4%)	
Respiratory failure	23 (4.7%)	47 (6.9%)	
Biventricular failure	89 (18.3%)	57 (8.4%)	
Other	16 (3.3%)	14 (2.1%)	
Cannulation approach			.001
Only central cannulation	105 (21.6%)	90 (13.2%)	
Only peripheral cannulation	224 (46.1%)	365 (53.5%)	
Mixed/switch cannulation	148 (30.5%)	210 (30.8%)	
Unknown	9 (1.9%)	17 (2.5%)	
ECMO duration, h	**112 (60-192)**	**122 (60.2-197)**	**.195**

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared with the overall population analysis.

TABLE E13. Postoperative outcomes stratified according to venoarterial extracorporeal membrane oxygenation (VA ECMO) implantation timing, and after exclusion of patients who received a VA ECMO with indication "failure to wean from cardiopulmonary bypass"

Variable	Intraoperative VA ECMO (n = 486)	Postoperative VA ECMO (n = 682)	*P* value
ICU stay, d	14.00 (6-25)	14.00 (6-28)	.787
Hospital stay, d	22.00 (9-39)	20.00 (9-39)	.473
Postoperative bleeding	277 (58.2%)	409 (60.8%)	.393
Requiring rethoracotomy	181 (39.9%)	258 (39.4%)	.901
Cannulation site bleeding	53 (11.2%)	89 (13.2%)	.318
Diffuse nonsurgical-related bleeding	100 (22.3%)	191 (29.7%)	.007
Neurologic complications			
Brain edema	17 (3.6%)	27 (4.1%)	.756
Cerebral hemorrhage	11 (2.3%)	27 (4.1%)	.131
Seizure	8 (1.7%)	11 (1.7%)	1.000
Stroke	56 (11.6%)	72 (10.7%)	.636
Vasospasm	1 (0.2%)	1 (0.2%)	1.000
Arrhythmia	141 (30.7%)	243 (38%)	.012
Leg ischemia	42 (8.9%)	70 (10.7%)	.365
Cardiac arrest	53 (11.5%)	144 (22.5%)	<.001
Pacemaker implant	10 (2.2%)	18 (2.8%)	.565
Bowel ischemia	**22 (4.8%)**	**47 (7.3%)**	**.101**
Right ventricular failure	80 (17.5%)	163 (25.6%)	.002
Acute kidney injury	**227 (49.3%)**	**362 (56.4%)**	**.023**
Pneumonia	99 (21.7%)	151 (23.8%)	.465
Septic shock	77 (16.9%)	130 (20.5%)	.138
Distributive syndrome	36 (7.9%)	67 (10.6%)	.143
ARDS	20 (4.3%)	47 (7.4%)	.041
MOF	154 (32%)	262 (38.7%)	.021
Embolism	20 (4.4%)	41 (6.5%)	.144
Postoperative procedures			
PCI	**13 (2.9%)**	**24 (3.8%)**	**.499**
Cardiac surgery	**106 (22.9%)**	**157 (24.6%)**	**.567**
Abdominal surgery	16 (3.6%)	40 (6.3%)	.051
Vascular surgery	61 (13.7%)	78 (12.4%)	.520
In-hospital mortality	270 (55.6%)	441 (64.7%)	.002

Data are reported as n (% as valid percentage excluding missing values) or median (interquartile range). *P* values by χ^2 (for categorical data) or Student *t* test (for parametric continuous data) and Mann–Whitney *U* test (for nonparametric continuous data) indicate statistically significant differences between intraoperative and postoperative VA ECMO groups. Text in bold indicates differences compared to the overall population analysis. *ICU*, Intensive care unit; *ARDS*, acute respiratory distress syndrome; *MOF*, multiorgan failure; *PCI*, percutaneous coronary intervention.