Features and outcomes of female and male patients requiring postcardiotomy extracorporeal life support

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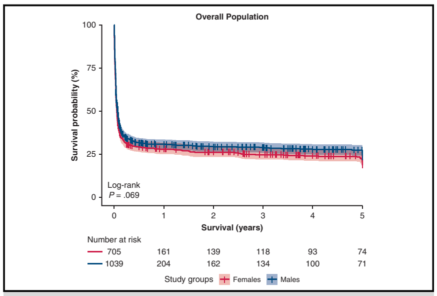
ABSTRACT

Objectives: Although cardiogenic shock requiring extracorporeal life support after cardiac surgery is associated with high mortality, the impact of sex on outcomes of postcardiotomy extracorporeal life support remains unclear with conflicting results in the literature. We compare patient characteristics, in-hospital outcomes, and overall survival between females and males requiring postcardiotomy extracorporeal life support.

Methods: This retrospective, multicenter (34 centers), observational study included adults requiring postcardiotomy extracorporeal life support between 2000 and 2020. Preoperative, procedural, and extracorporeal life support characteristics, complications, and survival were compared between females and males. Association between sex and in-hospital survival was investigated through mixed Cox proportional hazard models.

Results: This analysis included 1823 patients (female: 40.8%; median age: 66.0 years [interquartile range, 56.2-73.0 years]). Females underwent more mitral valve surgery (females: 38.4%, males: 33.1%, $P = .019$) and tricuspid valve surgery (feamales: 18%, males: 12.4%, $P < .001$), whereas males underwent more coronary artery surgery (females: 45.9%, males: 52.4%, $P = .007$). Extracorporeal life support implantation was more common intraoperatively in feamales (females: 64.1%, females: 59.1%) and postoperatively in males (females: 35.9%, males: 40.9%, $P = .036$). Ventricular unloading (females: 25.1%, males: 36.2%, $P < .001$) and intra-aortic balloon pumps (females: 25.8%, males: 36.8%, $P < .001$) were most frequently used in males. Females had more postoperative right ventricular failure (females: 24.1%, males: 19.1%, $P = .016$) and limb ischemia (females: 12.3%, males: 8.8%, $P = .23$). In-hospital mortality was 64.9% in females and 61.9% in males ($P = .199$) with no differences in 5-year survival (females: 20%, 95% CI, 17-23; males: 24%, 95% CI, 21-28; $P = .069$). Crude hazard ratio for in-hospital mortality in females was 1.12 (95% CI, 0.99-1.27; $P = .069$) and did not change after adjustments.

Conclusions: This study demonstrates that female and male patients requiring postcardiotomy extracorporeal life support have different preoperative and extracorporeal life support characteristics, as well as complications, without a statistical difference in in-hospital and 5-year survivals. (J Thorac Cardiovasc Surg 2024;■:1-11)



Differences between female and male patients in postcardiotomy venoarterial ECLS (95% CIs).

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CENTRAL MESSAGE

Patients' profiles and ECLS characteristics differ between females and males in postcardiotomy ECLS, but their in-hospital and postdischarge outcomes are comparable.

PERSPECTIVE

This study shows that female patients more often require postcardiotomy ECLS after valvular surgery, whereas male patients do after CABG. It supports the development of strategies to prevent right ventricular failure and limb ischemia particularly in females and suggests that sex differences should be integrated in each step of the ECLS decision-making and management processes.

See Commentary on page XXX.

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
ECLS	= extracorporeal life support
HR	= hazard ratio
IABP	= intra-aortic balloon pump
OR	= odds ratio

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Postcardiotomy cardiogenic shock requiring extracorporeal life support (ECLS) in adults is characterized by a relatively low incidence but a high morbidity and mortality.[1,2] Although sex differences in the incidence and outcomes of cardiovascular diseases have been reported,[3] the effect of sex on the incidence and outcomes of postcardiotomy ECLS remains unclear with conflicting results reported.[4-8] Moreover, the female population is often underrepresented in studies focusing on heart failure, mechanical circulatory support, or invasive interventions, and most current medical guidelines and protocols are not gender- or sex-specific.[3]

The reasons for possible sex differences are not yet fully understood and are likely multifactorial. Some potential factors that have been suggested include differences in

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Institutional Review Board approval was required for all centers, based on the Institutional Review Board approval of the coordinating center (MUMC+, No.: METC-2018-0788, date: December 19, 2018). Need for informed consent was waived based on the retrospective nature of the study, the emergency of the performed procedure, and the pseudonymization of shared data.

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baseline characteristics, comorbidities, and hormonal influences that vary with age.[3] However, the literature lacks a systematic analysis of all these factors in postcardiotomy ECLS. Understanding the potential sex differences in postcardiotomy ECLS could provide valuable insights for risk stratification, prognostication, and targeted interventions in this high-risk population. Thus, there is an urgent need to clarify this knowledge gap in the ECLS and cardiac surgery fields.

This study aims to describe sex-stratified characteristics, in-hospital outcomes, and long-term survival of patients undergoing cardiac surgery and requiring venoarterial ECLS. We hypothesized that females and males represent 2 distinct populations, marked by different preoperative characteristics, indications, and outcomes.

MATERIAL AND METHODS

Study Design

The current study is a secondary analysis of the Post-Cardiotomy Extra-Corporeal Life Support Study (ClinicalTrials.gov: NCT03857217), an international, multicenter, retrospective observational study collecting data from in 34 centers from 16 countries (Figures E1 and E2). Institutional Review Board approval was obtained at the coordinating center and required for all participating units (METC-2018-0788, December 2018). The need for informed consent was waived because of the retrospective nature of the study, the emergency of the performed procedure, and the pseudonymization of shared data. The current study is reported according to the Sex and Gender Equity in Research guidelines[9] and Strengthening the Reporting of Observational Studies in Epidemiology Statement.[10]

Patient Population

The Post-Cardiotomy Extra-Corporeal Life Support Study included adults (aged ≥18 years) requiring postcardiotomy ECLS between January 2000 and December 2020. Exclusion criteria included ECLS after discharge or before surgery, ECLS after noncardiac operations, and ECLS implantation not related to cardiac surgery hospitalization. For the current analysis, further exclusion criteria included missing data on sex or primary outcome, need for venovenous ECLS, and patients undergoing durable left ventricle assist device implantation or heart transplantation based on the previously described sex-related differences within these populations.[11-13] All included patients were categorized according to their self-reported biologically determined sex: male or female.[3,9,14,15] Within this article, "gender" describes the characteristics of females and males that are largely socially created, and "sex" encompasses characteristics that are biologically determined.

Data Collection and Outcomes

Data were collected and included in a dedicated electronic case report form (data.castoredc.com) according to the predefined protocol and variable definitions (Appendix E1). Follow-up data were collected through the review of the most recent medical records or contact with patients at discretion of the treating center. Full dataset was retained and centrally managed by the coordinating center. The primary outcome of interest was all-cause in-hospital mortality. Secondary outcomes included in-hospital complications and postdischarge survival.

Statistical Analysis

Data were merged and analyzed using SPSS 26.0 (IBM), and R 4.1.2 (R Foundation for Statistical Computing) (Appendix E1).

Demographic and clinical variables are expressed as numbers (valid percent on available data, excluding missing values; Table E1) for categorical variables and median (first and third quartiles) or mean and SD for continuous variables after evaluation of normality. Categorical data were compared between groups with Pearson's chi-square or Fisher exact test. Continuous variables were analyzed using the independent-samples t test or Mann–Whitney U test, as appropriate.

The associations between sex and both right ventricular failure and lower-limb ischemia were investigated using mixed-effects multivariable logistic regression models; the association between sex and in-hospital mortality was investigated using a mixed-effects Cox proportional hazards regression model. All models contained both fixed and random effects to account for dependency of observations due to clustering in centers and in years. Males were considered as the reference group in all models. The models were developed on 5 datasets after imputation of variables with less than 20% missing data. We report measures of association as hazard ratios (HRs) or odds ratios (ORs) with their 95% CIs and P values.

Overall survival was investigated with the Kaplan–Meier method, and comparisons were performed with log-rank test. Based on the possible variations in ECLS management over the study period, a sensitivity analysis was performed after exclusion of patients who received postcardiotomy ECLS before 2011 (2011-2020 cohort). A further sensitivity analysis was performed to include only patients who underwent coronary artery bypass grafting (CABG) or valvular operations. Subgroup analyses were conducted to investigate patients stratified by age groups (<50 years, 50-64.9 years, ≥65 years), and patients who underwent coronary artery bypass surgery, mitral valve surgery, and tricuspid valve surgery.

RESULTS

Preoperative, Surgical, and Extracorporeal Life Support Characteristics

The cohort included 1823 patients, of whom 743 were female (40.8%) and 1080 were male (59.2%, Figures E1 and E3). Their median age was 66.0 years (first and third quartiles: 56.2-73). Males were characterized by a cardiovascular profile with higher rates of smoking, previous myocardial infarction and percutaneous coronary interventions, coronary artery disease (CAD), and active endocarditis than females (Table 1). Overall, males more often presented with preoperative cardiogenic shock requiring vasopressors and emergency surgery. Females were more likely to be diagnosed with mitral and tricuspid valve disease and preoperative pulmonary hypertension (Table 1). Females more often underwent mitral and tricuspid valve surgery (Table 2) with higher rates of operations combining 2 or more procedures (females: n = 241/743, 32.4%; males: n = 265/1080, 24.5%; Figure 1, *A*). In the 2011-2020 cohort (n = 1443, 79.2%, Tables E2-E5), 3% (n = 17/567) of females underwent pulmonary endarterectomy compared with 1.4% (n = 12/876, P = .035) of males. CABG (Table 2) and isolated CABG were performed more frequently in males (females: n = 114/743, 15.3%; males: n = 256/1080, 23.7%; Figure 1, *A*).

Females received more intraoperative ECLS cannulations compared with higher rates of postoperative cannulations in males (Table 3). Failure to wean from cardiopulmonary bypass was the main ECLS indication (females: n = 306/717, 42.7%; males: n = 385/1066, 36.1%,

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TABLE 1. Preoperative patient characteristics

Variables	Females (n = 743)	Males (n = 1080)	*P* value
Age (y)	66.00 (57-74)	66.00 (56-72)	.119
Race			.003
Asian	38 (6.5%)	97 (12%)	
Black	4 (0.7%)	8 (1%)	
Hispanic	20 (3.4%)	38 (4.7%)	
White	471 (80.2%)	599 (74.3%)	
Other	21 (3.6%)	15 (1.9%)	
Unknown	33 (5.6%)	49 (6.1%)	
Body mass index (kg/m^2)	26.23 (23.4-30.7)	26.56 (24-29.8)	.477
Body surface area (m^2)	1.80 (1.7-2)	1.94 (1.8-2.1)	<.001
Comorbidities			
Hypertension	480 (67.6%)	730 (70%)	.293
Smoking	113 (19.3%)	312 (32.2%)	<.001
Diabetes mellitus	178 (24%)	298 (27.6%)	.083
Previous myocardial infarction	163 (21.9%)	312 (28.9%)	<.001
Myocardial infarction (last 30 d)	81 (11.4%)	150 (14.4%)	.073
Previous percutaneous coronary intervention	101 (13.7%)	196 (18.2%)	.012
Previous stroke	110 (14.8%)	140 (13%)	.268
Peripheral artery disease	112 (15.1%)	173 (16%)	.600
Atrial fibrillation	209 (28.1%)	260 (24.1%)	.056
Chronic obstructive pulmonary disease	82 (11.7%)	107 (10.1%)	.308
Pulmonary hypertension (>50 mm Hg)	170 (23.1%)	201 (18.6%)	.024
Previous cardiac surgery	171 (23%)	254 (23.5%)	.822
Preoperative creatinine (μmol/L)	96.4 (73.4-129)	103.45 (81-141.1)	<.001
Dialysis	49 (6.9%)	94 (8.9%)	.154
Left ventricular ejection fraction (%)	52.0 (40-60)	49.50 (34-60)	<.001
euroSCORE II*	7.60 (2.8-20)	7.01 (2.7-18.3)	.294
Preoperative condition			
NYHA class			.759
Class I	60 (8.4%)	77 (7.6%)	
Class II	162 (22.7%)	220 (21.6%)	
Class III	288 (40.4%)	411 (40.4%)	
Class IV	203 (28.5%)	310 (30.5%)	
Preoperative cardiogenic shock	142 (19.5%)	264 (24.7%)	.010
Preoperative cardiac arrest	75 (10.2%)	103 (9.6%)	.689
Preoperative intubation	82 (11.1%)	142 (13.1%)	.192
Preoperative septic shock	16 (2.3%)	33 (3.2%)	.303
Preoperative vasopressors	101 (13.7%)	189 (17.6%)	.031
Preoperative right ventricular failure	65 (10.5%)	81 (8.2%)	.131
Emergency surgery	182 (25%)	316 (29.4%)	.047
Urgent surgery	145 (19.8%)	201 (18.7%)	.543
Diagnosis			
CAD	335 (45.1%)	608 (56.3%)	<.001
Aortic vessel disease	129 (17.4%)	204 (18.9%)	.423
Aortic valve disease	287 (38.6%)	400 (37%)	.492
Mitral valve disease	299 (40.2%)	377 (34.9%)	.023
Tricuspid valve disease	144 (19.4%)	168 (15.6%)	.037
Pulmonary valve disease	6 (0.8%)	9 (0.8%)	1.000
Post-AMI ventricular septal rupture	19 (2.6%)	39 (3.6%)	.224
Free wall/papillary muscle rupture	11 (1.5%)	25 (2.3%)	.234
Active endocarditis	45 (6.1%)	101 (9.4%)	.011
Atrial septal defect	17 (2.3%)	14 (1.3%)	.139
Other diagnosis	67 (9%)	107 (9.9%)	.570

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *AMI*, acute myocardial infarction. *Data available for 70.1% of patients.

TABLE 2. Procedural characteristics

Variables	Females (n = 743)	Males (n = 1080)	*P* value
CABG	341 (45.9%)	566 (52.4%)	.007
Aortic valve surgery	305 (41%)	402 (37.2%)	.107
Mitral valve surgery	285 (38.4%)	357 (33.1%)	.019
Tricuspid valve surgery	134 (18%)	134 (12.4%)	<.001
Aortic surgery	145 (19.5%)	231 (21.4%)	.346
Pulmonary valve surgery	5 (0.7%)	7 (0.6%)	1.000
Atrial septal defect repair	18 (2.4%)	17 (1.6%)	.225
Ventricular septal defect repair	24 (3.2%)	43 (4%)	.448
Ventricular surgery	27 (3.6%)	47 (4.4%)	.471
Rhythm surgery	28 (3.8%)	38 (3.5%)	.799
Pulmonary embolectomy	10 (1.3%)	11 (1%)	.513
Pulmonary endarterectomy	26 (3.5%)	21 (1.9%)	.050
Off-pump surgery	18 (2.5%)	64 (6%)	<.001
Conversion to cardiopulmonary bypass	7 (36.8%)	18 (27.3%)	.410
Cardiopulmonary bypass time (min)	200 (135-290)	195 (132-282)	.431
Crossclamp time (min)	100 (65-150)	99 (61-152)	.297

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *CABG*, Coronary artery bypass grafting.

Figure 1, *B*) followed by cardiogenic shock (females: n = 157/717, 21.9%; males: n = 328/1066, 30.8%, *P* = .001). Distal limb perfusion, left ventricular unloading, and intra-aortic balloon pump (IABP) use were more frequent in males (Table 3).

Outcomes

Females had more postoperative right ventricular failure (OR, 1.38, 95% CI, 1.06-1.80, *P* = .016, model 1, Table E6). This effect became somewhat smaller after adjustments (OR, 1.32, 95% CI, 1.00-1.74, *P* = .0521, model 5). Males more often developed septic shock (Table 4), whereas leg ischemia was more frequent in females. In a multivariable mixed-effects logistic regression model and after adjustment for body surface area, distal perfusion, age, history of distal vessel disease, preoperative vasopressor use, bleeding at cannulation site, and extracorporeal cardiopulmonary resuscitation, females had higher odds for leg ischemia (OR, 1.53,

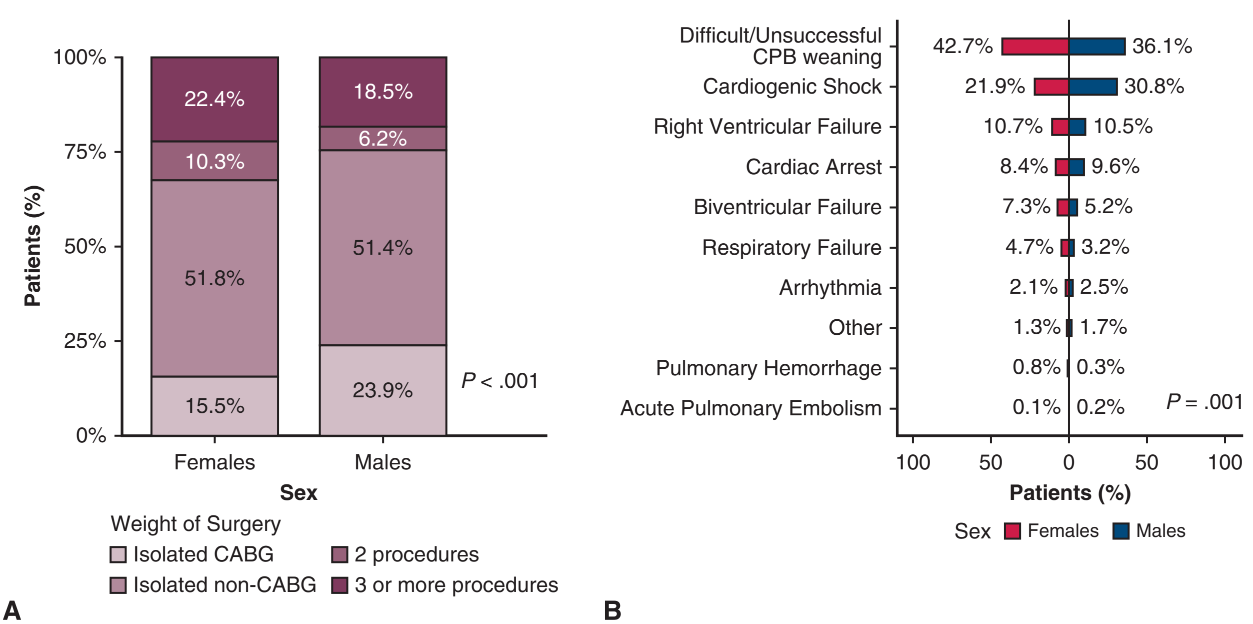

FIGURE 1. Surgical details and ECLS indications. Distribution of weight of surgery (A) and indication for ECLS (B) by sex. *CABG*, Coronary artery bypass grafting; *CPB*, cardiopulmonary bypass.

TABLE 3. Details on extracorporeal life support

Variables	Females (n = 743)	Males (n = 1080)	*P* value
ECLS implantation timing			.036
Intraoperative	476 (64.1%)	638 (59.1%)	
Postoperative	267 (35.9%)	442 (40.9%)	
Cannulation approach			.547
Only central cannulation	125 (16.8%)	177 (16.4%)	
Only peripheral cannulation	335 (45.1%)	523 (48.4%)	
Mixed/switch cannulation	265 (35.7%)	355 (32.9%)	
Unknown	18 (2.4%)	25 (2.3%)	
Left ventricular unloading	155 (25.1%)	312 (36.2%)	<.001
IABP during any time of hospitalization	188 (25.8%)	395 (36.8%)	<.001
IABP implantation timing			.633
Preoperative	56 (29.8%)	127 (32.2%)	
Intraoperative	132 (70.2%)	268 (67.8%)	
Distal femoral perfusion in patients with peripheral cannulation	217 (68%)	371 (75.4%)	.024
ECLS duration (h)	118 (60.2-194.5)	120.00 (56.8-192)	.989

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *ECLS*, Extracorporeal life support; *IABP*, intra-aortic balloon pump.

95% CI, 1.00-2.36, *P* = .0517, Table E7). The number of units of postoperatively transfused erythrocyte concentrates was similar in both females (median: 11, first to third quartile: 4-21) and males (median: 10, first to third quartile: 4-21; *P* = .434. Table E8). In-hospital mortality was 64.9% in females (n = 482) and 61.9% in males (n = 668, *P* = .199) with 715 deaths during extracorporeal support (39.2%) and 442 deaths after weaning (23.1%). In a mixed-effects Cox model with random center and year effects, females showed an HR of 1.12 (95% CI, 0.99-1.27, *P* = .069; Figure 2) for in-hospital mortality compared with males. Adjustment for age (model 1), preoperative characteristics (model 2), intraoperative variables (model 3), and ECLS variables (model 4) did not change the results. The HR decreased to 1.08 (95% CI, 0.95-1.22, *P* = .248) after adjustment for postoperative complications (model 5). When adding the interaction term between sex and age to the models, no effect modification by age was observed (*P* values for interaction > .228). Median overall follow-up time was 21 days (first and third quartiles: 7-147), and median follow-up for hospital survivors was 730 days (first and third quartiles: 91-1801). Median survival at 5 years was 20% (95% CI, 17-23) for female patients and 24% (95% CI, 21-28) for male patients. Overall, survival was similar for both groups (*P* = .069, Figure 3), also when considering the 2011-2020 subcohort (*P* = .06, Figure E4). The cohort of patients who underwent CABG and valvular surgery showed a worse survival for females (*P* = .04, Tables E9-E12, Figure E4), but this was not confirmed after subgroup analyses of patients who underwent CABG (*P* = .39, Tables E13-E16, Figure E5), mitral valve surgery (*P* = .07, Tables E17-E20, Figure E6), and tricuspid valve surgery (*P* = .78, Tables E21-E24, Figure E7) or stratified by age groups (<50 years: *P* = .14, 50-65 years: *P* = .74, >65 years: *P* = .16, Figure E8).

DISCUSSION

Female and male patients requiring postcardiotomy ECLS have different preoperative characteristics and ECLS indications and complications, but comparable in-hospital and long-term survival. This study has 4 main findings (Figure 4). First, males requiring postcardiotomy ECLS are mainly affected by CAD requiring surgical revascularization and are characterized by a cardiovascular profile including smoking, diabetes mellitus, previous myocardial infarction, and percutaneous coronary intervention. Females requiring postcardiotomy ECLS undergo more mitral and tricuspid valve operations than males. Second, females more often receive intraoperative ECLS cannulation for difficult or unsuccessful weaning from cardiopulmonary bypass, whereas males require more postoperative ECLS initiation for cardiogenic shock and undergo IABP implantation. Third, females are more likely to experience postoperative right ventricular failure and leg ischemia compared with males. Fourth, in-hospital and long-term survivals were comparable between female and male patients.

Sex and gender differences have been increasingly addressed in all fields of medicine,[3,12,13] including cardiac surgery where female sex has been reported as a risk factor for postoperative morbidity and mortality.[16] Within the cardiac surgery population, up to 4% of patients might experience postcardiotomy cardiogenic shock requiring ECLS.[1,2] Nevertheless, females have always represented only 20% to 30% of patients included in most studies on postcardiotomy ECLS,[4] and results on sex-related differences have been

TABLE 4. Postoperative outcomes

Variables	Females (n = 743)	Males (n = 1080)	*P* value
Intensive care unit stay (d)	14 (6-27)	13 (5-24)	.150
Hospital stay (d)	18 (7-36)	19 (8-36)	.672
Postoperative bleeding	418 (57.3%)	612 (57.5%)	.961
Requiring re-thoracotomy	284 (41.3%)	395 (38.3%)	.227
Cannulation site bleeding	98 (13.5%)	121 (11.4%)	.187
Diffuse no surgical-related bleeding	165 (25.5%)	269 (26.9%)	.567
Neurological complications			
Cerebral hemorrhage	22 (3.2%)	31 (3%)	.887
Stroke	81 (11%)	110 (10.2%)	.641
Arrhythmia	230 (34.4%)	332 (32.9%)	.526
Leg ischemia	85 (12.3%)	90 (8.8%)	.023
Cardiac arrest	123 (18.4%)	160 (15.8%)	.183
Pacemaker implantation	22 (3.3%)	30 (3%)	.774
Bowel ischemia	34 (5.1%)	64 (6.3%)	.339
Right ventricular failure	156 (24.1%)	191 (19.1%)	.016
Acute kidney injury	373 (56.3%)	552 (54.6%)	.514
Pneumonia	134 (20.7%)	227 (22.8%)	.330
Septic shock	91 (14.1%)	178 (17.9%)	.048
Distributive shock syndrome	52 (8.1%)	103 (10.3%)	.142
Acute respiratory distress syndrome	41 (6.1%)	51 (5%)	.381
Embolism	42 (6.5%)	52 (5.2%)	.278
Postoperative procedures			
Percutaneous coronary intervention	15 (2.4%)	31 (3.1%)	.444
Cardiac surgery	157 (23.5%)	228 (22.6%)	.678
Abdominal surgery	23 (3.7%)	48 (4.8%)	.265
Vascular surgery	61 (9.6%)	97 (9.8%)	1.000
In-hospital mortality	482 (64.9%)	668 (61.9%)	.199
In-hospital mortality timing			.709
Deceased on support	294 (39.6%)	421 (39.0%)	
Deceased after weaning	179 (24.1%)	243 (22.5%)	
Death time unknown	9 (1.2%)	4 (0.4%)	
Main cause of death			.162
Multiorgan failure	165 (36.2%)	238 (38.1%)	
Sepsis	25 (5.5%)	49 (7.8%)	
Persistent heart failure	177 (38.8%)	219 (35%)	
Distributive shock	5 (1.1%)	17 (2.7%)	
Bleeding	31 (6.8%)	29 (4.6%)	
Neurological injury	24 (5.3%)	31 (5%)	
Bowel ischemia	6 (1.3%)	14 (2.2%)	
Other	23 (5%)	28 (4.5%)	

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles).

contradictory.[4-6,8] In the current study, males are characterized by the typical profile of patients with CAD undergoing CABG surgery, in some cases with emergency indications and preoperative vasopressors. Females are more likely to have pulmonary hypertension and undergo mitral-tricuspid valve surgery requiring elective operations with combined procedures. Several studies reported a higher percentage of CAD[4,5] and diabetes mellitus[6,8] in males requiring ECLS for cardiogenic shock or postcardiotomy support. Yet, to the best of our knowledge, only Biancari and colleagues[4] reported higher rates of tricuspid valve surgery in females (6.6%) compared with males (2.4%).

The different preoperative profile between male and female patients also explains the different ECLS cannulation timing, left ventricular unloading, and IABP use. The typical CAD profile in males is more often associated

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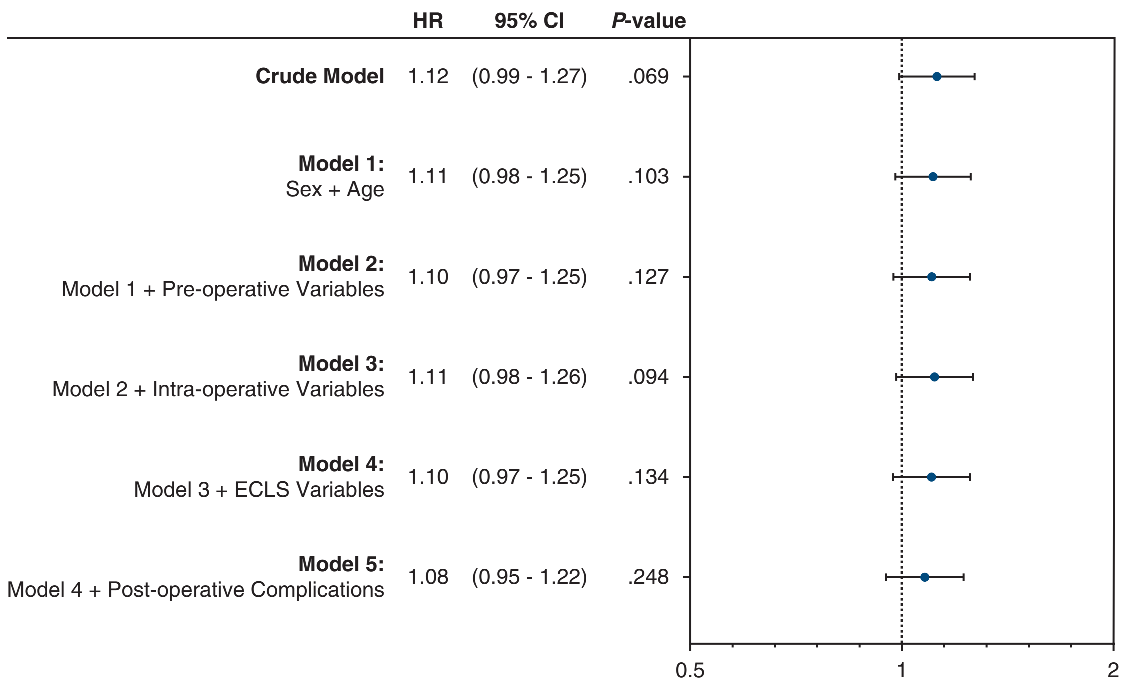

FIGURE 2. HRs for in-hospital mortality in females. In a mixed-effects Cox model with random center and year effects: crude model, adjustment for age (model 1), preoperative characteristics (model 2), intraoperative variables (model 3), ECLS variables (model 4), and postoperative complications (model 5). *HR*, Hazard ratio; *ECLS*, extracorporeal life support.

with postoperative ECLS initiation due to any postoperative situation (ie, bypass graft occlusion, recent myocardial infarction) inducing cardiogenic shock.[17] The presence of ischemic cardiomyopathy, as well as recent myocardial infarction, can also elucidate the more common use of IABPs (including preoperative) or other unloading strategies to allow myocardial recovery of the ischemic left ventricle in males.[1,18] Females affected by valve diseases more often require intraoperative ECLS initiation for difficult or unsuccessful weaning from cardiopulmonary

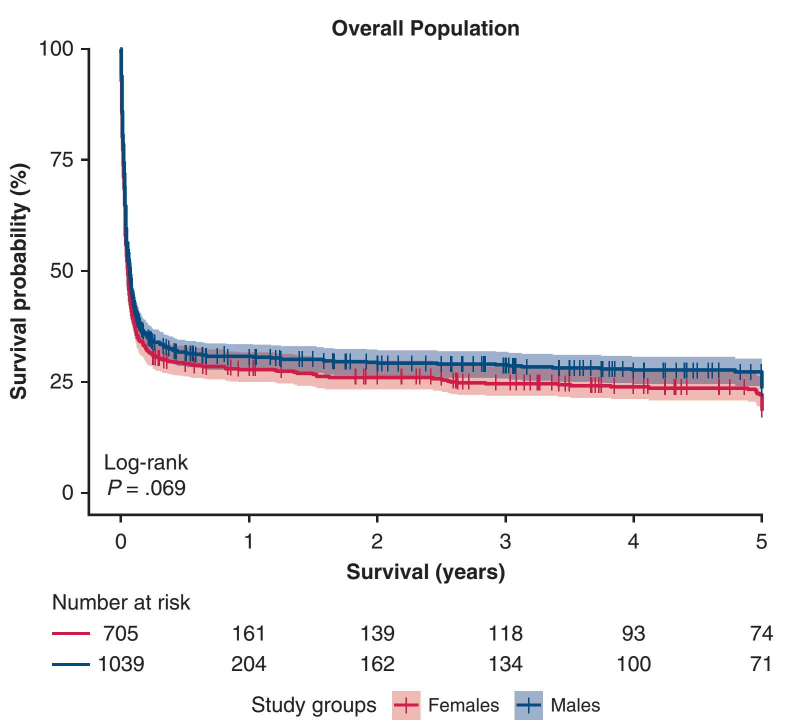

FIGURE 3. Five-year survival in females and males. Kaplan–Meier survival curves with 95% CIs.

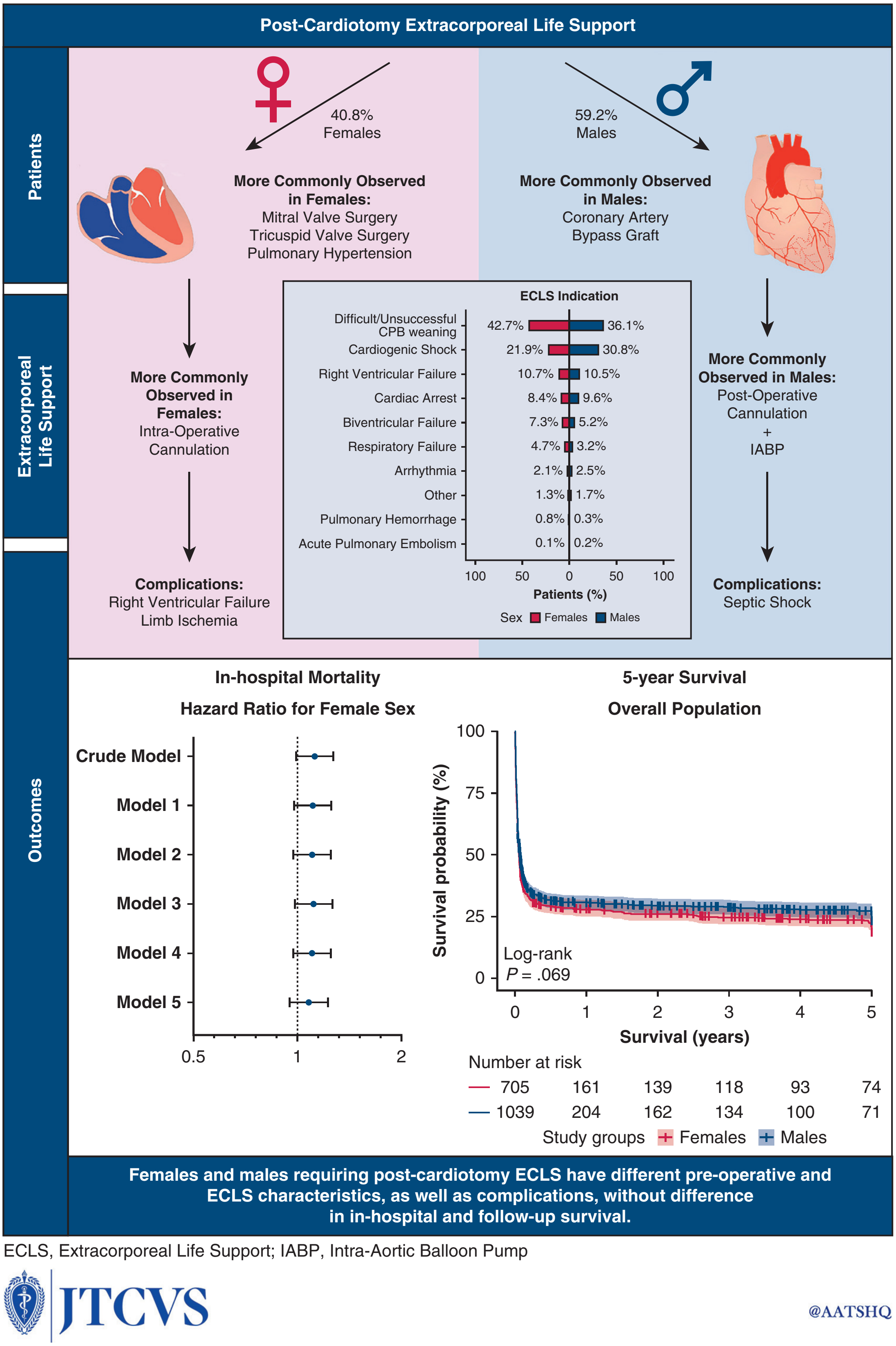

FIGURE 4. Graphical abstract. From the Post-Cardiotomy Extracorporeal Life Support Study 1 (n = 1823). This study demonstrates that females and males requiring postcardiotomy ECLS have different preoperative diagnoses, surgical indications, and ECLS characteristics, as well as complications, without a statistically significant difference in in-hospital and 5-year survivals. *IABP*, Intra-aortic balloon pump.

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bypass. Indeed, it has been demonstrated that in case of tricuspid valvular surgery an intraoperative initiation of ECLS may be associated with improvement in postoperative hemodynamics and a 35.5% in-hospital mortality compared with a 68.8% mortality for postoperative cannulation.[19] The role of intraoperative ECLS still needs to be clarified in case of pulmonary hypertension and right ventricular impairment, which can be associated with mitral and tricuspid valvular surgery.[20]

Differences in surgical indications are reflected by the postoperative complication profiles. Indeed, 24.1% of females developed postoperative right ventricular failure, which is a possible complication after mitral or tricuspid surgery. Among these females, 31.1% (n = 46/150, data not shown) required ECLS for right ventricular failure, 43.6% (n = 68/156, data not shown) were cannulated postoperatively, and 82.1% (n = 128/156, data not shown) died in the hospital. Moreover, preoperative pulmonary hypertension and preexisting right ventricular impairment seem to be associated with the occurrence of such a complication after surgery. Further studies are required to understand if a prophylactic intraoperative ECLS initiation in selected cases with a high risk of right ventricular failure could prevent these dramatic outcomes. Moreover, more attention must be paid to an early initiation of left ventricular unloading strategies to prevent left ventricular distension and right ventricular afterload increase.[21]

Leg ischemia complicates 12.3% of ECLS runs in females, in line with a reported incidence of 7% to 17%[8,22,23] associated with smaller blood vessels or shorter stature. In the current study, distal limb perfusion was used less frequently in females (68%) who underwent femoral cannulation compared with males (75.4%), and the use of vasopressors seemed to be associated with the occurrence of limb ischemia. Regular use of distal limb perfusion has been encouraged to prevent limb ischemia, yet this is still not routinely implemented in all centers.[24] Sex-specific benefits of distal limb perfusion must be investigated, but the results from this study encourage the regular use of distal limb perfusion in females. Very small vessels can be perfused with pediatric cannulas or 6F, 7F, and 8F armed introducers.[25]

Postoperative septic shock occurred more often in males (17.9%) than in females (14.1%) with 73.6% and 79.1% mortality (data not shown), respectively. This might be explained by active endocarditis, which was more prevalent in males, and this might have driven the development of postoperative shock.[8] Patients receiving postcardiotomy ECLS experience an infection risk ranging from 9% to 65%[1] due to multiple cannulation sites, mechanical ventilation, and surgical wounds. Moreover, Li and colleagues[26] demonstrated that nosocomial infections increase the relative risk of death after ECLS by 32%.

Despite these differences, in-hospital and long-term survival were comparable in males and females. Contradictory evidence exists in literature on this topic. Female sex has been identified as a risk factor for in-hospital mortality.[4,7] Chang and colleagues[6] identified an OR of 1.01 (95% CI, 0.87-1.18) for in-hospital mortality in females, mirroring larger studies addressing sex differences in ECLS.[5,8] Finally, an analysis of 7185 postcardiotomy ECLS runs included in the Extracorporeal Life Support Organization Registry did not identify female sex as a determinant of hospital death.[27] These discrepancies might be due to variations in included populations and ethnical groups, geographical and temporal differences, sample size, and local policies, but also nonclinical factors, including financial, historical, cultural, and ethical factors.[28] Overall, based on the results of the current study, females have a crude HR of 1.12 (95% CI, 0.99-1.27) for in-hospital mortality, indicating that female sex should not be considered as a risk factor in the patients' selection process for postcardiotomy ECLS. After adjustment, we noticed that the HR for females decreased to 1.08 (95% CI, 0.95-1.22) when adding complications to the mixed Cox model. Although not statistically significant, this result may suggest that clinicians should focus on preventing postoperative and ECLS-related complications to benefit in-hospital mortality.

Study Limitations

Our study is observational by nature, preventing causal inferences.[29] Because data collected focused on in-hospital variables, this study could not investigate potential prehospital sex-related differences. Moreover, postcardiotomy ECLS retrospective observational studies, by design, suffer from confounding by indication. Despite this, we adopted a prevalent observational descriptive statistical approach to remain as close as possible to the observed reality. This study analyzed patients on the basis of their self-reported biologically determined sex, but no genetic tests were conducted to verify the chromosome panel and differences based on gender identity, and related socially determined variables were not addressed.[9,14,15] Thus, we cannot exclude a gender bias for the absence of recognition of ischemic heart disease presentation in females.[30] Variable definitions were assigned at the time of study design and do not express the most recent scientific findings. For this reason, results on right ventricular failure are to be considered with caution. Multiple scoring systems (eg, Society of Thoracic Surgeons, Postcardiotomy Extracorporeal Membrane Oxygenation score, or Vasoactive-Inotropic Score) to stratify patients for disease severity were not included in the study database. Caution should be applied in the interpretation of data regarding postoperative transfusions due to a high percentage of missing data (n = 901/1824; 49.4%) and to logistic regression models for limb ischemia due to the lower number of observed events. Information on disability, functional status, and quality of life after discharge was not available. A partial overlapping with previously reported series cannot be excluded. Because ECLS volumes might vary over time per center and this study included data between 2000 and 2020, we did not study center-volume effects. However, we took center and year effects into account using mixed-effects regression analyses and performed sensitivity analyses excluding patients undergoing operation before 2011.

CONCLUSIONS

Females and males requiring postcardiotomy ECLS are two different clinical populations, marked by different preoperative characteristics, surgical indications, and ECLS features. Females experience more limb ischemia and right ventricular failure. Despite this, in-hospital and long-term survival did not statistically significantly differ between females and males, indicating that sex should not be considered as an exclusion criterion or a negative factor for survival at the moment of ECLS initiation. Nevertheless, more attention to sex-specific ECLS features and complications is advised to improve outcomes. New studies are necessary to investigate the effect of gender in the ECLS field in terms of patients' access to health care, clinicians' gender perception in the decision-making process, and post-ECLS long-term care.

Conflict of Interest Statement

R.L. is a consultant for Medtronic, Getinge, Abiomed, and LivaNova; Advisory Board Member of Eurosets, Hemocue, and Xenios (honoraria as research funding). D.W. is a consultant/proctor for Abbott and a scientific advisor for Xenios. K.R. reports honorarium from Baxter and Fresenius 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.

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

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APPENDIX E1. SUPPLEMENTAL METHODS

Diversity Information and Authors' Contributions

The coordinating team for the current sub-study of the Post-Cardiotomy Extra-Corporeal Life Support Study (PELS-1) was developed to adhere as much as possible with the "3G" principles to mitigate personnel gaps in gender (sex), generation, and geography.[E1] Furthermore, the team was designed to include different specialties and expertise and comply with a multidisciplinary approach. The details of the study's leadership group are as follows:

- S.M.: Surgeon, overall PELS clinical trial coordinator and Principal Investigator of the current PELS sub-study. Nationality: Italian. Role: Concept/design. Study coordination. Data collection. Data cleaning. Statistics. Data analysis/interpretation. Drafting article.
- B.C.T.vB.: Internist, intensivist, and epidemiologist. Nationality: Dutch. Role: Concept/design. Statistics. Data analysis/interpretation. Drafting article.
- J.M.R.: Surgeon. Nationality: Belgian. Role: Role: Concept/design. Data cleaning. Data analysis/interpretation. Drafting article.
- M.E.D.P.: Intensivist. Nationality: Italian. Role: Concept/design. Data cleaning. Data analysis/interpretation. Drafting article.
- R.L.: Senior surgeon, supervisor, and PELS Chief Investigator. Nationality: Italian. Role: Concept/design. Study coordination. Data analysis/interpretation. Drafting article. Supervision.

The complete PELS consists of a large consortium of 34 hospitals from 16 countries and 5 continents including Europe, North America, South America, Asia, and Australia to promote inclusion of authors and patients of different ethnicities. Each center has been encouraged to include in the study group a senior principal investigator and a young investigator to promote gender and generation diversity. Each center is represented in the authors list of all PELS articles by at least 1 author, with alternance of senior and young investigators based on internal choice of each center and the contribution of each author to the development of the specific study. Because of the limitations to the number of authors of most journals, all investigators who are not added in the main authors list are listed in the PELS Investigators list in the Supplementary material. All PELS articles are shared within the PELS collaborative group, and all authors and investigators are invited to contribute to the development of each study and manuscript revision.

Data Collection

The following predefined groups of data were collected:

- Demographic data: sex, age, race
- Patients' characteristics: European System for Cardiac Operative Risk Evaluation, length, weight, serum creatinine level, left ventricular ejection fraction, and 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 (LVAD), New York Heart Association (NYHA) 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 edema, 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, postacute myocardial infarction ventricular septal rupture, free wall/papillary muscle rupture, graft failure, active endocarditis, atrial septal defect, post-LVAD right ventricular failure, other diagnosis
- Coronary surgery: arterial graft, number of distal arterial anastomoses, left internal thoracic artery, right internal thoracic artery, radial artery, gastroepiploic artery, other arterial graft, venous graft, number of distal venous anastomoses, 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, additional pacemaker/implantable cardioverter defibrillator procedure, ventricular septal defect closure, atrial septal defect closure, ventricular surgery, pericardiectomy, pulmonary embolectomy/endarterectomy, other cardiac surgery, other cardiac surgery description
- Extracorporeal circulation: extracorporeal circulation duration, crossclamp duration, circulation arrest, cardioplegia characteristics, off-pump conversion
- Extracorporeal membrane oxygenation variables, 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 re-thoracotomy, cannulation site bleeding, diffuse no surgical-related bleeding), neurological 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 shock 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.

Variable Definitions

The following definitions were used for the main study variables:

- Sex: our research and article have been developed in accordance with the international World Health Organization definitions of sex and gender where "gender" describes those characteristics of females and males that are largely socially created (including concepts such as cisgender and transgender), and "sex" encompasses those that are biologically determined (https://www.who.int/genomics/gender/en/). The same distinction is mirrored by the definitions of gender and sex given by several other international institutions such as the World Health Organization Regional Office for Europe (https://www.euro.who.int/en/health-topics/health-determinants/gender/gender-definitions), the Office for National Statistics, and UK government (https://www.ons.gov.uk/economy/environmentalaccounts/articles/whatisthedifferencebetweensexandgender/2019-02-21) or the Canadian Institutes of Health Research (https://cihr-irsc.gc.ca/e/48642.html). Despite these definitions, sex and gender often are mistakenly used interchangeably in scientific literature, health policy, and legislation. In our study, we defined our patients based on biologically determined sex (male/female) and did not include a further analysis of gender identity.[E2-E4]
- Hypertension: systolic blood pressure more than 140 mm Hg or diastolic blood pressure more than 90 mm Hg,[E5] or use of antihypertensive agents to maintain normal blood pressure
- Smoking: active (smoking during the past 30 days) and more than 100 cigarettes during lifetime
- Chronic obstructive pulmonary disease: diagnosis of chronic obstructive pulmonary disease, any Gold classification[E6]
- Peripheral arterial disease: claudication, carotid occlusion or more than 50% stenosis, amputation for arterial disease or previous, or planned intervention on the abdominal aorta, limb arteries, or carotids[E7]
- Pulmonary hypertension: systolic pulmonary artery pressure more than 50 mm Hg
- 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, neurological function, renal function, presence of active endocarditis, preoperative state, procedural urgency, and procedure type[E7]
- NYHA class: Functional class of dyspnea according to the classification as proposed by the NYHA
- Preoperative cardiogenic shock: preoperative state with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, with worsening acidosis or lactate levels[E8]
- Preoperative cardiac arrest: preoperative cardiopulmonary resuscitation in the 24 hours before surgery
- Preoperative septic shock: septic patients with vasopressor requirement to maintain mean arterial pressure greater than 65 mm Hg and serum lactate levels greater than 2 mmol/L in the absence of hypovolemia[E9]
- Preoperative right ventricular failure: evidence of right-sided structural or functional abnormalities in combination with clinical symptoms and signs of right ventricular failure[E10]
- Preoperative biventricular failure: biventricular dysfunction accompanied by both signs and symptoms of right-sided and left-sided heart failure[E11]
- Emergency surgery: surgery before the beginning of the next working day after the decision to operate is made[E7]
- 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[E7]
- 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

- Active endocarditis: patients still on antibiotic treatment for endocarditis at the time of surgery[E7]
- Post-LVAD right ventricular failure: right ventricular failure as described previously in presence of LVAD
- Ventricular surgery: surgery performed to restore structural ventricular function, especially in case of ventricular aneurysm formation or rupture
- Rhythm surgery: surgical (epicardial or endo-epicardial) ablation performed for atrial or ventricular arrhythmia
- Failure to wean: failure to wean from cardiopulmonary bypass 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 or lactate levels[E8]
- Right ventricular failure: evidence of right-sided structural or functional abnormalities in combination with clinical symptoms and signs of right ventricular failure[E10]
- Respiratory failure: reversible pulmonary disease that cannot be managed anymore 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[E11]
- 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
- Stroke: neurological dysfunction caused by focal brain or retinal ischemia with clinical symptoms lasting less more than 24 hours, with or without permanent disability
- Transient ischemic attack: a brief episode of neurological dysfunction caused by focal brain or retinal ischemia with clinical symptoms lasting less than 1 hour, without evidence of acute brain infarction[E12]
- Arrhythmia: any atrial or ventricular arrhythmia lasting more than 30 seconds
- Leg ischemia: clinical signs of lower-extremity ischemia requiring intervention (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 mean arterial pressure more than 65 mm Hg and serum lactate levels greater than 2 mmol/L in the absence of hypovolemia[E9]
- Distributive shock syndrome: mean arterial pressure less than 50 mm Hg with cardiac index more than 2.5 L/min/m^2, right atrial pressure less than 5 mm Hg, left atrial pressure less than 10 mm Hg, and low systemic vascular resistance (<800 dyne/s/cm^{-5}) during intravenous norepinephrine infusion (>0.5 μg/kg/min)[E13]
- Acute respiratory distress syndrome: acute diffuse inflammatory lung injury requiring invasive mechanical ventilation of extracorporeal membrane oxygenation
- Multiorgan failure: hypometabolic state with involvement of more than 1 organ as established by biochemical or radiological analysis

Statistical Analysis

Data were merged and analyzed using SPSS 26.0 (IBM), and R 4.1.2 (R Foundation for Statistical Computing) (Appendix E1). The full cohort was categorized into 2 study groups (females and males) for comparisons. Missing data analysis was conducted with the *mice*: *Multivariate Imputation by Chained Equations* R package.[E14] The percentage of missing values was calculated for each variable and reported in Table E1. Missing data patterns were investigated and identified as missing completely at random.

Descriptive statistics were conducted on available data only, and no imputations were performed for this purpose. Normality was investigated with Kolmogorov-Smirnov, Shapiro-Wilk, and direct inspection of histograms as appropriate. Demographic and clinical variables are expressed as numbers (valid percent on available data, excluding missing values) for categorical variables and median (interquartile range) or mean and SD for continuous variables. Categorical data were compared between groups with Pearson's chi-square or Fisher exact test. Continuous variables were analyzed using the independent-samples t test or Mann–Whitney U test, as appropriate. Stacked bar plots were designed to represent the distributions of levels within each categorical variable and compare them between study groups. We described the population characteristics and preoperative variables, intraoperative variables, variables while on ECLS, and postoperative complications stratified for males and females.

To estimate the associations between sex and postoperative right ventricular failure and lower-limb ischemia, we conducted a mixed-effects multivariable logistic regression using the *lme4*: *Linear Mixed-Effects Models using 'Eigen' and S4* R package.[E15] The random effect was used to account for dependency of observations due to clustering in centers and in years. For both outcomes, we first estimated a crude model, which was subsequently first adjusted for sets of variables (Appendix E1) deemed potential confounders for the

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association with the outcome. For the association with right ventricular failure, we used the following models:

Model 1: crude model with variable "sex"

Model 2: sex, pulmonary hypertension

Model 3: sex, pulmonary hypertension, left ventricular unloading

Model 4: sex, age, body mass index, dialysis, myocardial infarction, atrial fibrillation, chronic obstructive pulmonary disease, pulmonary hypertension, previous cardiac surgery, left ventricular ejection fraction, cardiogenic shock, urgent surgery, emergency surgery, cardiac arrest, acute pulmonary edema, preoperative right ventricular failure

Model 5: sex, age, pulmonary hypertension, previous cardiac surgery, left ventricular ejection fraction, acute pulmonary edema, preoperative right ventricular failure, cardiopulmonary bypass time, mitral valve surgery, tricuspid valve surgery, postoperative ECLS implantation, postoperative bleeding requiring re-thoracotomy, postoperative acute kidney injury, left ventricular unloading

For the association with lower-limb ischemia. we used the following models:

Model 1: crude model with variable "sex"

Model 2: sex, body surface area

Model 3: sex, body surface area, distal perfusion

Model 4: sex, body surface area, distal perfusion, age, history of peripheral vessel disease, preoperative vasopressors, bleeding at cannulation site, extracorporeal cardiopulmonary resuscitation

To estimate the associations between sex and in-hospital mortality, we conducted a mixed-effects Cox proportional hazards regression, using the *coxme*: *Mixed Effects Cox Models* R package. The random effect was used to account for dependency of observations due to clustering in centers and in years. The proportional hazards assumption was tested with Schoenfeld residuals, and nonlinearity for continuous variables was tested with Martingale residuals. We first estimated a crude model, which was subsequently first adjusted for age, then for sets of variables (Appendix E1) deemed potential confounders for the association with mortality at patient selection, intraoperative decisions, and for ECMO management, based on clinical practice and literature.[E16-E20] For the association with in-hospital mortality, we used the following models:

Model 1: age

Model 2: demographic data and preoperative variables: age, body mass index, dialysis, previous myocardial infarction, stroke, atrial fibrillation, diabetes, chronic obstructive pulmonary disease, peripheral artery disease, pulmonary hypertension, previous cardiac surgery, preoperative left ventricular ejection fraction, cardiogenic shock, urgency status (elective, urgent, emergency surgery), cardiac arrest, septic shock, preoperative IABP, right ventricular failure

Model 3: demographic data, preoperative and intraoperative variables. Model 2 + cardiopulmonary bypass time, coronary artery bypass surgery, aortic valve surgery, mitral valve surgery, tricuspid valve surgery, aortic surgery, other types of surgery (including all types of surgery other than those previously listed)

Model 4: demographic data, preoperative, intraoperative and ECMO variables; model 3 + ECLS implant timing, ECLS indication, cannulation approach

Model 5: demographic data, preoperative, intraoperative, ECMO variables, and postoperative complications; model 4 + bleeding requiring re-thoracotomy, postoperative cerebral hemorrhage, postoperative stroke, leg ischemia, postoperative cardiac arrest, postoperative bowel ischemia, postoperative acute kidney injury, postoperative septic shock, postoperative right ventricular failure

The mixed-effects Cox proportional hazards and logistic regression models were developed on 5 imputed datasets after imputation of variables with less than 20% missing data. Variables with more missing data were omitted from the models. We used the *mice*: *Multivariate Imputation by Chained Equations* R package[E14] for the imputation process. Five imputed datasets were created with "cart" method, mixed-Cox models were run on each of these datasets and results were pooled (*junkka/ehahelper*: *Helper Functions for Event History Analysis* R package) to obtain estimates as HRs with their 95% CIs and *P* values. Based on the hormonal variation in the different ages of females, effect modification of sex and the outcome by age was investigated by adding an interaction term between sex and age to the models.

Overall survival was investigated with the Kaplan–Meier method and comparisons were performed with log-rank test (*survival* and *survminer* R packages). Patients' loss to follow-up was included in survival analyses and considered censored at the time of their last control. Curves were truncated when the number of patients at risk from the study group (females) dropped below 10% of the initial sample (at 5 years).

Based on the possible variations in ECLS management over the study period. a sensitivity analysis[E21] was performed after exclusion of patients who received a postcardiotomy ECLS before 2011. A further sensitivity analysis was performed to include only patients who underwent CABG or valvular operations. Subgroup analyses were conducted to investigate overall survival in patients who underwent coronary artery bypass surgery, mitral valve surgery, and tricuspid valve surgery.

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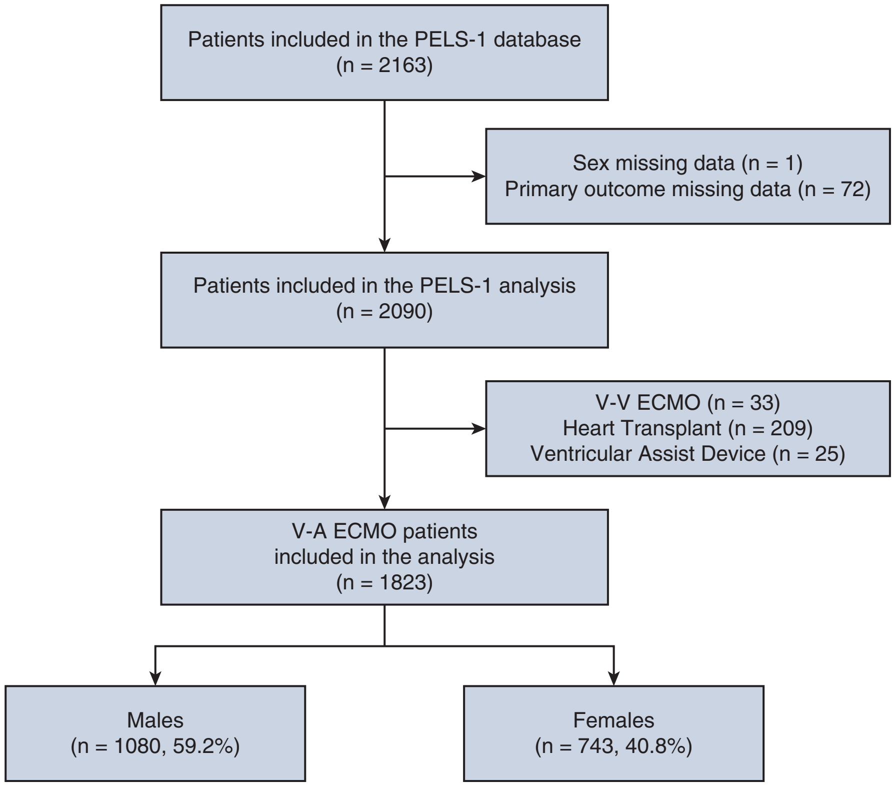

FIGURE E1. Flow-chart describing the patients included in the current study. *PELS-1*, Post-Cardiotomy Extra-Corporeal Life Support Study; *VV-ECMO*, venovenous extracorporeal membrane oxygenation; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation.

FIGURE E2. Bar chart representing the yearly variations of female-male ratio of patients included in the current analysis of the Post-Cardiotomy Extracorporeal Life Support Study 1 reported as percentages.

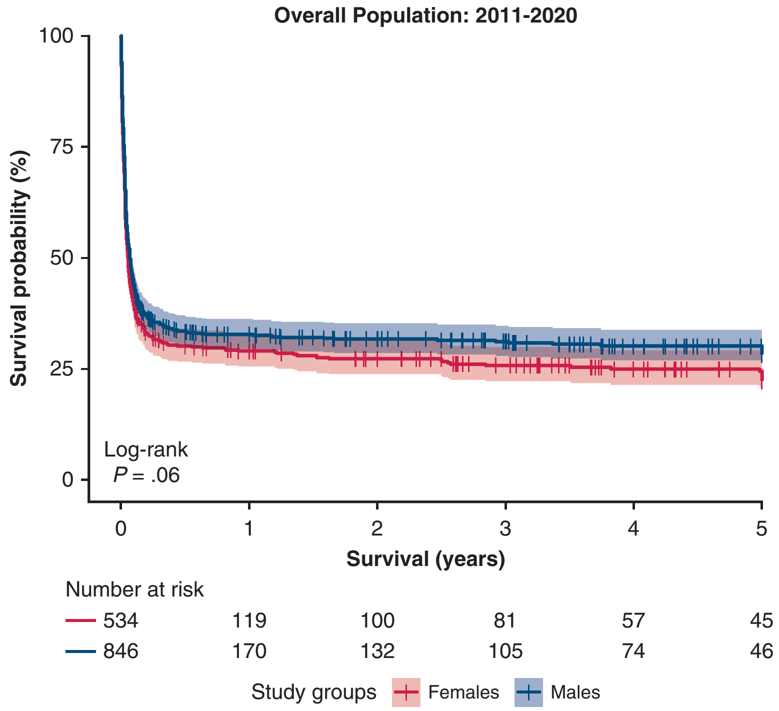

FIGURE E3. Overall Kaplan–Meier survival curves with 95% confidence limit of patients who had venoarterial ECLS for postcardiotomy support between 2011 and 2020. Groups are defined according to sex.

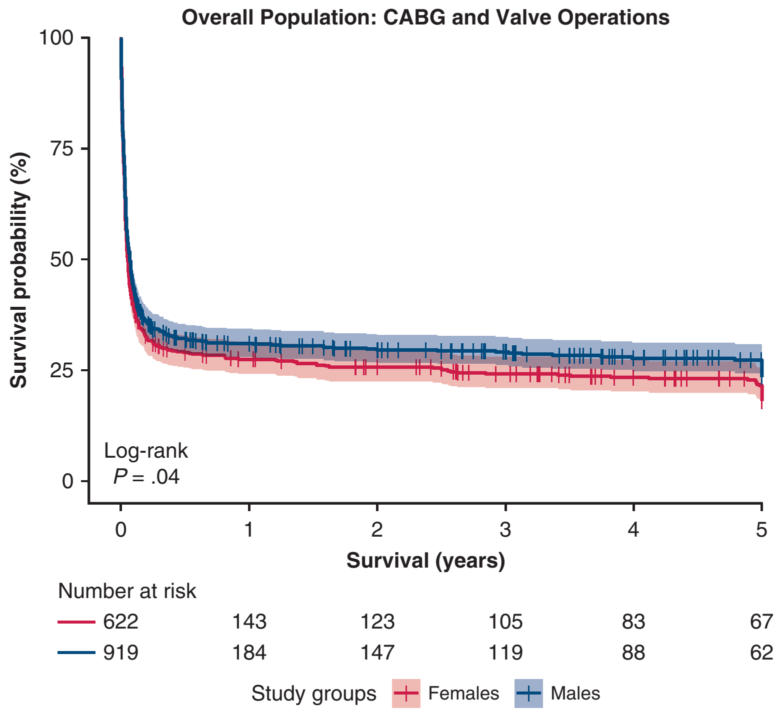

FIGURE E4. Overall Kaplan–Meier survival curves with 95% confidence limit of patients who underwent CABG or valvular surgery and required ECLS. Groups are defined according to sex. *CABG*, Coronary artery bypass grafting.

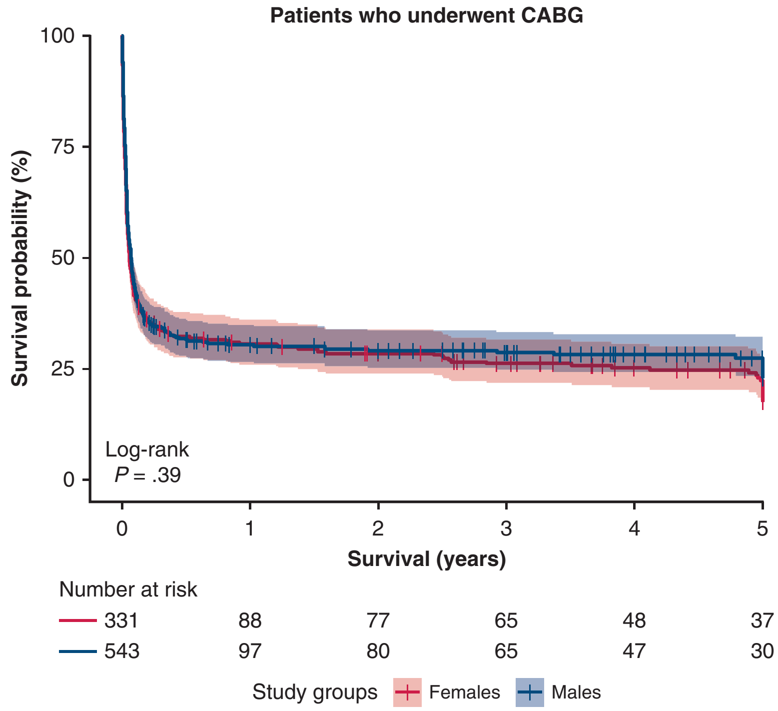

FIGURE E5. Overall Kaplan–Meier survival curves with 95% confidence limit of patients who underwent CABG surgery and required ECLS. Groups are defined according to sex. *CABG*, Coronary artery bypass grafting.

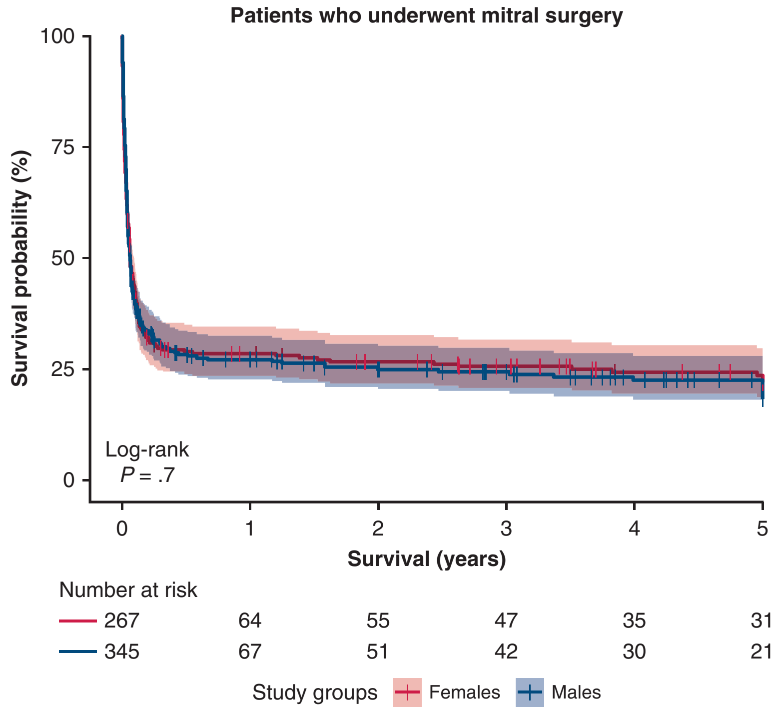

FIGURE E6. Overall Kaplan–Meier survival curves with 95% confidence limit of patients who underwent mitral valve surgery and required ECLS. Groups are defined according to sex.

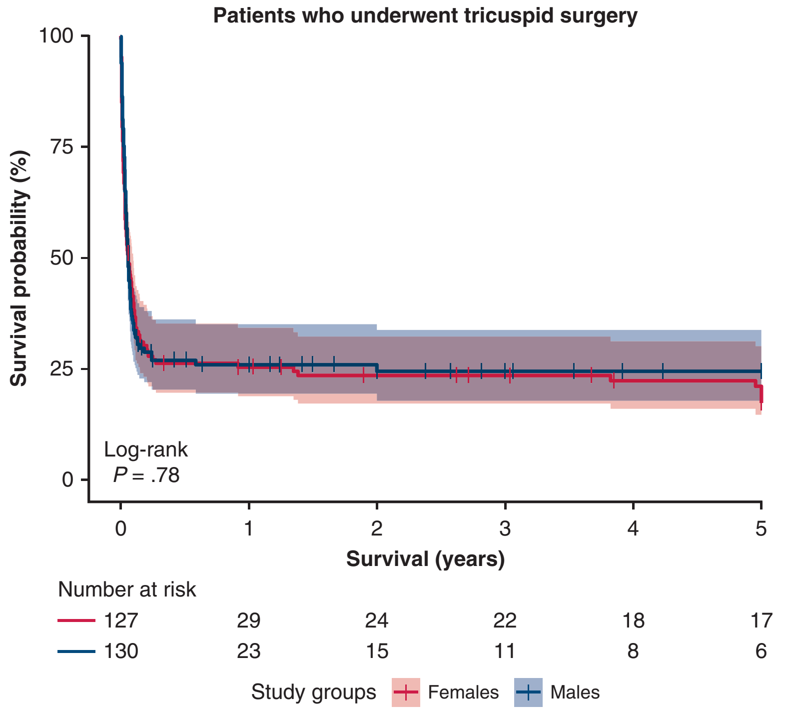

FIGURE E7. Overall Kaplan–Meier survival curves with 95% confidence limit of patients who underwent tricuspid valve surgery and required ECLS. Groups are defined according to sex.

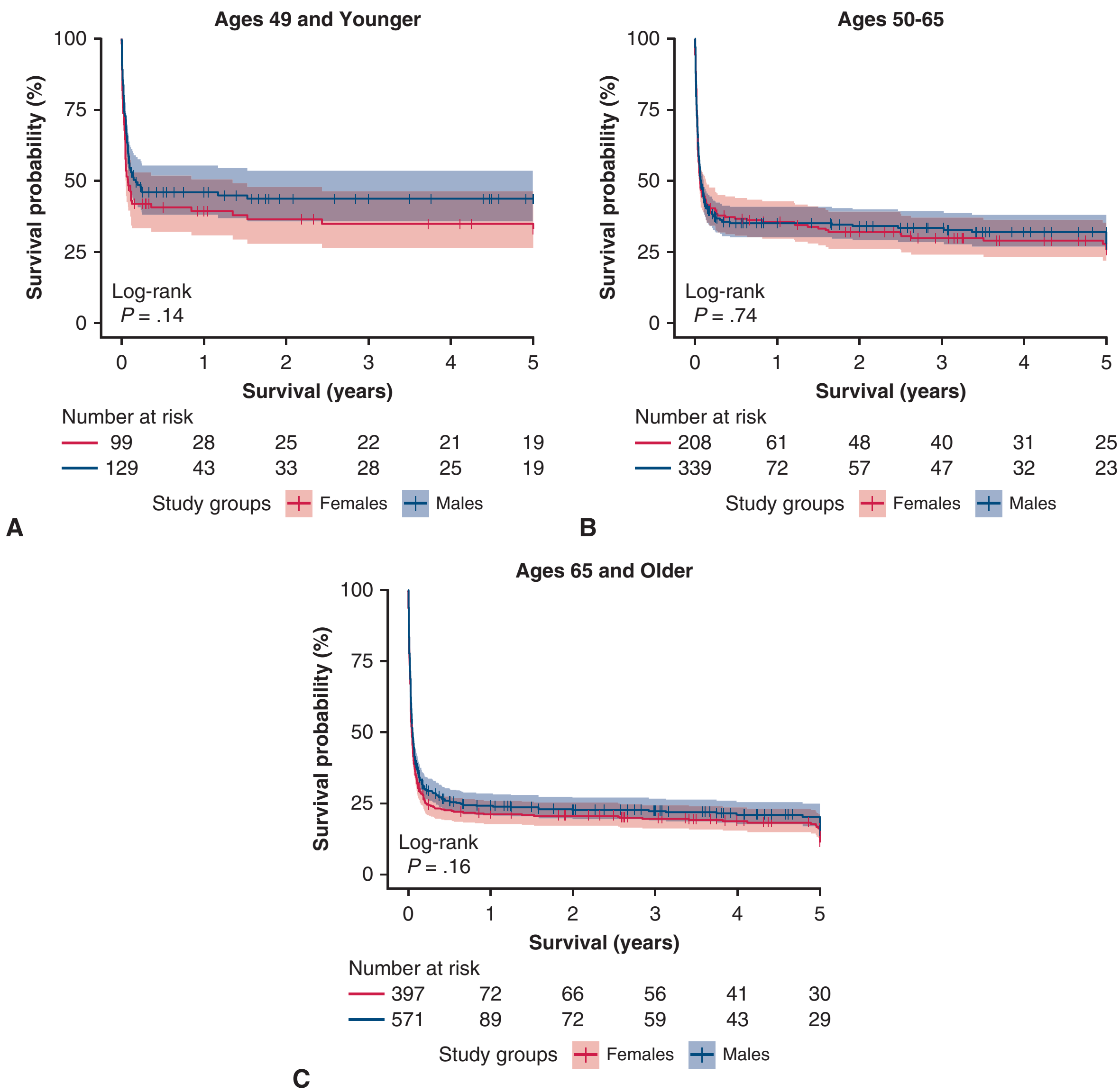

FIGURE E8. Overall Kaplan–Meier survival curves with 95% confidence limit of patients who underwent postcardiotomy ECLS stratified by age: <50 years (A), 50 to 64.9 years (B), ≥65 years (C). Groups are defined according to sex.

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TABLE E1. Complete and missing cases for each study variable

Variables	Complete cases	Missing cases
Age (y)	1822 (99.9%)	1 (0.1%)
Ethnicity	1823 (100%)	0 (0%)
Body mass index (kg/m^2)	1812 (99.4%)	11 (0.6%)
Body surface area (m^2)	1812 (99.4%)	11 (0.6%)
Comorbidities		
Hypertension	1753 (96.2%)	70 (3.8%)
Dialysis	1764 (96.8%)	59 (3.2%)
Previous myocardial infarction	1823 (100%)	0 (0%)
Myocardial infarction (last 30 d)	1753 (96.2%)	70 (3.8%)
Smoking	1555 (85.3%)	268 (14.7%)
Previous stroke	1823 (100%)	0 (0%)
Atrial fibrillation	1822 (99.9%)	1 (0.1%)
Diabetes mellitus	1823 (100%)	0 (0%)
Implanted pacemaker	1672 (91.7%)	151 (8.3%)
Implanted cardioverter-defibrillator	1670 (91.6%)	153 (8.4%)
Previous percutaneous coronary intervention	1810 (99.3%)	13 (0.7%)
Chronic obstructive pulmonary disease	1758 (96.4%)	65 (3.6%)
Peripheral artery disease	1823 (100%)	0 (0%)
Pulmonary hypertension (>50 mm Hg)	1814 (99.5%)	9 (0.5%)
Previous cardiac surgery	1823 (100%)	0 (0%)
Preoperative creatinine (μmol/L)	1700 (93.3%)	123 (6.7%)
Left ventricular ejection fraction (%)	1736 (95.2%)	87 (4.8%)
euroSCORE II	1278 (70.1%)	545 (29.9%)
Preoperative condition		
NYHA class	1731 (95.0%)	92 (5.0%)
Preoperative cardiogenic shock	1799 (98.7%)	24 (1.3%)
Preoperative intubation	1822 (99.9%)	1 (0.1%)
Preoperative cardiac arrest	1802 (98.8%)	21 (1.2%)
Preoperative septic shock	1744 (95.7%)	79 (4.3%)
Preoperative vasopressors	1811 (99.3%)	12 (0.7%)
Preoperative acute pulmonary edema	1742 (95.6%)	81 (4.4%)
Preoperative right ventricular failure	1603 (87.9%)	220 (12.1%)
Emergency surgery	1804 (99.0%)	19 (1.0%)
Urgent surgery	1807 (99.1%)	16 (0.9%)
Diagnosis		
CAD	1823 (100%)	0 (0%)
Aortic vessel disease	1823 (100%)	0 (0%)
Aortic valve disease	1823 (100%)	0 (0%)
Mitral valve disease	1823 (100%)	0 (0%)
Tricuspid valve disease	1823 (100%)	0 (0%)
Pulmonary valve disease	1823 (100%)	0 (0%)
Postacute myocardial infarction ventricular septal rupture	1823 (100%)	0 (0%)
Free wall/papillary muscle rupture	1823 (100%)	0 (0%)
Active endocarditis	1823 (100%)	0 (0%)
Atrial septal defect	1823 (100%)	0 (0%)
Post–left ventricular assist device right ventricular failure	1823 (100%)	0 (0%)
Other diagnosis	1823 (100%)	0 (0%)
Weight of surgery	1823 (100%)	0 (0%)
CABG	1823 (100%)	0 (0%)
Aortic valve surgery	1823 (100%)	0 (0%)
Mitral valve surgery	1822 (99.9%)	1 (0.1%)

(Continued)

TABLE E1. Continued

Variables	Complete cases	Missing cases
Tricuspid valve surgery	1823 (100%)	0 (0%)
Aortic surgery	1823 (100%)	0 (0%)
Pulmonary valve surgery	1823 (100%)	0 (0%)
Atrial septal defect repair	1823 (100%)	0 (0%)
Ventricular septal defect repair	1823 (100%)	0 (0%)
Ventricular surgery	1823 (100%)	0 (0%)
Rhythm surgery	1823 (100%)	0 (0%)
Pulmonary embolectomy	1823 (100%)	0 (0%)
Pulmonary endarterectomy	1823 (100%)	0 (0%)
Off-pump surgery	1793 (98.4%)	30 (1.6%)
Cardiopulmonary bypass time (min)	1651 (90.6%)	172 (9.4%)
Crossclamp time (min)	1641 (90.0%)	182 (10%)
ECLS indication	1783 (97.8%)	40 (2.2%)
Cannulation approach	1823 (100%)	0 (0%)
Chest status	1332 (73%)	492 (27%)
Implant timing	1823 (100%)	0 (0%)
IABP	1801 (98.8%)	22 (1.2%)
Left ventricular vent	1479 (81.1%)	344 (18.9%)
Extracorporeal membrane oxygenation duration (h)	1791 (98.2%)	32 (1.8%)
Intensive care unit stay (d)	1753 (96.2%)	70 (3.8%)
Hospital stay (d)	1759 (96.5%)	64 (3.5%)
Postoperative bleeding	1795 (98.5%)	28 (1.5%)
Requiring re-thoracotomy	1718 (94.2%)	105 (5.8%)
Cannulation site bleeding	1791 (98.2%)	32 (1.8%)
Diffuse no surgical-related bleeding	1648 (90.4%)	175 (9.6%)
Neurological complications		
Cerebral hemorrhage	1720 (94.3%)	103 (5.7%)
Stroke	1812 (99.4%)	11 (0.6%)
Arrhythmia	1678 (92.0%)	145 (8.0%)
Leg ischemia	1714 (94.0%)	109 (6.0%)
Cardiac arrest	1679 (92.1%)	144 (7.9%)
Pacemaker implant	1678 (92%)	145 (8.0%)
Bowel ischemia	1679 (92.1%)	144 (7.9%)
Right ventricular failure	1644 (90.2%)	179 (9.8%)
Acute kidney injury	1674 (91.8%)	149 (8.2%)
Pneumonia	1644 (90.2%)	179 (9.8%)
Septic shock	1642 (90.1%)	181 (9.9%)
Distributive shock	1641 (90.0%)	182 (10.0%)
Acute respiratory distress syndrome	1678 (92.0%)	145 (8.0%)
Multiorgan failure	1807 (99.1%)	16 (0.9%)
Embolism	1646 (90.3%)	177 (9.7%)
Postoperative procedures		
Percutaneous coronary intervention	1620 (88.9%)	203 (11.1%)

(Continued)

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TABLE E1. Continued

Variables	Complete cases	Missing cases
Cardiac surgery	1679 (92.1%)	144 (7.9%)
Abdominal surgery	1620 (88.9%)	203 (11.1%)
Vascular surgery	1624 (89.1%)	199 (10.9%)
In-hospital mortality	1823 (100%)	0 (0%)
In-hospital mortality - timing	1810 (99.3%)	13 (0.7%)

Sensitivity analysis after excluding patients who received treatments before 2011. *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *CABG*, coronary artery bypass grafting; *ECLS*, extracorporeal life support; *IABP*, intra-aortic balloon pump.

TABLE E2. Preoperative characteristics of patients who received treatment in the decade 2011-2020

Variables	Females (n = 567)	Males (n = 876)	*P* value
Age (y)	66.27 (57-74)	66.00 (56-72)	.073
Race			.029
Asian	36 (7.9%)	91 (13.5%)	
Black	4 (0.9%)	8 (1.2%)	
Hispanic	19 (4.2%)	38 (5.6%)	
White	354 (77.5%)	481 (71.3%)	
Other	14 (3.1%)	12 (1.8%)	
Unknown	30 (6.6%)	45 (6.7%)	
Body mass index (kg/m^2)	26.03 (23.3-30.1)	26.60 (24.2-29.8)	.089
Body surface area (m^2)	1.79 (1.6-1.9)	1.95 (1.8-2.1)	<.001
Comorbidities			
Hypertension	371 (69%)	589 (70%)	.719
Smoking	93 (19.7%)	243 (30.1%)	<.001
Diabetes mellitus	**128 (22.6%)**	**241 (27.5%)**	**.036**
Previous myocardial infarction	120 (21.2%)	252 (28.8%)	.001
Myocardial infarction (last 30 d)	**53 (9.9%)**	**120 (14.3%)**	**.016**
Previous percutaneous coronary intervention	76 (13.5%)	162 (18.5%)	.013
Previous stroke	86 (15.2%)	108 (12.3%)	.133
Peripheral artery disease	78 (13.8%)	132 (15.1%)	.541
Atrial fibrillation	156 (27.5%)	208 (23.8%)	.121
Chronic obstructive pulmonary disease	52 (9.7%)	82 (9.5%)	.926
Pulmonary hypertension (>50 mm Hg)	132 (23.6%)	152 (17.4%)	.004
Previous cardiac surgery	123 (21.7%)	204 (23.3%)	.520
Preoperative creatinine (μmol/L)	92.0 (71-123.8)	104.00 (80.4-141)	<.001
Dialysis	40 (7.3%)	78 (9%)	.278
Left ventricular ejection fraction (%)	52.5 (40-60)	48.00 (34-60)	.001
euroSCORE II	6.99 (2.8-18.2)	6.95 (2.7-17.3)	.538
Preoperative condition			
NYHA class			.882
Class I	47 (8.7%)	67 (8.1%)	
Class II	123 (22.7%)	183 (22%)	
Class III	224 (41.3%)	337 (40.6%)	
Class IV	149 (27.4%)	244 (29.4%)	
Preoperative cardiogenic shock	107 (19.1%)	219 (25.2%)	.008
Preoperative intubation	62 (11%)	116 (13.2%)	.219
Preoperative cardiac arrest	45 (8.1%)	72 (8.3%)	.921
Preoperative septic shock	14 (2.6%)	30 (3.6%)	.350
Preoperative vasopressors	72 (12.8%)	153 (17.5%)	.017
Preoperative acute pulmonary edema	37 (6.9%)	64 (7.6%)	.672
Preoperative right ventricular failure	50 (10.2%)	67 (8.3%)	.232
Emergency surgery	131 (23.7%)	250 (28.7%)	.043
Urgent surgery	113 (20.3%)	159 (18.2%)	.334
Diagnosis			
CAD	252 (44.4%)	489 (55.8%)	<.001
Aortic vessel disease	106 (18.7%)	178 (20.3%)	.457
Aortic valve disease	209 (36.9%)	322 (36.8%)	1.000
Mitral valve disease	233 (41.1%)	303 (34.6%)	.014
Tricuspid valve disease	118 (20.8%)	145 (16.6%)	.043
Pulmonary valve disease	5 (0.9%)	9 (1%)	1.000
Post-AMI ventricular septal rupture	13 (2.3%)	31 (3.5%)	.211
Free wall/papillary muscle rupture	8 (1.4%)	17 (1.9%)	.539
Active endocarditis	**40 (7.1%)**	**88 (10%)**	**.058**
Atrial septal defect	13 (2.3%)	13 (1.5%)	.312
Other diagnosis	57 (10.1%)	90 (10.3%)	.929

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). Text in bold indicates differences compared with the main analysis. *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *AMI*, acute myocardial infarction.

TABLE E3. Procedural characteristics of patients who received treatment in the decade 2011-2020

Variables	Females (n = 567)	Males (n = 876)	*P* value
CABG	255 (45%)	458 (52.3%)	.007
Aortic valve surgery	230 (40.6%)	327 (37.3%)	.224
Mitral valve surgery	222 (39.2%)	287 (32.8%)	.013
Tricuspid valve surgery	109 (19.2%)	114 (13%)	.002
Aortic surgery	118 (20.8%)	201 (22.9%)	.363
Pulmonary valve surgery	4 (0.7%)	7 (0.8%)	1
Atrial septal defect repair	14 (2.5%)	15 (1.7%)	.34
Ventricular septal defect repair	18 (3.2%)	33 (3.8%)	.662
Ventricular surgery	26 (4.6%)	40 (4.6%)	1
Rhythm surgery	25 (4.4%)	32 (3.7%)	.491
Pulmonary embolectomy	8 (1.4%)	8 (0.9%)	.443
Pulmonary endarterectomy	**17 (3%)**	**12 (1.4%)**	**.035**
Off-pump surgery	15 (2.7%)	56 (6.5%)	.001
Conversion to cardiopulmonary bypass	7 (43.8%)	15 (25.9%)	.218
Cardiopulmonary bypass time (min)	201 (135-297)	195 (134-280)	.431
Crossclamp time (min)	103 (68-152)	103 (63-153)	.455

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). Text in bold indicates differences compared with the main analysis. *CABG*, Coronary artery bypass grafting.

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TABLE E4. Details on extracorporeal life support of patients who received treatment in the decade 2011-2020

Variables	Females (n = 567)	Males (n = 876)	*P* value
ECLS implantation timing			**.078**
Intraoperative	**358 (63.1%)**	**512 (54.8%)**	
Postoperative	**209 (36.9%)**	**364 (41.6%)**	
Cannulation approach			.075
Only central cannulation	15 (2.6%)	17 (1.9%)	
Only peripheral cannulation	92 (16.2%)	127 (14.5%)	
Mixed/switch cannulation	241 (42.5%)	433 (49.4%)	
Unknown	219 (38.6%)	299 (34.1%)	
Left ventricular unloading	126 (26.3%)	247 (35%)	.002
IABP during any time of hospitalization	125 (22.6%)	286 (32.9%)	<.001
IABP implantation timing			**.033**
Preoperative	**27 (21.6%)**	**92 (32.2%)**	
Intraoperative	**98 (78.4%)**	**194 (67.8%)**	
Distal femoral perfusion in patients with peripheral cannulation	158 (69.3%)	313 (77.9%)	.022
ECLS duration (h)	120 (64-204.4)	120.00 (60-199)	.935

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). Text in bold indicates differences compared with the main analysis. *ECLS*, Extracorporeal life support; *IABP*, intra-aortic balloon pump.

TABLE E5. Postoperative outcomes of patients who received treatment in the decade 2011-2020

Variables	Females (n = 567)	Males (n = 876)	*P* value
Intensive care unit stay (d)	14 (6-28)	13.00 (5-23)	.082
Hospital stay (d)	19 (7-37)	19.00 (9-36)	.997
Postoperative bleeding	307 (55.4%)	480 (55.7%)	.913
Requiring re-thoracotomy	213 (40.7%)	302 (36.2%)	.096
Cannulation site bleeding	66 (12%)	104 (12.1%)	1
Diffuse no surgical-related bleeding	114 (23.4%)	193 (24%)	.84
Neurological complications			
Cerebral hemorrhage	18 (3.4%)	24 (2.9%)	.63
Stroke	66 (11.7%)	88 (10.1%)	.383
Arrhythmia	172 (33.7%)	262 (31.9%)	.509
Leg ischemia	**50 (9.5%)**	**71 (8.5%)**	**.558**
Cardiac arrest	85 (16.7%)	126 (15.3%)	.537
Pacemaker implantation	19 (3.7%)	23 (2.8%)	.42
Bowel ischemia	27 (5.3%)	54 (6.6%)	.409
Right ventricular failure	116 (23.7%)	145 (17.9%)	.012
Acute kidney injury	266 (52.6%)	417 (50.9%)	.572
Pneumonia	102 (20.8%)	178 (22%)	.627
Septic shock	68 (13.9%)	148 (18.3%)	.038
Distributive syndrome	45 (9.2%)	91 (11.3%)	.262
Acute respiratory distress syndrome	25 (4.9%)	35 (4.3%)	.59
Embolism	29 (5.9%)	38 (4.7%)	.365
Postoperative procedures			
Percutaneous coronary intervention	14 (2.9%)	29 (3.6%)	.526
Cardiac surgery	127 (24.9%)	203 (24.7%)	1
Abdominal surgery	18 (3.7%)	39 (4.8%)	.402
Vascular surgery	37 (7.6%)	89 (11%)	.053
In-hospital mortality	364 (64.2%)	530 (60.5%)	.165
In-hospital mortality timing			.520
Deceased on support	222 (61.0%)	341 (64.3%)	
Deceased after weaning	133 (36.6%)	185 (34.9%)	
Main cause of death			.388
Multiorgan failure	132 (38.9%)	192 (38.9%)	
Sepsis	20 (5.9%)	37 (7.5%)	
Persistent heart failure	123 (36.3%)	171 (34.7%)	
Distributive shock	4 (1.2%)	15 (3%)	
Bleeding	23 (6.8%)	23 (4.7%)	
Neurological injury	16 (4.7%)	24 (4.9%)	
Bowel ischemia	5 (1.5%)	13 (2.6%)	
Other	16 (4.7%)	18 (3.7%)	

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). Text in bold indicates differences compared with the main analysis.

TABLE E6. Odds ratios for variables associated with postoperative right ventricular failure

Variables	Full cohort (n = 1823)			
		95% CI		
	OR	Lower limit	Upper limit	*P* value
Model 1: crude model with a random intercept for hospital and year				
Sex (Reference: Male)	1.38	1.06	1.80	.0160
Model 2: Model 1 + preoperative pulmonary hypertension				
Sex (Reference: Male)	1.37	1.08	1.74	.0090
Pulmonary hypertension (>50 mm Hg)	1.63	1.19	2.24	.0032
Model 3: Model 2 + left ventricular unloading				
Sex (Reference: Male)	1.36	1.07	1.73	.0115
Pulmonary hypertension (>50 mm Hg)	1.62	1.18	2.22	.0036
Left ventricular unloading	0.64	0.41	1.00	.0486
Model 4: Model 1 + demographic data and preoperative variables				
Sex (Reference: Male)	1.32	1.00	1.75	.0464
Age (y)	1.00	0.99	1.01	.8609
Body mass index	1.01	0.98	1.04	.4587
Dialysis	1.17	0.72	1.89	.5295
Myocardial infarction	0.88	0.62	1.25	.4752
Atrial fibrillation	0.83	0.60	1.13	.2349
Chronic obstructive pulmonary disease	0.78	0.48	1.25	.2984
Pulmonary hypertension (>50 mm Hg)	1.50	1.04	2.17	.0308
Previous cardiac surgery	1.00	0.73	1.38	.9784
Left ventricular ejection fraction	1.01	1.00	1.02	.0358
Cardiogenic shock	0.86	0.58	1.28	.4639
Urgent surgery	1.04	0.72	1.51	.8334
Emergency surgery	0.90	0.59	1.38	.6241
Cardiac arrest	1.27	0.78	2.07	.3238
Acute pulmonary edema	0.93	0.54	1.61	.8014
Preoperative right ventricular failure	4.34	2.84	6.63	<.001
Model 5: Variables influencing right ventricular function				
Sex (Reference: Male)	1.32	1.00	1.74	.0521
Age (y)	1.00	0.98	1.01	.5143
Pulmonary hypertension (>50 mm Hg)	1.40	0.97	2.03	.0752
Previous cardiac surgery	1.01	0.74	1.40	.9290
Left ventricular ejection fraction	1.01	1.00	1.02	.0168
Acute pulmonary edema	0.88	0.52	1.46	.6109
Preoperative right ventricular failure	4.04	2.67	6.12	.0000
Cardiopulmonary bypass time (min)	1.00	1.00	1.00	.81
Mitral valve surgery	1.15	0.85	1.57	.3674
Tricuspid valve surgery	1.13	0.74	1.71	.5716
Postoperative ECLS implantation	1.15	0.85	1.57	.3708
Postoperative bleeding requiring re-thoracotomy	1.17	0.89	1.56	.2611
Postoperative acute kidney injury	1.39	1.03	1.87	.0309
Left ventricular unloading	0.72	0.43	1.19	.1991

ECLS, Extracorporeal life support.

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TABLE E7. Odds ratios for variables associated with postoperative lower ischemia

	Full cohort (n = 1823)			
		95% CI		
Variables	OR	Lower limit	Upper limit	*P* value
Model 1: crude model with a random intercept for hospital and year				
Sex (Reference: Male)	1.42	0.95	2.12	.0838
Model 2: Model 1 + body surface area				
Sex (Reference: Male)	1.40	0.93	2.13	.1095
Body surface area (m^2)	0.91	0.37	2.29	.8474
Model 3: Model 2 + distal perfusion				
Sex (Reference: Male)	1.41	0.93	2.13	.1082
Body surface area (m^2)	0.91	0.37	2.29	.8484
Distal perfusion	1.03	0.64	1.65	.8985
Model 4: Model 1 + variables influencing limb ischemia				
Sex (Reference: Male)	1.53	1.00	2.36	.0517
Body surface area (m^2)	0.80	0.31	2.10	.6538
Distal perfusion	1.12	0.69	1.81	.6488
Age (y)	0.98	0.97	1.00	.0485
History of peripheral vessel disease	1.34	0.72	2.50	.3499
Preoperative vasopressors	2.04	1.27	3.29	.0033
Bleeding at cannulation site	2.09	1.24	3.52	.0058
Extracorporeal cardiopulmonary resuscitation	1.41	0.75	2.64	.2836

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TABLE E8. Postoperative transfusions

	Females (n = 743)		Males (n = 1080)		
Variables		Missing values		Missing values	*P* value
Postoperative transfusions (number of packed red blood cells)	11 (4-21)	407 (54.8%)	10 (4-21)	494 (45.7%)	.434

Data are reported as n (%) or median (first and third quartiles).

TABLE E9. Preoperative characteristics of patients who underwent coronary artery bypass or valvular surgery

	Females (n = 649)	Males (n = 952)	*P* value
Age (y)	67.00 (58-74)	67.00 (57-72.1)	.157
Race			<.001
Asian	34 (5.2%)	81 (8.5%)	
Black	3 (0.5%)	5 (0.5%)	
Hispanic	16 (2.5%)	35 (3.7%)	
White	413 (63.5%)	538 (56.4%)	
Other	20 (3.1%)	11 (1.2%)	
Unknown	164 (25.2%)	284 (29.8%)	
Body mass index (kg/m^2)	26.27 (23.5-30.6)	26.54 (24-29.8)	.685
Body surface area (m^2)	1.80 (1.7-2)	1.93 (1.8-2.1)	<.001
Comorbidities			
Hypertension	425 (68.5%)	660 (71.5%)	.233
Smoking	97 (19.2%)	277 (32.4%)	<.001
Diabetes mellitus	169 (26%)	283 (29.7%)	.109
Previous myocardial infarction	149 (22.9%)	294 (30.8%)	<.001
Myocardial infarction (last 30 d)	76 (12.3%)	132 (14.3%)	.249
Previous percutaneous coronary intervention	94 (14.6%)	175 (18.4%)	.044
Previous stroke	96 (14.8%)	125 (13.1%)	.342
Peripheral artery disease	96 (14.8%)	158 (16.6%)	.334
Atrial fibrillation	**195 (30%)**	**243 (25.5%)**	**.047**
Chronic obstructive pulmonary disease	73 (11.9%)	100 (10.7%)	.463
Pulmonary hypertension (>50 mm Hg)	**144 (22.4%)**	**181 (19%)**	**.103**
Previous cardiac surgery	151 (23.2%)	228 (23.9%)	.757
Preoperative creatinine (μmol/L)	**79.0 (48-169)**	**92.00 (57-189.9)**	**.103**
Dialysis	44 (7.1%)	88 (9.4%)	.111
Left ventricular ejection fraction (%)	50.0 (38.5-60)	47.02 (32-60)	.006
euroSCORE II	7.60 (2.9-20.7)	7.28 (2.8-19)	.430
Preoperative condition			
NYHA class			.714
Class I	39 (6.2%)	54 (6%)	
Class II	148 (23.6%)	198 (21.9%)	
Class III	264 (42.1%)	376 (41.5%)	
Class IV	176 (28.1%)	277 (30.6%)	
Preoperative cardiogenic shock	118 (18.5%)	231 (24.4%)	.006
Preoperative cardiac arrest	69 (10.8%)	97 (10.3%)	.755
Preoperative intubation	65 (10%)	121 (12.7%)	.102
Preoperative septic shock	15 (2.4%)	31 (3.4%)	.293
Preoperative vasopressors	**87 (13.6%)**	**162 (17.1%)**	**.059**
Preoperative right ventricular failure	53 (9.9%)	69 (7.9%)	.206
Emergency surgery	**147 (23.1%)**	**268 (28.2%)**	**.025**
Urgent surgery	129 (20.2%)	171 (18%)	.268
Diagnosis			
CAD	319 (49.1%)	582 (61%)	<.001
Aortic vessel disease	94 (14.5%)	150 (15.7%)	.490
Aortic valve disease	280 (43.1%)	391 (41%)	.404
Mitral valve disease	295 (45.4%)	375 (39.3%)	.015
Tricuspid valve disease	138 (21.2%)	162 (17%)	.032
Pulmonary valve disease	5 (0.8%)	8 (0.8%)	.879
Post-AMI ventricular septal rupture	8 (1.2%)	18 (1.9%)	.307
Free wall/papillary muscle rupture	11 (1.7%)	23 (2.4%)	.327
Active endocarditis	45 (6.9%)	99 (10.4%)	.018
Atrial septal defect	13 (2%)	9 (0.9%)	.074
Other diagnosis	30 (4.6%)	71 (7.4%)	.022

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). Text in bold indicates differences compared with the main analysis. *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *AMI*, acute myocardial infarction.

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TABLE E10. Intraoperative characteristics of patients who underwent coronary artery bypass or valvular surgery

Variables	Females (n = 649)	Males (n = 952)	*P* value
CABG	341 (52.5%)	566 (59.3%)	.006
Aortic valve surgery	305 (46.9%)	402 (42.1%)	.058
Mitral valve surgery	285 (43.8%)	357 (37.4%)	.010
Tricuspid valve surgery	134 (20.6%)	134 (14%)	<.001
Aortic surgery	111 (17.1%)	173 (18.1%)	.586
Pulmonary valve surgery	5 (0.8%)	7 (0.7%)	.935
Atrial septal defect repair	14 (2.2%)	12 (1.3%)	.163
Ventricular septal defect repair	12 (1.8%)	21 (2.2%)	.623
Ventricular surgery	14 (2.2%)	25 (2.6%)	.551
Rhythm surgery	24 (3.7%)	32 (3.4%)	.717
Pulmonary embolectomy	3 (0.5%)	3 (0.3%)	.691
Pulmonary endoarterectomy	4 (0.6%)	4 (0.4%)	.722
Off-pump surgery	15 (2.4%)	58 (6.1%)	<.001
Conversion to Cardiopulmonary bypass	6 (40%)	16 (27.1%)	.355
Cardiopulmonary bypass time (min)	198 (135-288)	195 (132-277)	.452
Crossclamp time (min)	102 (68-150)	102 (62-152)	.265

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *CABG*, Coronary artery bypass grafting.

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TABLE E11. Details on extracorporeal life support of patients who underwent coronary artery bypass or valvular surgery

Variables	Females (n = 649)	Males (n = 952)	*P* value
ECLS implantation timing			.049
Intraoperative	410 (63.1%)	555 (58.2%)	
Postoperative	240 (36.9%)	399 (41.8%)	
Cannulation approach			.454
Only central cannulation	104 (16%)	157 (16.5%)	
Only peripheral cannulation	295 (45.4%)	465 (48.7%)	
Mixed/switch cannulation	236 (36.3%)	310 (32.5%)	
Unknown	15 (2.3%)	22 (2.3%)	
Left ventricular unloading	143 (26.3%)	291 (38.1%)	<.001
IABP during any time of hospitalization	176 (27.7%)	363 (38.3%)	<.001
IABP implantation timing			.699
Preoperative	50 (28.4%)	109 (30%)	
Intraoperative	126 (71.6%)	254 (70%)	
ECLS duration (h)	117 (62-192)	120.00 (60-195)	.734

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *ECLS*, Extracorporeal life support; *IABP*, intra-aortic balloon pump.

TABLE E12. Postoperative outcomes of patients who underwent coronary artery bypass or valvular surgery

Variables	Females (n = 649)	Males (n = 952)	*P* value
Intensive care unit stay (d)	14 (6-27)	13.00 (6-24)	.339
Hospital stay (d)	18 (7-36)	19.00 (8-36)	.479
Postoperative bleeding	366 (57.4%)	543 (57.6%)	.913
Requiring re-thoracotomy	245 (41%)	350 (38.4%)	.313
Cannulation site bleeding	89 (14%)	107 (11.4%)	.121
Diffuse no surgical-related bleeding	143 (25.4%)	248 (28%)	.282
Neurological complications			
Cerebral hemorrhage	21 (3.5%)	28 (3.1%)	.684
Stroke	69 (10.7%)	94 (9.9%)	.620
Arrhythmia	198 (34.1%)	304 (34%)	.964
Leg ischemia	75 (12.4%)	81 (9%)	.031
Cardiac arrest	112 (19.3%)	151 (16.9%)	.234
Pacemaker implantation	18 (3.1%)	28 (3.1%)	.974
Bowel ischemia	29 (5%)	53 (5.9%)	.446
Right ventricular failure	136 (24.3%)	169 (19.1%)	.019
Acute kidney injury	327 (56.8%)	482 (53.9%)	.283
Pneumonia	119 (21.3%)	199 (22.5%)	.566
Septic shock	75 (13.4%)	159 (18%)	.021
Distributive shock syndrome	44 (7.9%)	91 (10.3%)	.123
Acute respiratory distress syndrome	33 (5.7%)	45 (5%)	.584
Embolism	34 (6.1%)	43 (4.9%)	.321
Postoperative procedures			
Percutaneous coronary intervention	14 (2.6%)	28 (3.2%)	.497
Cardiac surgery	142 (24.4%)	211 (23.6%)	.712
Abdominal surgery	21 (3.9%)	44 (5%)	.305
Vascular surgery	59 (10.8%)	86 (9.8%)	.560
In-hospital mortality	425 (65.4%)	587 (61.5%)	.116
In-hospital mortality timing			.351
Deceased on support	256 (39.9%)	363 (38.2%)	
Deceased after weaning	160 (25.0%)	220 (23.2%)	
Main cause of death			.249
Multiorgan failure	148 (36.7%)	210 (38.5%)	
Sepsis	24 (6.0%)	46 (8.4%)	
Persistent heart failure	153 (38.0%)	194 (35.5%)	
Distributive shock	5 (1.2%)	15 (2.7%)	
Bleeding	26 (6.5%)	21 (3.8%)	
Neurological injury	21 (5.2%)	25 (4.6%)	
Bowel ischemia	5 (1.2%)	10 (1.8%)	
Other	21 (5.2%)	25 (4.6%)	

Subgroup analysis of patients who underwent coronary artery bypass surgery. Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles).

TABLE E13. Preoperative characteristics of patients who underwent coronary artery bypass surgery

Variables	Females (n = 333)	Males (n = 552)	*P* value
Age (y)	68.00 (60-74.2)	67.00 (59-72.4)	.050
Race			<.001
Asian	20 (5.9%)	60 (10.6%)	
Black	0 (0%)	3 (0.5%)	
Hispanic	6 (1.8%)	23 (4.1%)	
White	229 (67.2%)	297 (52.5%)	
Other	13 (3.8%)	5 (0.9%)	
Unknown	73 (21.4%)	178 (31.4%)	
Body mass index (kg/m^2)	26.64 (23.9-31.1)	26.58 (24.2-29.8)	.506
Body surface area (m^2)	1.83 (1.7-2)	1.94 (1.8-2.1)	<.001
Comorbidities			
Hypertension	252 (75.7%)	417 (75.5%)	.965
Smoking	56 (21.6%)	179 (34.6%)	<.001
Diabetes mellitus	110 (32.3%)	199 (35.2%)	.372
Previous myocardial infarction	126 (37%)	241 (42.6%)	.094
Myocardial infarction (last 30 d)	66 (19.8%)	116 (21%)	.670
Previous percutaneous coronary intervention	73 (21.7%)	126 (22.3%)	.823
Previous stroke	43 (12.6%)	67 (11.8%)	.730
Peripheral artery disease	68 (19.9%)	117 (20.7%)	.792
Atrial fibrillation	71 (20.8%)	117 (20.7%)	.968
Chronic obstructive pulmonary disease	48 (15.2%)	64 (11.6%)	.123
Pulmonary hypertension (>50 mm Hg)	64 (19%)	89 (15.8%)	.210
Previous cardiac surgery	61 (17.9%)	82 (14.5%)	.173
Preoperative creatinine (μmol/L)	97.3 (76.9-132)	102.00 (81.3-132.7)	.023
Dialysis	21 (6.6%)	57 (10.3%)	.066
Left ventricular ejection fraction (%)	45.0 (30-60)	43.00 (30-55)	.121
euroSCORE II	8.70 (3.6-21.7)	7.81 (2.9-19)	.102
Preoperative condition			
NYHA class			.502
Class I	27 (8.2%)	36 (6.7%)	
Class II	81 (24.6%)	116 (21.6%)	
Class III	125 (38.0%)	210 (39.0%)	
Class IV	96 (29.2%)	176 (32.7%)	
Preoperative cardiogenic shock	66 (19.9%)	159 (28.3%)	.005
Preoperative cardiac arrest	50 (14.8%)	64 (11.4%)	.138
Preoperative intubation	30 (8.8%)	80 (14.1%)	.018
Preoperative septic shock	7 (2.1%)	12 (2.2%)	.957
Preoperative vasopressors	43 (12.8%)	110 (19.5%)	.010
Preoperative right ventricular failure	23 (8.3%)	27 (5.2%)	.087
Emergency surgery	94 (28.7%)	191 (33.9%)	.108
Urgent surgery	63 (19%)	96 (17%)	.447
Diagnosis			
Aortic vessel disease	52 (15.2%)	73 (12.9%)	.320
Aortic valve disease	124 (36.4%)	178 (31.4%)	.128
Mitral valve disease	114 (33.4%)	164 (29%)	.159
Tricuspid valve disease	48 (14.1%)	60 (10.6%)	.117
Pulmonary valve disease	3 (0.9%)	0 (0%)	.025
Post-AMI ventricular septal rupture	4 (1.2%)	13 (2.3%)	.227
Free wall/papillary muscle rupture	4 (1.2%)	11 (1.9%)	.378
Active endocarditis	14 (4.1%)	29 (5.1%)	.485
Atrial septal defect	5 (1.5%)	3 (0.5%)	.160
Other diagnosis	11 (3.2%)	33 (5.8%)	.077

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *AMI*, acute myocardial infarction.

TABLE E14. Procedural characteristics of patients who underwent coronary artery bypass surgery

Variables	Females (n = 333)	Males (n = 552)	*P* value
Aortic valve surgery	139 (40.8%)	169 (29.9%)	<.001
Mitral valve surgery	100 (29.3%)	145 (25.6%)	.223
Tricuspid valve surgery	45 (13.2%)	36 (6.4%)	<.001
Aortic surgery	65 (19.1%)	80 (14.1%)	.050
Pulmonary valve surgery	3 (0.9%)	0 (0%)	.053
Atrial septal defect repair	5 (1.5%)	3 (0.5%)	.160
Ventricular septal defect repair	6 (1.8%)	12 (2.1%)	.706
Ventricular surgery	2 (0.6%)	18 (3.2%)	.010
Rhythm surgery	9 (2.6%)	16 (2.8%)	.867
Pulmonary embolectomy	1 (0.3%)	2 (0.4%)	1.000
Pulmonary endoarterectomy	1 (0.3%)	2 (0.4%)	1.000
Off-pump surgery	15 (4.6%)	57 (10.2%)	.003
Conversion to Cardiopulmonary bypass	6 (40%)	14 (24.6%)	.331
Cardiopulmonary bypass time (min)	216 (147-316)	190 (124-267)	<.001
Crossclamp time (min)	103 (70-156)	92 (56-142)	.002

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles).

TABLE E15. Details on extracorporeal life support of patients who underwent coronary artery bypass surgery

Variables	Females (n = 333)	Males (n = 552)	*P* value
ECLS implantation timing			.003
Intraoperative	230 (67.4%)	325 (57.4%)	
Postoperative	111 (32.6%)	241 (42.6%)	
Cannulation approach			.050
Only central cannulation	56 (16.4%)	95 (16.8%)	
Only peripheral cannulation	134 (39.3%)	256 (45.2%)	
Mixed/switch cannulation	146 (42.8%)	197 (34.8%)	
Unknown	5 (1.5%)	18 (3.2%)	
Left ventricular unloading	83 (28.1%)	202 (45.7%)	<.001
IABP during any time of hospitalization	108 (32.4%)	272 (48.1%)	<.001
IABP implantation timing			.464
Preoperative	40 (37%)	90 (33.1%)	
Intraoperative	68 (63%)	182 (66.9%)	
ECLS duration (h)	115 (64-192)	120.00 (61.4-207.5)	.215

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *ECLS*, Extracorporeal life support; *IABP*, intra-aortic balloon pump.

TABLE E16. Postoperative outcomes of patients who underwent coronary artery bypass surgery

	Females (n = 333)	Males (n = 552)	*P* value
Intensive care unit stay (d)	13 (6-28)	13.00 (6-23)	.425
Hospital stay (d)	19 (7-37)	19.00 (8-34)	.868
Postoperative bleeding	190 (56.9%)	313 (55.9%)	.722
Requiring re-thoracotomy	130 (41.8%)	206 (38.0%)	.275
Cannulation site bleeding	50 (15%)	63 (11.3%)	.102
Diffuse no surgical-related bleeding	61 (20.5%)	142 (26.6%)	.049
Neurological complications			
Cerebral hemorrhage	9 (2.8%)	16 (2.9%)	.895
Stroke	39 (11.5%)	63 (11.2%)	.866
Arrhythmia	111 (35.7%)	190 (35.4%)	.928
Leg ischemia	46 (14.3%)	50 (9.2%)	.022
Cardiac arrest	64 (20.6%)	93 (17.3%)	.239
Pacemaker implantation	7 (2.3%)	13 (2.4%)	.875
Bowel ischemia	17 (5.5%)	33 (6.1%)	.686
Right ventricular failure	62 (21%)	96 (18.1%)	.304
Acute kidney injury	176 (57.9%)	293 (54.6%)	.35
Pneumonia	60 (20.3%)	115 (21.7%)	.630
Septic shock	36 (12.2%)	84 (15.8%)	.155
Distributive shock syndrome	21 (7.1%)	47 (8.9%)	.389
Acute respiratory distress syndrome	18 (5.8%)	25 (4.7%)	.469
Embolism	21 (7.1%)	25 (4.7%)	.149
Postoperative procedures			
Percutaneous coronary intervention	3 (1.1%)	18 (3.4%)	.043
Cardiac surgery	73 (23.5%)	132 (24.6%)	.716
Abdominal surgery	9 (3.2%)	26 (4.9%)	.236
Vascular surgery	39 (13.6%)	52 (9.8%)	.103
In-hospital mortality	213 (62.5%)	345 (61.0%)	.651
In-hospital mortality timing			.956
Deceased on support	125 (37.4%)	206 (36.5%)	
Deceased after weaning	81 (24.3%)	138 (24.4%)	
Main cause of death			.550
Multiorgan failure	64 (32.0%)	127 (39.4%)	
Sepsis	16 (8.0%)	23 (7.1%)	
Persistent heart failure	83 (41.5%)	119 (37.0%)	
Distributive shock	2 (1.0%)	8 (2.5%)	
Bleeding	11 (5.5%)	11 (3.4%)	
Neurological injury	10 (5.0%)	16 (5.0%)	
Bowel ischemia	3 (1.5%)	5 (1.6%)	
Other	11 (5.5%)	13 (4.0%)	

Subgroup analysis of patients who underwent mitral valve surgery. Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles).

TABLE E17. Preoperative characteristics of patients who underwent mitral valve surgery

Variables	Females (n = 285)	Males (n = 356)	*P* value
Age (y)	66.00 (58-74)	67.00 (56.5-72)	.836
Race			.122
Asian	13 (4.6%)	21 (5.9%)	
Black	3 (1.1%)	0 (0%)	
Hispanic	9 (3.2%)	9 (2.5%)	
White	177 (62.1%)	215 (60.2%)	
Other	10 (3.5%)	5 (1.4%)	
Unknown	73 (25.6%)	107 (30%)	
Body mass index (kg/m^2)	26.06 (23.6-30)	26.52 (23.7-29.8)	.552
Body surface area (m^2)	1.80 (1.7-2)	1.93 (1.8-2.1)	<.001
Comorbidities			
Hypertension	177 (65.1%)	237 (69.5%)	.245
Smoking	48 (21%)	88 (29%)	.034
Diabetes mellitus	72 (25.3%)	96 (26.9%)	.641
Previous myocardial infarction	45 (15.8%)	85 (23.8%)	.012
Myocardial infarction (last 30 d)	23 (8.5%)	35 (10.3%)	.447
Previous percutaneous coronary intervention	42 (14.8%)	65 (18.3%)	.224
Previous stroke	47 (16.5%)	59 (16.5%)	.990
Peripheral artery disease	33 (11.6%)	49 (13.7%)	.418
Atrial fibrillation	124 (43.5%)	136 (38.1%)	.165
Chronic obstructive pulmonary disease	35 (12.9%)	37 (10.7%)	.403
Pulmonary hypertension (>50 mm Hg)	90 (32%)	104 (29.2%)	.443
Previous cardiac surgery	80 (28.1%)	111 (31.1%)	.405
Preoperative creatinine (μmol/L)	98.15 (79.6-133.5)	109.62 (87.4-153.9)	<.001
Dialysis	18 (6.6%)	44 (12.8%)	.012
Left ventricular ejection fraction (%)	50.00 (37-60)	50.00 (37.5-60)	.608
euroSCORE II	8.32 (3.7-21.9)	8.03 (3.1-22.9)	.820
Preoperative condition			
NYHA class			.535
Class I	7 (2.5%)	9 (2.7%)	
Class II	60 (21.7%)	62 (18.3%)	
Class III	115 (41.7%)	160 (47.2%)	
Class IV	94 (34.1%)	108 (31.9%)	
Preoperative cardiogenic shock	52 (18.4%)	83 (23.3%)	.135
Preoperative cardiac arrest	21 (7.6%)	28 (8%)	.830
Preoperative intubation	38 (13.4%)	45 (12.6%)	.772
Preoperative septic shock	8 (3%)	17 (5%)	.204
Preoperative vasopressors	42 (14.8%)	66 (18.5%)	.208
Preoperative right ventricular failure	26 (10.6%)	37 (11.6%)	.722
Emergency surgery	48 (17.4%)	79 (22.3%)	.126
Urgent surgery	60 (21.5%)	74 (20.9%)	.854
Diagnosis			
CAD	110 (38.6%)	182 (51%)	.002
Aortic vessel disease	16 (5.6%)	27 (7.6%)	.326
Aortic valve disease	96 (33.7%)	133 (37.3%)	.348
Tricuspid valve disease	100 (35.1%)	107 (30%)	.168
Pulmonary valve disease	1 (0.4%)	0 (0%)	.444
Post-AMI ventricular septal rupture	6 (2.1%)	3 (0.8%)	.195
Free wall/papillary muscle rupture	10 (3.5%)	22 (6.2%)	.125
Active endocarditis	19 (6.7%)	52 (14.6%)	.001
Atrial septal defect	8 (2.8%)	3 (0.8%)	.069
Other diagnosis	17 (6%)	22 (6.2%)	.917

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *AMI*, acute myocardial infarction.

TABLE E18. Procedural characteristics of patients who underwent mitral valve surgery

Variables	Females (n = 285)	Males (n = 356)	*P* value
CABG	100 (35.1%)	145 (40.6%)	.152
Aortic valve surgery	101 (35.4%)	130 (36.4%)	.798
Tricuspid valve surgery	101 (35.4%)	102 (28.6%)	.063
Aortic surgery	19 (6.7%)	41 (11.5%)	.037
Pulmonary valve surgery	1 (0.4%)	0 (0%)	.444
Atrial septal defect repair	9 (3.2%)	5 (1.4%)	.130
Ventricular septal defect repair	6 (2.1%)	4 (1.1%)	.317
Ventricular surgery	10 (3.5%)	10 (2.8%)	.608
Rhythm surgery	21 (7.4%)	21 (5.9%)	.449
Pulmonary embolectomy	1 (0.4%)	2 (0.6%)	1.000
Pulmonary endoarterectomy	1 (0.4%)	2 (0.6%)	1.000
Cardiopulmonary bypass time (min)	209.00 (156-291)	221.00 (161-298)	.224
Crossclamp time (min)	119.00 (86-160)	128.00 (86-175)	.095

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *CABG*, Coronary artery bypass grafting.

TABLE E19. Details on extracorporeal life support of patients who underwent mitral valve surgery

Variables	Females (n = 285)	Males (n = 356)	*P* value
ECLS implantation timing			.003
Intraoperative	183 (64.2%)	223 (62.5%)	
Postoperative	102 (35.8%)	134 (37.5%)	
Cannulation approach			.178
Only central cannulation	41 (14.4%)	70 (19.6%)	
Only peripheral cannulation	134 (47%)	164 (45.9%)	
Mixed/switch cannulation	100 (35.1%)	117 (32.8%)	
Unknown	10 (3.5%)	6 (1.7%)	
Left ventricular unloading	63 (26.1%)	94 (32%)	.141
IABP during any time of hospitalization	75 (26.8%)	124 (35%)	.591
IABP implantation timing			.588
Preoperative	22 (29.3%)	32 (25.8%)	
Intraoperative	53 (70.7%)	92 (74.2%)	
ECLS duration (h)	119.13 (72-194.3)	120.00 (62.4-191.8)	.448

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *ECLS*, Extracorporeal life support; *IABP*, intra-aortic balloon pump.

TABLE E20. Postoperative outcomes of patients who underwent mitral valve surgery

Variables	Females (n = 285)	Males (n = 356)	*P* value
Intensive care unit stay (d)	14.50 (7-29)	12.00 (5-24)	.117
Hospital stay (d)	21.00 (8-40)	18.00 (7-39)	.595
Postoperative bleeding	164 (58.6%)	211 (59.4%)	.826
Requiring re-thoracotomy	105 (39.3%)	137 (39.9%)	.877
Cannulation site bleeding	46 (16.4%)	39 (11%)	.047
Diffuse no surgical-related bleeding	65 (26.4%)	90 (28%)	.685
Neurological complications			
Cerebral hemorrhage	9 (3.4%)	10 (3%)	.783
Stroke	25 (8.8%)	34 (9.6%)	.756
Arrhythmia	87 (33.3%)	100 (30.1%)	.403
Leg ischemia	32 (12%)	27 (8.2%)	.118
Cardiac arrest	45 (17.3%)	42 (12.7%)	.112
Pacemaker implantation	8 (3.1%)	13 (3.9%)	.578
Bowel ischemia	12 (4.6%)	26 (7.8%)	.11
Right ventricular failure	62 (24.8%)	77 (23.8%)	.774
Acute kidney injury	150 (57.3%)	191 (58.1%)	.844
Pneumonia	65 (25.9%)	76 (23.5%)	.5
Septic shock	39 (15.6%)	69 (21.4%)	.08
Distributive shock syndrome	23 (9.2%)	42 (13%)	.163
Acute respiratory distress syndrome	17 (6.5%)	12 (3.6%)	.104
Embolism	15 (6%)	23 (7.1%)	.6
Postoperative procedures			
Percutaneous coronary intervention	6 (2.5%)	5 (1.6%)	.439
Cardiac surgery	63 (24.2%)	76 (23%)	.718
Abdominal surgery	12 (5%)	17 (5.3%)	.847
Vascular surgery	23 (9.5%)	25 (7.8%)	.484
In-hospital mortality	187 (65.6%)	234 (65.5%)	.986
In-hospital mortality timing			.847
Deceased on support	109 (38.4%)	143 (40.2%)	
Deceased after weaning	77 (27.1%)	90 (25.3%)	
Main cause of death			.780
Multiorgan failure	79 (44.1%)	90 (40.5%)	
Sepsis	12 (6.7%)	24 (10.8%)	
Persistent heart failure	60 (33.5%)	73 (32.9%)	
Distributive shock	3 (1.7%)	5 (2.3%)	
Bleeding	8 (4.5%)	8 (3.6%)	
Neurological injury	6 (3.4%)	7 (3.2%)	
Bowel ischemia	2 (1.1%)	6 (2.7%)	
Other	9 (5%)	9 (4.1%)	

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). Subgroup analysis of patients who underwent tricuspid valve surgery.

TABLE E21. Preoperative characteristics of patients who underwent tricuspid valve surgery

Variables	Females (n = 127)	Males (n = 128)	*P* value
Age (y)	67.50 (59-74)	68.02 (58.9-73.8)	.601
Race			.365
Asian	16 (11.9%)	9 (6.7%)	
Black	2 (1.5%)	0 (0%)	
Hispanic	2 (1.5%)	1 (0.7%)	
White	79 (59%)	80 (59.7%)	
Other	4 (3%)	4 (3%)	
Unknown	31 (23.1%)	40 (29.9%)	
Body mass index (kg/m^2)	26.82 (24-31)	26.95 (23.7-29.6)	.460
Body surface area (m^2)	1.83 (1.7-2)	1.90 (1.8-2)	.009
Comorbidities			
Hypertension	83 (65.4%)	81 (63.3%)	.730
Smoking	16 (14.7%)	31 (28.4%)	.013
Diabetes mellitus	32 (23.9%)	31 (23.1%)	.885
Previous myocardial infarction	14 (10.4%)	25 (18.7%)	.057
Myocardial infarction (last 30 d)	4 (3.1%)	4 (3.1%)	1.000
Previous percutaneous coronary intervention	15 (11.3%)	26 (19.5%)	.062
Previous stroke	16 (11.9%)	22 (16.4%)	.293
Peripheral artery disease	10 (7.5%)	16 (11.9%)	.216
Atrial fibrillation	74 (55.2%)	70 (52.2%)	.624
Chronic obstructive pulmonary disease	16 (12.5%)	18 (13.8%)	.749
Pulmonary hypertension (>50 mm Hg)	48 (36.4%)	57 (42.5%)	.303
Previous cardiac surgery	42 (31.3%)	47 (35.1%)	.517
Preoperative creatinine (μmol/L)	107.42 (85.6-141)	109.18 (85.7-152.1)	.476
Dialysis	9 (7.1%)	15 (11.5%)	.220
Left ventricular ejection fraction (%)	55.00 (40-60)	50.00 (40-60)	.159
euroSCORE II	9.01 (4.4-20.7)	9.80 (3.7-21.1)	.698
Preoperative condition			
NYHA class			.071
Class I	4 (3.1%)	1 (0.8%)	
Class II	29 (22.3%)	16 (12.3%)	
Class III	63 (48.5%)	77 (59.2%)	
Class IV	34 (26.2%)	36 (27.7%)	
Preoperative cardiogenic shock	18 (13.5%)	20 (15%)	.726
Preoperative cardiac arrest	6 (4.5%)	6 (4.5%)	1.000
Preoperative intubation	13 (9.7%)	8 (6%)	.256
Preoperative septic shock	2 (1.6%)	4 (3.1%)	.684
Preoperative vasopressors	15 (11.2%)	17 (12.8%)	.690
Preoperative right ventricular failure	22 (19.5%)	23 (18.9%)	.904
Emergency surgery	11 (8.5%)	23 (17.3%)	.033
Urgent surgery	35 (26.5%)	22 (16.5%)	.048
Diagnosis			
CAD	46 (34.3%)	53 (39.6%)	.376
Aortic vessel disease	12 (9%)	12 (9%)	1.000
Aortic valve disease	50 (37.3%)	53 (39.6%)	.706
Mitral valve disease	100 (74.6%)	104 (77.6%)	.567
Tricuspid valve disease	117 (87.3%)	120 (89.6%)	.567
Pulmonary valve disease	2 (1.5%)	0 (0%)	.498
Post-AMI ventricular septal rupture	2 (1.5%)	1 (0.7%)	1.000
Free wall/papillary muscle rupture	0 (0%)	0 (0%)	NA
Active endocarditis	7 (5.2%)	9 (6.7%)	.606
Atrial septal defect	5 (3.7%)	4 (3%)	1.000
Other diagnosis	6 (4.5%)	16 (11.9%)	.026

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *AMI*, acute myocardial infarction; *NA*, not available.

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TABLE E22. Procedural characteristics of patients who underwent tricuspid valve surgery

Variables	Females (n = 127)	Males (n = 128)	*P* value
CABG	45 (33.6%)	36 (26.9%)	.231
Aortic valve surgery	52 (38.8%)	47 (35.1%)	.527
Mitral valve surgery	101 (75.4%)	102 (76.1%)	.887
Aortic surgery	15 (11.2%)	15 (11.2%)	1.000
Pulmonary valve surgery	2 (1.5%)	0 (0%)	.498
Atrial septal defect repair	5 (3.7%)	6 (4.5%)	.758
Ventricular septal defect repair	3 (2.2%)	3 (2.2%)	1
Ventricular surgery	2 (1.5%)	1 (0.7%)	1.000
Rhythm surgery	13 (9.7%)	5 (3.7%)	.051
Pulmonary embolectomy	1 (0.7%)	0 (0%)	1.000
Pulmonary endoarterectomy	1 (0.7%)	0 (0%)	1.000
Cardiopulmonary bypass time (min)	218.00 (146-289)	211.00 (158-285)	.801
Crossclamp time (min)	121.00 (88-160)	118.00 (84-161)	.669

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *CABG*, Coronary artery bypass grafting.

TABLE E23. Details on extracorporeal life support of patients who underwent tricuspid valve surgery

Variables	Females (n = 127)	Males (n = 128)	*P* value
ECLS implantation timing			.543
Intraoperative	82 (61.2%)	77 (57.5%)	
Postoperative	52 (38.8%)	57 (42.5%)	
Cannulation approach			.235
Only central cannulation	22 (16.4%)	27 (20.1%)	
Only peripheral cannulation	61 (45.5%)	58 (43.3%)	
Mixed/switch cannulation	45 (33.6%)	48 (35.8%)	
Unknown	6 (4.5%)	1 (0.7%)	
Left ventricular unloading	24 (21.6%)	29 (26.6%)	.387
IABP during any time of hospitalization	25 (19.7%)	36 (27.1%)	.16
IABP implantation timing			.727
Preoperative	5 (20%)	5 (13.9%)	
Intraoperative	20 (80%)	31 (86.1%)	
ECLS duration (h)	123.00 (56.2-195.8)	131.27 (72-192)	.822

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles). *ECLS*, Extracorporeal life support; *IABP*, intra-aortic balloon pump.

TABLE E24. Postoperative outcomes of patients who underwent tricuspid valve surgery

Variables	Females (n = 127)	Males (n = 128)	*P* value
Intensive care unit stay (d)	14.00 (6-31)	12.00 (6-20.5)	.188
Hospital stay (d)	21.00 (7-39)	18.00 (9-33)	.613
Postoperative bleeding	69 (52.3%)	84 (63.2%)	.073
Requiring re-thoracotomy	56 (44.8%)	50 (38.5%)	.305
Cannulation site bleeding	16 (12.1%)	18 (13.5%)	.731
Diffuse no surgical-related bleeding	26 (23%)	43 (36.4%)	.026
Neurological complications			
Cerebral hemorrhage	1 (0.8%)	3 (2.4%)	.37
Stroke	5 (3.7%)	6 (4.5%)	.739
Arrhythmia	37 (31.4%)	41 (33.1%)	.776
Leg ischemia	10 (7.9%)	8 (6.4%)	.65
Cardiac arrest	19 (16.2%)	13 (10.5%)	.188
Pacemaker implantation	5 (4.2%)	6 (4.8%)	.822
Bowel ischemia	3 (2.5%)	9 (7.3%)	.091
Right ventricular failure	32 (28.1%)	35 (28.7%)	.916
Acute kidney injury	79 (64.2%)	69 (57%)	.25
Pneumonia	33 (28.7%)	34 (28.3%)	.951
Septic shock	18 (15.8%)	32 (26.9%)	.039
Distributive shock syndrome	10 (8.8%)	14 (11.7%)	.466
Acute respiratory distress syndrome	9 (7.6%)	3 (2.4%)	.062
Embolism	6 (5.3%)	8 (6.6%)	.674
Postoperative procedures			
Percutaneous coronary intervention	3 (2.7%)	1 (0.9%)	.361
Cardiac surgery	21 (17.8%)	31 (25.2%)	.162
Abdominal surgery	3 (2.7%)	3 (2.6%)	1
Vascular surgery	5 (4.5%)	7 (5.9%)	.617
In-hospital mortality	95 (70.9%)	92 (68.7%)	.690
In-hospital mortality timing			.720
Deceased on support	55 (42%)	60 (44.8%)	
Deceased after weaning	37 (28.2%)	32 (23.9%)	
Main cause of death			.285
Multiorgan failure	39 (43.8%)	26 (29.2%)	
Sepsis	6 (6.7%)	11 (12.4%)	
Persistent heart failure	31 (34.8%)	38 (42.7%)	
Distributive shock	2 (2.2%)	1 (1.1%)	
Bleeding	4 (4.5%)	5 (5.6%)	
Neurological injury	3 (3.4%)	2 (2.2%)	
Bowel ischemia	0 (0%)	3 (3.4%)	
Other	4 (4.5%)	3 (3.4%)	

Data are reported as n (% as valid percentage excluding missing values) or median (first and third quartiles).

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