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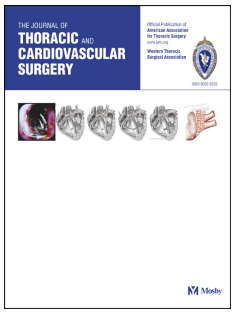

Features and Outcomes of Females and Males Requiring Postcardiotomy Extracorporeal Life Support

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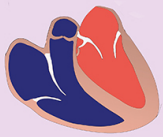
Post-Cardiotomy Extracorporeal Life Support

Patients

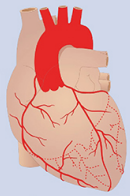
40.8% Females



More Commonly Observed in Females:
Mitral Valve Surgery
Tricuspid Valve Surgery
Pulmonary Hypertension

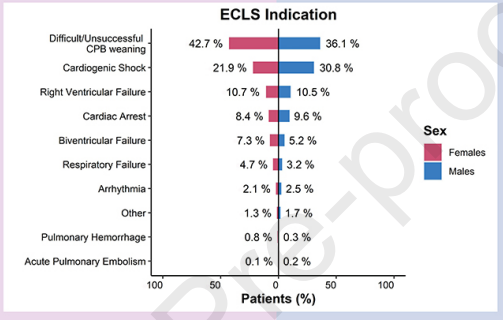
59.2% Males

More Commonly Observed in Males:
Coronary Artery Bypass Graft



Extracorporeal Life Support

More Commonly Observed in Females:
Intra-Operative



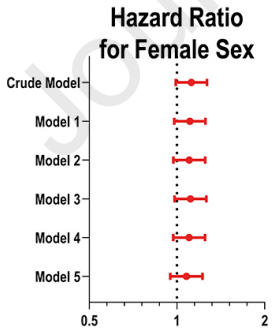
More Commonly Observed in Males:
Post-Operative Cannulation
+
IABP

Complications:
Right Ventricular Failure
Limb Ischemia

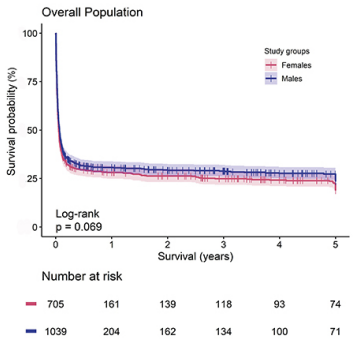
Complications:
Septic Shock

Outcomes

In-hospital Mortality



5-year Survival



Females and males requiring post-cardiotomy ECLS have different pre-operative and ECLS characteristics, as well as complications, without difference in in-hospital and follow-up survival.

ECLS, Extracorporeal Life Support; IABP, Intra-Aortic Balloon Pump

Features and Outcomes of Females and Males Requiring Postcardiotomy Extracorporeal Life Support

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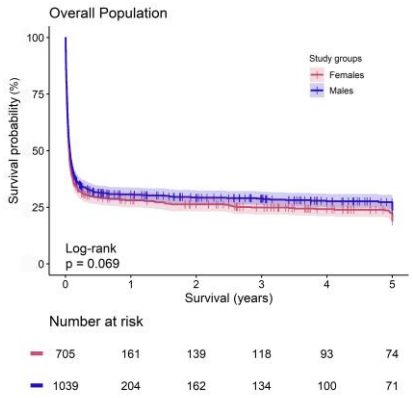
Word count: 4421

Abbreviations and Acronyms:

CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CI	Confidence interval
ECLS	Extracorporeal life support
HR	Hazard ratio
IABP	Intra-aortic balloon pump
IRB	Institutional review board
PELS-1	Post-cardiotomy extracorporeal life support study
SAGER	Sex and Gender Equity in Research
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

Central Picture



Differences between females and males in post-cardiotomy veno-arterial ECLS. (95% confidence intervals)

Central message:

Patients' profiles and ECLS characteristics differ between females and males in post-cardiotomy ECLS but their in-hospital and post-discharge outcomes are comparable.

Perspective statement:

This study shows that females require more often post-cardiotomy ECLS after valvular surgery, while males after coronary artery bypass surgery. It supports the development of strategies to prevent right ventricular failure and limb ischemia particularly in females and it suggests that sex differences should be integrated in each step of the ECLS decision-making and management processes.

Abstract

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

Methods: This retrospective, multicentre (34 centres), observational study included adults requiring post-cardiotomy ECLS between 2000 and 2020. Pre-operative, procedural, and ECLS characteristics, complications, and survival were compared between females and males. Association between sex and in-hospital survival was investigated through mixed-Cox proportional hazards models.

Results: This analysis included 1823 patients [females:40.8%; median age:66.0 (interquartile range:56.2-73.0 years)]. Females underwent more mitral (females:38.4%, males:33.1%, p=0.019) and tricuspid (females:18%, males:12.4%, p<0.001) valve surgery, while males had more coronary artery surgery (females:45.9%, males:52.4%, p=0.007). ECLS implantation was more common intra-operatively in females (females:64.1%, males:59.1%) and post-operatively in males (females:35.9%, males:40.9%, p=0.036). Ventricular unloading (females:25.1%, males:36.2%, p<0.001) and intra-aortic balloon pump (females: 25.8%, males:36.8%, p<0.001) were most frequently used in males. Females suffered more post-operative right ventricular failure (females:24.1%, males:19.1%, p=0.016) and limb ischemia (females:12.3%, males:8.8%, p=0.23). In-hospital mortality was 64.9% in females and 61.9% in males (p=0.199) with no differences in 5-year survival (females:20%, 95%CI:17-23; males:24%, 95%CI:21-28;p=0.069). Crude hazard ratio for in-hospital mortality in females was 1.12 (95%CI: 0.99-1.27,p=0.069) and did not change after adjustments.

Conclusions: This study demonstrates that females and males requiring post-cardiotomy ECLS have different pre-operative and ECLS characteristics, as well as complications, without a statistical difference in in-hospital and 5-year survival.

Word count abstract: 250

Keywords: Mechanical Circulatory Support, Extracorporeal Life Support, Post-cardiotomy Cardiogenic Shock, Cardiac Surgery, Acute Heart Failure, Sex differences.

Introduction

Post-cardiotomy 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 previously been reported[3], the effect of sex on the incidence and outcomes of post-cardiotomy 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 including differences in baseline characteristics, comorbidities, and hormonal influences which vary with age[3]. However, literature lacks a systematic analysis of all these factors in post-cardiotomy ECLS. Understanding the potential sex differences in post-cardiotomy ECLS could provide valuable insights for risk stratification, prognostication, and targeted interventions in this high-risk population. Thus, an urgent need to clarify this knowledge gap in the ECLS and cardiac surgery fields is present.

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

Methods

Study Design

The current study is a secondary analysis of the Post-cardiotomy Extra-Corporeal Life Support Study (PELS, ClinicalTrials.gov: NCT03857217): an international, multi-centre, retrospective observational study collecting data from in 34 centres from 16 countries (Supplemental Figure 1 and 2). Institutional Review Board approval was obtained at the coordinating centre and required for all participating units (METC-

2018-0788, December 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. 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

PELS included adults (≥18 years old) requiring post-cardiotomy ECLS between January 2000 and December 2020. Exclusion criteria included ECLS after discharge or before surgery, ECLS after non-cardiac operations, 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 veno-venous 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/female[3,9,14,15]. Within this manuscript, 'Gender' describes those characteristics of women and men that are largely socially created, while 'Sex' encompasses those 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 pre-defined protocol and variable definitions (Supplementary methods). Follow-up data were collected through the review of the most recent medical records or contact with patients at discretion of the treating centre. Full dataset was retained and centrally managed by the coordinating centre. The primary outcome of interest was all-cause in-hospital mortality. Secondary outcomes included in-hospital complications and post-discharge survival.

Statistical Analysis

Data were merged and analysed using SPSS 26.0 (IBM,New York,USA), and R 4.1.2 (R Foundation for Statistical Computing,Vienna,Austria) (Supplemental methods).

Demographic and clinical variables are expressed as numbers (valid percent on available data, excluding missing values; Supplemental table 1) for categorical variables and median (1^{st} and 3^{rd} quartile) or mean and standard deviation for continuous variables, after evaluation of normality. Categorical data were compared between groups with Pearson's chi-Square, or Fisher's exact test. Continuous variables were analysed 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 centres and in years. The models were developed on five datasets after imputation of variables with <20% missing data. We report measures of association as hazard ratios (HRs) or odds ratios (OR) with their 95% confidence intervals (CIs) and additionally their 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 post-cardiotomy ECLS before 2011 (2011-2020 cohort). A further sensitivity analysis was performed to include only patients who underwent coronary artery bypass graft (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. A two-sided p-value of < 0.05 and a p-interaction of < 0.1 were considered statistically significant.

Results

Pre-operative, Surgical and ECLS Characteristics

The cohort included 1823 patients of whom 743 females (40.8%) and 1080 males (59.2%, Supplemental figure 1 and 3). Median age was 66.0 years (1st and 3rd quartile: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 presented more often with pre-operative cardiogenic shock, requiring vasopressors and emergency surgery. Females were more likely to be diagnosed with mitral and tricuspid valve disease, and pre-operative pulmonary hypertension (Table1). Females underwent more often mitral and tricuspid valve surgery (Table 2) with higher rates of operations combining ≥2 procedure (females: n=241/743,32.4%; males: n=265/1080,24.5%; Figure 1A). In the 2011-2020 cohort (n=1443,79.2%, Supplemental tables 2-5), 3% (n=17/567) of females underwent pulmonary endarterectomy compared to 1.4% (n=12/876, p=0.035) of males. CABG (Table 2) and isolated CABG were more frequent in males (females: n=114/743,15.3%; males: n=256/1080,23.7%; Figure 1A).

Females received more intra-operative ECLS cannulations compared to higher rates of post-operative 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%, Figure 1B) followed by cardiogenic shock (females: n=157/717,21.9%; males: n=328/1066,30.8%, p=0.001). Distal limb perfusion, left ventricular unloading and intra-aortic balloon pump (IABP) were more frequent in males (Table 3).

Outcomes

Females suffered more post-operative right ventricular failure (RVF, OR:1.38, 95%CI:1.06-1.80, p=0.016, model 1, Supplemental Table 6). This effect became somewhat smaller after adjustments (OR:1.32, 95%CI:1.00-1.74, p=0.0521, model 5),). Males developed more often septic shock (Table 4), while leg ischemia was more frequent in females. In a multivariable mixed-effects logistic regression model and after adjustment for body surface are, distal perfusion, age, history of distal vessel disease, pre-operative

vasopressor use, bleeding at cannulation site and ECPR, females had higher odds on leg ischemia (OR:1.53, 95%CI:1.00-2.36, p=0.0517, Supplemental Table 7). Number of units of post-operatively transfused erythrocyte concentrates was similar in both females (median:11, 1st-3rd quartile:4-21) and males (median:10, 1st-3rd quartile:4-21; P=0.434. Supplemental Table 8). In-hospital mortality was 64.9% in females (n=482) and 61.9% in males (n=668, p=0.199) with 715 deaths during extracorporeal support (39.2%) and 442 deaths after weaning (23.1%). In a mixed-effects Cox model with random centre and year effects, females showed a hazard of 1.12 (95%CI:0.99-1.27, p=0.069; Figure 2) for in-hospital mortality compared to males. Adjustment for age (model 1), pre-operative characteristics (model 2), intra-operative variables (model 3) and ECLS variables (model 4) did not change results. The HR dropped to 1.08 (95%CI:0.95-1.22, p=0.248) after adjustment for post-operative complications (model 5). When adding interaction term between sex and age to the models, no effect modification by age was observed (p-values for interaction >0.228). Median overall follow-up time was 21 (1st and 3rd quartile: 7-147) days, while median follow-up for hospital survivors was 730 (1st and 3rd quartile: 91-1801) days. Median survival at 5 years was 20% (95% CI: 17-23) for female and 24% (95% CI: 21-28). Overall, survival was similar for both groups (p=0.069, Figure 3), also when considering the 2011-2020 sub-cohort (p=0.06, Supplemental figure 4). The cohort of patients who underwent CABG and valvular surgery showed a worse survival for females (p=0.04, Supplemental Table 9-12, Supplemental Figure 4), but this was not confirmed after subgroup analyses of patients who underwent CABG (p=0.39, Supplemental Tables 13-16, Supplemental figure 5), mitral valve surgery (p=0.07, Supplemental Tables 17-20, Supplemental figure 6), tricuspid valve surgery (p=0.78, Supplemental Tables 21-24, Supplemental figure 7) or stratified by age groups (<50 years old: p=0.14, 50-65 years old: p=0.74, >65 years old: p=0.16, Supplemental figure 8).

Comment

Females and males requiring post-cardiotomy ECLS have different pre-operative characteristics, ECLS indications and complications, but comparable in-hospital and long-term survival. This study has four main findings (Figure 4). First, males requiring post-cardiotomy 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. Contrarily, females requiring post-cardiotomy ECLS undergo more mitral and tricuspid valve operations than males. Second, females receive more often intra-operative ECLS cannulation for difficult or unsuccessful weaning from cardiopulmonary bypass, while males require more post-operative ECLS initiation for cardiogenic shock and undergo IABP implantation. Third, females are more likely to experience post-operative right ventricular failure and leg ischemia compared to males. Fourth, in-hospital and long-term survival rates were comparable between females and males.

Sex and gender differences have been increasingly addressed in all field of medicine[3,12,13], including cardiac surgery where female sex has been reported as a risk factor for post-operative morbidity and mortality[16]. Within the cardiac surgery population, up to 4% of patients might experience post-cardiotomy cardiogenic shock requiring ECLS[1,2]. Nevertheless, females have always represented only 20-30% of patients included in most studies on post-cardiotomy ECLS[4] and results about sex-related differences have been contradictory[4-6,8]. In the current study, males are characterized by the typical profile of CAD patients undergoing CABG surgery, in some cases with emergency indications and pre-operative vasopressors. Contrarily, females are more likely to have pulmonary hypertension and 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 and/or post-cardiotomy support. Yet, to the best of our knowledge, only Biancari et al. reported higher rates of tricuspid valve surgery in females (6.6%) compared to males (2.4%).

The different pre-operative profile between males and females also explains the different ECLS cannulation timing, left ventricular unloading and IABP use. The typical CAD profile in males is more often associated with post-operative ECLS initiation due to any post-operative situation (i.e. 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 IABP (including pre-operative) or other unloading strategies to allow myocardial recovery of the ischemic left ventricle in males[1,18]. Females

affected by valve diseases require more often intraoperative ECLS initiation for difficult or unsuccessful weaning from cardiopulmonary bypass. Indeed, it has been demonstrated that in case of tricuspid valvular surgery an intra-operative initiation of ECLS may be associated with improvement in post-operative hemodynamics and a 35.5% in-hospital mortality compared to a 68.8% mortality for post-operative cannulation[19]. The role of intra-operative ECLS still needs to be clarified in case of pulmonary hypertension and right ventricular impairment, which can be associated to mitral and tricuspid valvular surgery[20].

Differences in surgical indications are reflected by the post-operative complication profiles. Indeed, 24.1% of females developed post-operative right ventricular failure, which is a possible complication after mitral and/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 post-operatively and 82.1% (n=128/156, data not shown) died in hospital. Moreover, pre-operative pulmonary hypertension and pre-existing 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 intra-operative ECLS initiation in selected cases with 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 7-17%[8,22,23], associated to smaller blood vessels or the shorter stature. In the current study, distal limb perfusion was used less frequently in females (68%) who underwent femoral cannulation compared to men (75.4%), and the use of vasopressors seemed associated with the occurrence of limb ischemia. Regular use of distal limb perfusion has been encouraged to prevent limb ischemia, yet they are still not routinely implemented in all centres[24]. Sex-specific benefits of distal limb perfusion still must be investigated but results from this study encourage the regular use of distal limb perfusion in females here very small vessels can be perfused with paediatric cannulas or a 6-7-8 Fr armed introducers[25].

Post-operative septic shock occurred more often in males (17.9%) than 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 as this might have driven the development of post-operative shock[8]. Post-cardiotomy ECLS patients experience an infection risk ranging from 9% to 65%[1] due to multiple cannulation sites, mechanical ventilation and surgical wounds. Moreover, Li et al. demonstrated that nosocomial infections increase the relative risk of death after ECLS by 32%[26].

Despite the above-mentioned 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 risk factor for in-hospital mortality [4,7]. Differently, Chang et al. identified an odds ratio 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 7,185 post-cardiotomy ECLS runs included in the Extracorporeal Life Support Organization Registry did not identify female sex as determinant of hospital death[27]. These discrepancies might be due to variations in included populations and ethnical groups, geographical and temporal differences, sample size, local policies, but also non-clinical factors, including financial, historical, cultural and ethical factors[28]. Overall, based on the results of the current study, females have a crude hazard ratio 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 post-cardiotomy ECLS. After adjustment, we noticed that females' hazard ratio dropped 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 post-operative and ECLS-related complications to benefit in-hospital mortality.

Our study is observational by nature, preventing causal inferences[29]. Since data collected focused on in-hospital variables, this study could not investigate potential prehospital sex-related differences. Moreover, post-cardiotomy 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 analysed patients based on 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 ischaemic heart disease presentation

in women[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 (such as The 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 post-operative 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. As ECLS volumes might vary over time per centre and this study included data between 2000 and 2020, we did not study centre volume effects. However, we took centre and year effects into account using mixed effects regression analyses and we performed sensitivity analyses excluding patients operated before 2011 were performed.

In conclusion, females and males requiring post-cardiotomy ECLS are two different clinical populations, marked by different pre-operative 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 for 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 patient's access to health care, clinicians' gender perception in the decision-making process and post-ECLS long-term care.

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Tables

Table 1 - Pre-operative patients' characteristics.

	Females (n=743)	Males (n=1080)	P-value
Age (years)	66.00(57-74)	66.00(56-72)	0.119
Race			0.003
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/m2)	26.23(23.4-30.7)	26.56(24-29.8)	0.477
Body surface area (m2)	1.80(1.7-2)	1.94(1.8-2.1)	<0.001
Comorbidities			
Hypertension	480(67.6%)	730(70%)	0.293
Smoking	113(19.3%)	312(32.2%)	<0.001
Diabetes mellitus	178(24%)	298(27.6%)	0.083
Previous myocardial infarction	163(21.9%)	312(28.9%)	<0.001
Myocardial infarction (last 30 days)	81(11.4%)	150(14.4%)	0.073
Previous percutaneous coronary intervention	101(13.7%)	196(18.2%)	0.012
Previous stroke	110(14.8%)	140(13%)	0.268
Peripheral artery disease	112(15.1%)	173(16%)	0.600
Atrial fibrillation	209(28.1%)	260(24.1%)	0.056
Chronic obstructive pulmonary disease	82(11.7%)	107(10.1%)	0.308
Pulmonary hypertension (>50 mmHg)	170(23.1%)	201(18.6%)	0.024
Previous cardiac surgery	171(23%)	254(23.5%)	0.822
Preoperative creatinine (µmol/L)	96.4(73.4-129)	103.45(81-141.1)	<0.001
Dialysis	49(6.9%)	94(8.9%)	0.154
Left ventricular ejection fraction (%)	52.0(40-60)	49.50(34-60)	<0.001
Euroscore II*	7.60(2.8-20)	7.01(2.7-18.3)	0.294
Preoperative condition			
New York Heart Association class			0.759
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%)	0.010
Preoperative cardiac arrest	75(10.2%)	103(9.6%)	0.689
Preoperative intubation	82(11.1%)	142(13.1%)	0.192
Preoperative septic shock	16(2.3%)	33(3.2%)	0.303
Preoperative vasopressors	101(13.7%)	189(17.6%)	0.031
Preoperative right ventricular failure	65(10.5%)	81(8.2%)	0.131
Emergency surgery	182(25%)	316(29.4%)	0.047
Urgent surgery	145(19.8%)	201(18.7%)	0.543
Diagnosis			
Coronary artery disease	335(45.1%)	608(56.3%)	<0.001
Aortic vessel disease	129(17.4%)	204(18.9%)	0.423
Aortic valve disease	287(38.6%)	400(37%)	0.492
Mitral valve disease	299(40.2%)	377(34.9%)	0.023
Tricuspid valve disease	144(19.4%)	168(15.6%)	0.037
Pulmonary valve disease	6(0.8%)	9(0.8%)	1.000
Post-AMI ventricular septal rupture	19(2.6%)	39(3.6%)	0.224
Free wall/Papillary muscle rupture	11(1.5%)	25(2.3%)	0.234
Active endocarditis	45(6.1%)	101(9.4%)	0.011
Atrial septal defect	17(2.3%)	14(1.3%)	0.139
Other diagnosis	67(9%)	107(9.9%)	0.570

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). *Data available for 70.1% of patients. AMI. Acute Myocardial Infarction.

Table 2 - Procedural characteristics

	Females (n=743)	Males (n=1080)	p-value
Coronary artery bypass graft	341(45.9%)	566(52.4%)	0.007
Aortic valve surgery	305(41%)	402(37.2%)	0.107
Mitral valve surgery	285(38.4%)	357(33.1%)	0.019
Tricuspid valve surgery	134(18%)	134(12.4%)	<0.001
Aortic surgery	145(19.5%)	231(21.4%)	0.346
Pulmonary valve surgery	5(0.7%)	7(0.6%)	1.000
Atrial septal defect repair	18(2.4%)	17(1.6%)	0.225
Ventricular septal defect repair	24(3.2%)	43(4%)	0.448
Ventricular surgery	27(3.6%)	47(4.4%)	0.471
Rhythm surgery	28(3.8%)	38(3.5%)	0.799
Pulmonary embolectomy	10(1.3%)	11(1%)	0.513
Pulmonary endarterectomy	26(3.5%)	21(1.9%)	0.050
Off-pump surgery	18(2.5%)	64(6%)	<0.001
Conversion to cardiopulmonary bypass	7(36.8%)	18(27.3%)	0.410
Cardiopulmonary bypass time (min)	200(135-290)	195(132-282)	0.431
Crossclamp time (min)	100(65-150)	99(61-152)	0.297

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

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Table 3 - Details on Extracorporeal Life Support.

	Females (n=743)		Males (n=1080)		P-value
ECLS implantation timing					0.036
Intraoperative	476	(64.1%)	638	(59.1%)	
Postoperative	267	(35.9%)	442	(40.9%)	
Cannulation approach					0.547
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%)	<0.001
IABP during any time of hospitalization	188	(25.8%)	395	(36.8%)	<0.001
IABP implantation timing					0.633
Pre-operative	56	(29.8%)	127	(32.2%)	
Intra-operative	132	(70.2%)	268	(67.8%)	
Distal femoral perfusion in patients with peripheral cannulation	217	(68%)	371	(75.4%)	0.024
ECLS duration (hours)	118	(60.2-194.5)	120.00	(56.8-192)	0.989

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).
ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

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Table 4 - Postoperative outcomes.

	Females (n=743)	Males (n=1080)	P-value
Intensive care unit stay (days)	14(6-27)	13(5-24)	0.150
Hospital stay (days)	18(7-36)	19(8-36)	0.672
Postoperative bleeding	418(57.3%)	612(57.5%)	0.961
Requiring re-thoracotomy	284(41.3%)	395(38.3%)	0.227
Cannulation site bleeding	98(13.5%)	121(11.4%)	0.187
Diffuse no-surgical related bleeding	165(25.5%)	269(26.9%)	0.567
Neurological complications			
Cerebral haemorrhage	22(3.2%)	31(3%)	0.887
Stroke	81(11%)	110(10.2%)	0.641
Arrhythmia	230(34.4%)	332(32.9%)	0.526
Leg ischemia	85(12.3%)	90(8.8%)	0.023
Cardiac arrest	123(18.4%)	160(15.8%)	0.183
Pacemaker implantation	22(3.3%)	30(3%)	0.774
Bowel ischemia	34(5.1%)	64(6.3%)	0.339
Right ventricular failure	156(24.1%)	191(19.1%)	0.016
Acute kidney injury	373(56.3%)	552(54.6%)	0.514
Pneumonia	134(20.7%)	227(22.8%)	0.330
Septic shock	91(14.1%)	178(17.9%)	0.048
Distributive shock syndrome	52(8.1%)	103(10.3%)	0.142
Acute respiratory distress syndrome	41(6.1%)	51(5%)	0.381
Embolism	42(6.5%)	52(5.2%)	0.278
Postoperative procedures			
Percutaneous coronary intervention	15(2.4%)	31(3.1%)	0.444
Cardiac surgery	157(23.5%)	228(22.6%)	0.678
Abdominal surgery	23(3.7%)	48(4.8%)	0.265
Vascular surgery	61(9.6%)	97(9.8%)	1.000
In-hospital mortality	482(64.9%)	668(61.9%)	0.199
In-hospital mortality timing			0.709
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			0.162
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 (1st and 3rd quartile).

Figures

Figure 1 – Surgical details and extracorporeal life support indications. Distribution of weight of surgery (A) and indication to extracorporeal life support (ECLS; B) by sex.

Figure 2 – Hazard ratios for in-hospital mortality in females. In a mixed-effects Cox model with random centre and year effects: crude model, adjustment for age (Model 1), pre-operative characteristics (Model 2), intra-operative variables (Model 3), ECLS variables (Model 4), post-operative complications (Model 5).

Figure 3 – 5-year survival in females and males. Kaplan-Meier survival curves with 95% confidence intervals.

Figure 4 – Graphical abstract. From the Post-cardiotomy Extracorporeal Life Support (PELS-1 study, n=1823) study. This study demonstrates that females and males requiring post-cardiotomy extracorporeal life support (ECLS) have different pre-operative diagnoses, surgical indications and ECLS characteristics, as well as complications, without a statistically significant difference in in-hospital and 5-year survival. IABP, Intra-Aortic Balloon Pump.

Supplemental Figure 1 –– Flow-chart describing the patients included in the current study.

Supplemental Figure 2 – Bar chart representing the yearly variations of females-males ratio of patients included in the current analysis of the PELS-1 study reported as percentages.

Supplemental Figure 3 - Overall Kaplan-Meier survival curves with 95% confidence limit of patients who had veno-arterial extracorporeal life support for post-cardiotomy support between 2011 and 2020. Groups are defined according to sex.

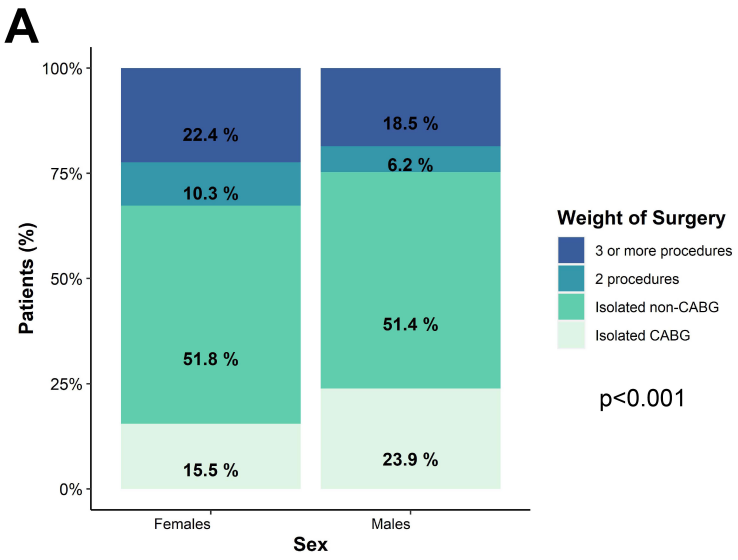
Supplemental Figure 4 - Overall Kaplan-Meier survival curves with 95% confidence limit of patients who underwent coronary artery bypass graft (CABG) or valvular surgery and required extracorporeal life support. Groups are defined according to sex.

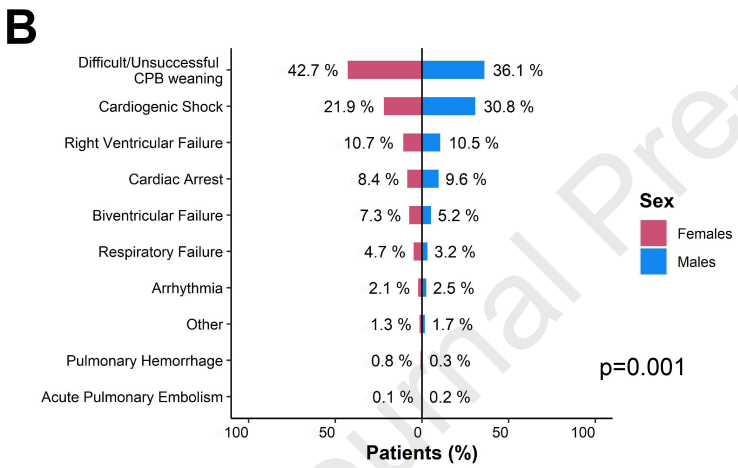
Supplemental Figure 5 - Overall Kaplan-Meier survival curves with 95% confidence limit of patients who underwent coronary artery bypass graft (CABG) surgery and required extracorporeal life support. Groups are defined according to sex.

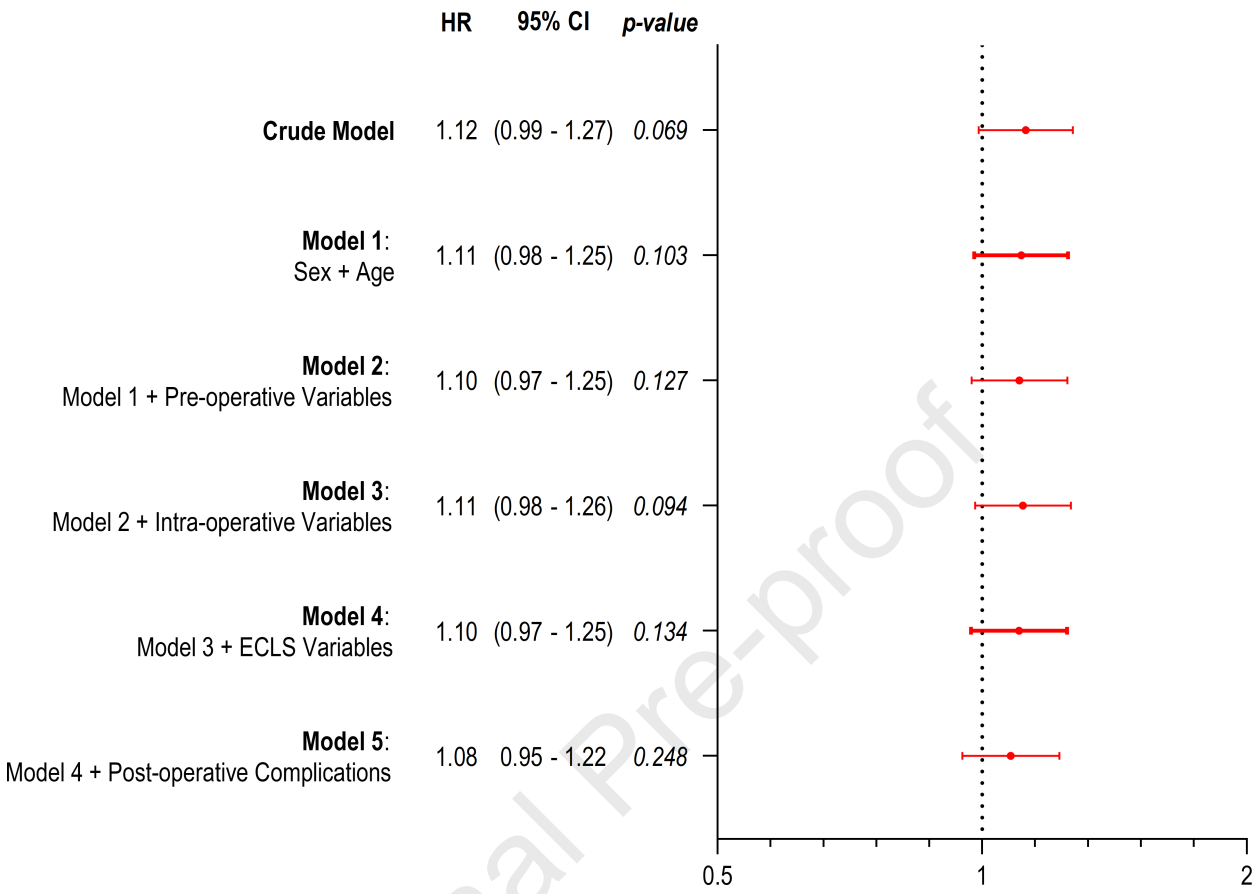
Supplemental Figure 6 - Overall Kaplan-Meier survival curves with 95% confidence limit of patients who underwent mitral valve surgery and required extracorporeal life support. Groups are defined according to sex.

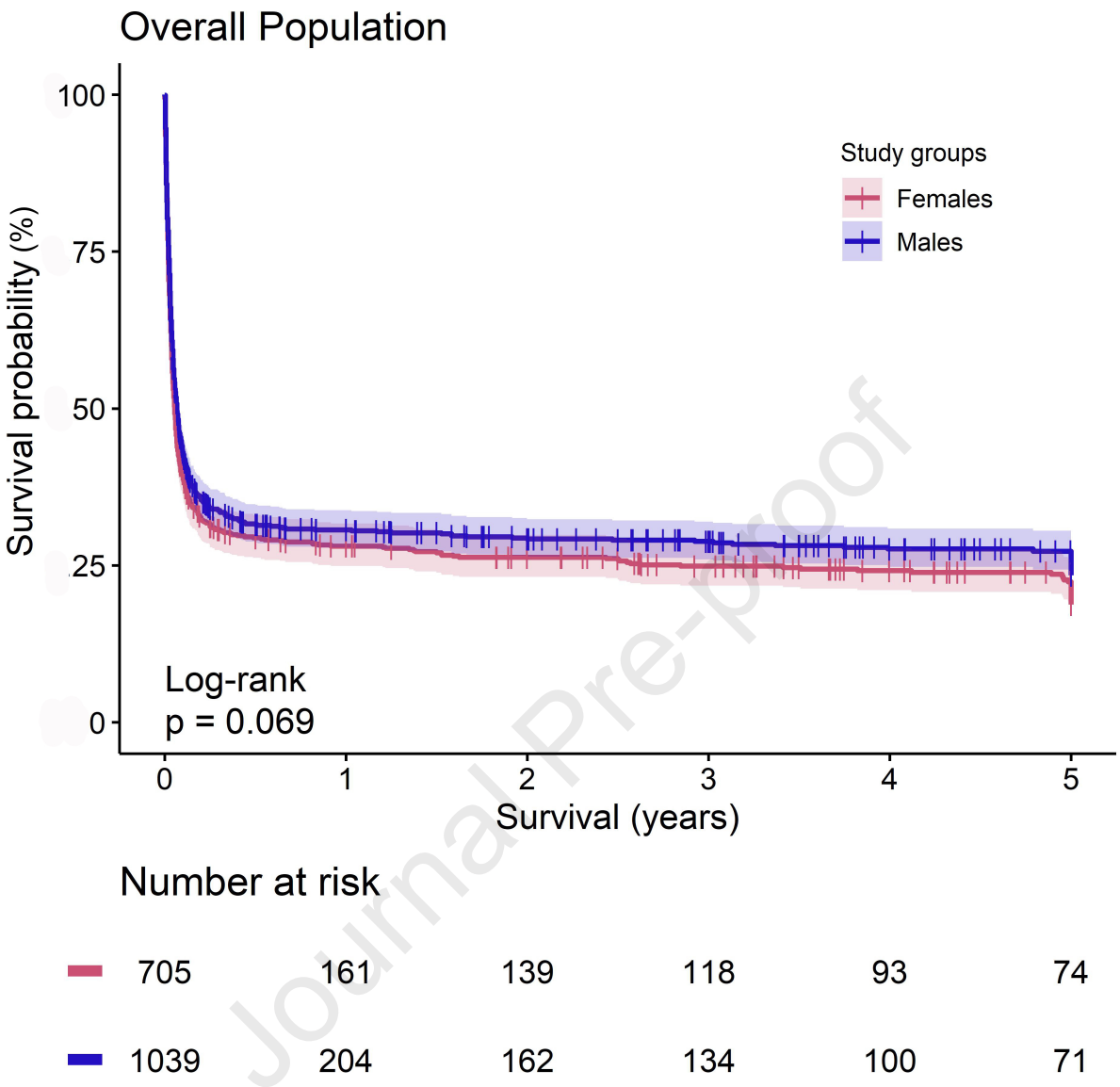
Supplemental Figure 7 - Overall Kaplan-Meier survival curves with 95% confidence limit of patients who underwent tricuspid valve surgery and required extracorporeal life support. Groups are defined according to sex.

Supplemental Figure 8 - Overall Kaplan-Meier survival curves with 95% confidence limit of patients who underwent post-cardiotomy extracorporeal life support stratified by age: <50 years (A), 50-64.9 years (B), ≥65 years (C). Groups are defined according to sex.





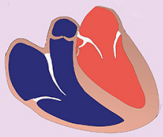




Post-Cardiotomy Extracorporeal Life Support

Patients

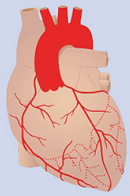
40.8% Females



More Commonly Observed in Females:
Mitral Valve Surgery
Tricuspid Valve Surgery
Pulmonary Hypertension

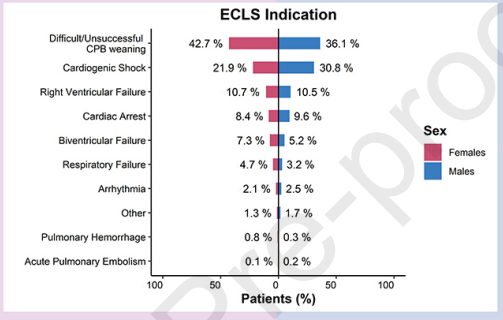
59.2% Males

More Commonly Observed in Males:
Coronary Artery Bypass Graft



Extracorporeal Life Support

More Commonly Observed in Females:
Intra-Operative



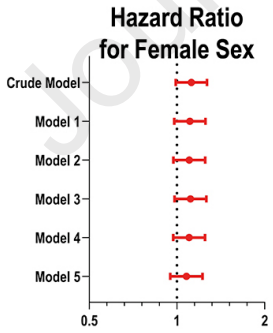
More Commonly Observed in Males:
Post-Operative Cannulation
+
IABP

Complications:
Right Ventricular Failure
Limb Ischemia

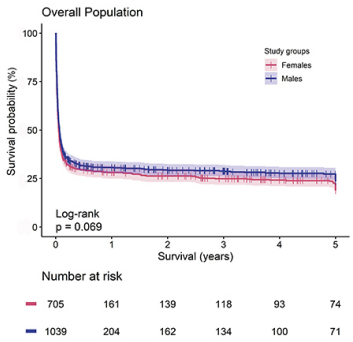
Complications:
Septic Shock

Outcomes

In-hospital Mortality

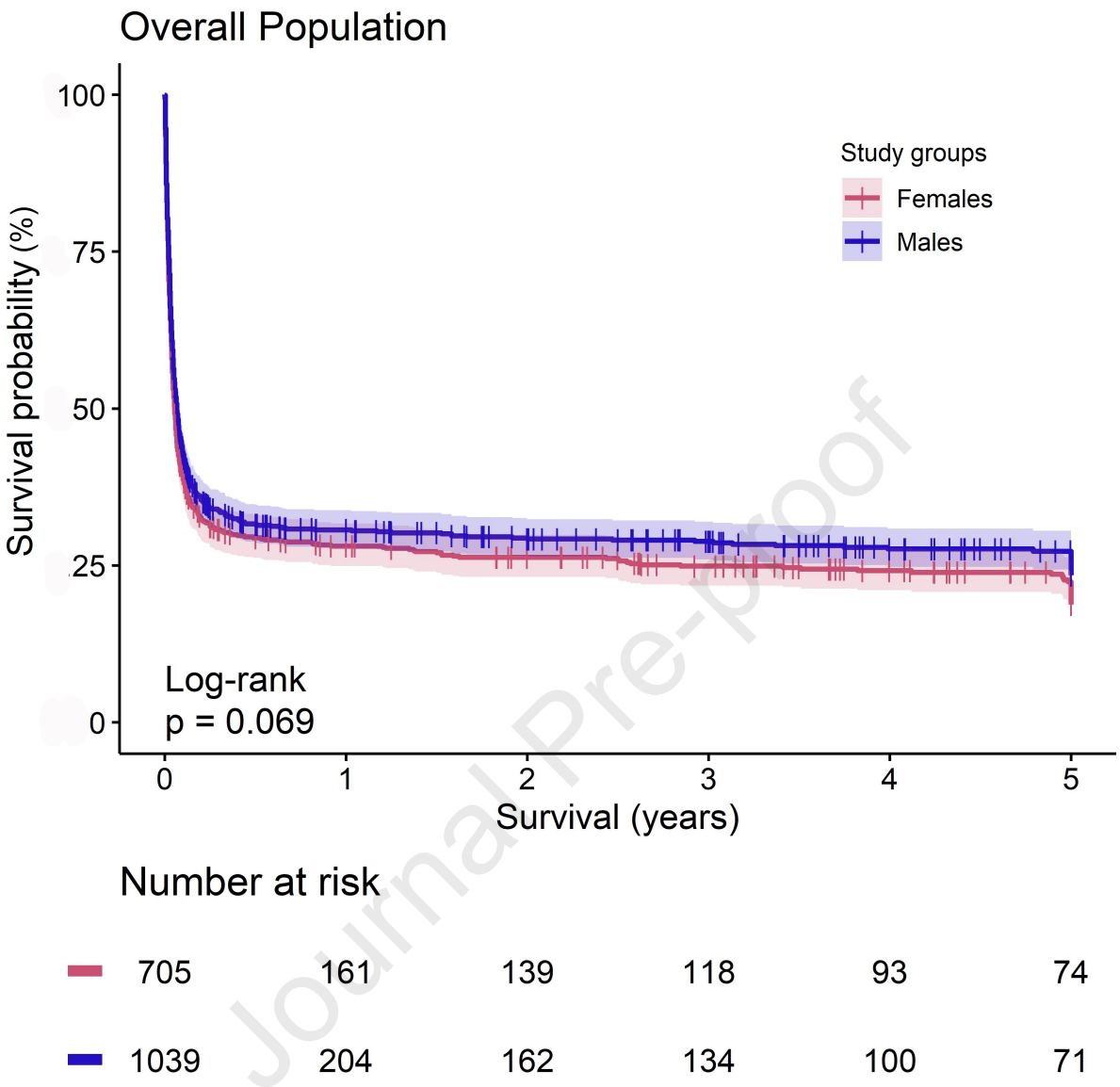


5-year Survival



Females and males requiring post-cardiotomy ECLS have different pre-operative and ECLS characteristics, as well as complications, without difference in in-hospital and follow-up survival.

ECLS, Extracorporeal Life Support; IABP, Intra-Aortic Balloon Pump



Electronic Supplementary Material

Features and Outcomes of Females and Males Requiring Postcardiotomy Extracorporeal Life Support

The PELS Multi-Centre Cohort Study

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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 complain as much as possible with the "3G" principles to mitigate personnel gaps in gender (sex), generation, and geography [1]. Furthermore. the team was designed to include different specialties and expertise and comply with a multi-disciplinary approach. Hereafter the details of the study's leadership group:

- SM: under-40 female 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.
- BvB: 40-year-old male internist, intensivist and epidemiologist. Nationality: Dutch. Role: Concept/design. Statistics. Data analysis/interpretation. Drafting article.
- JMR: under-40 female surgeon. Nationality: Belgian. Role: Role: Concept/design. Data cleaning. Data analysis/interpretation. Drafting article.
- MEDP: under-50 female intensivist. Nationality: Italian. Role: Concept/design. Data cleaning. Data analysis/interpretation. Drafting article.
- RL: senior surgeon, supervisor, and PELS Chief Investigator. Nationality: Italian. Role: Concept/design. Study coordination. Data analysis/interpretation. Drafting article. Supervision.

The complete PELS study 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 ethnicity. Each centre has been encouraged to include in the study group a senior principal investigator and a young investigator to promote gender and generation diversity. Each centre is represented in the authors list of all PELS articles by at least one author, with alternance of senior and young investigators based on internal choice of each centre and the contribution of each author to the development of the specific study. Due to 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 materials. 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: EuroSCORE, length, weight, serum creatinine level, left ventricular ejection fraction, comorbidities (hypertension, chronic kidney disease requiring dialysis, previous myocardial infarction, previous endocarditis, smoking, previous stroke, atrial fibrillation, previous pulmonary embolism, diabetes mellitus, previous transient ischemic attack (TIA), implanted pacemaker (PM), implanted implantable cardioverter defibrillator (ICD), previous percutaneous coronary intervention (PCI), chronic obstructive pulmonary disease (COPD), 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 oedema, preoperative intra-aortic balloon pump (IABP), preoperative right ventricular failure, preoperative biventricular failure.
- Diagnosis: coronary artery disease, aortic vessel disease, aortic valve disease, mitral valve disease, tricuspid valve disease, pulmonary valve disease, post-acute myocardial infarction (AMI) 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 mammary artery (LIMA), right internal mammary artery (RIMA), radial artery, gastro-epiploic artery (GEA), 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 PM-/ICD procedure, ventricular septal defect (VSD) closure, atrial septal defect (ASD) closure, ventricular surgery, pericardiectomy, pulmonary embolectomy/endarterectomy, other cardiac surgery, other cardiac surgery description.
- Extracorporeal circulation (ECC): ECC duration, cross-clamp duration, circulation arrest, cardioplegia characteristics, off-pump conversion.
- Extracorporeal membrane oxygenation (ECMO) variables: ECMO indication, chest status, cannulation approach, use of left ventricular vent, ECMO duration (hours), configuration change, ECMO monitoring.
- In-hospital outcomes: deceased in hospital, deceased timing, intensive care unit (ICU) 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 oedema, cerebral haemorrhage, 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 (ARDS), multi-organ failure, embolism
- Postoperative procedures: PCI, 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 manuscript have been developed in accordance to the international World Health Organization (WHO) definitions of sex and gender where 'Gender' describes those characteristics of women and men that are largely socially created (including concepts such as cisgender and transgender). while '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 WHO Regional Office for Europe (https://www.euro.who.int/en/health-topics/health-determinants/gender/gender-definitions), the Office for National Statistics (ONS) and United Kingdom 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 are often 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 we did not include a further analysis of gender identity [2-4].
- Hypertension: Systolic blood pressure >140mmHg or diastolic blood pressure >90mmHg[5], 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
- COPD: Diagnosis of chronic obstructive pulmonary disease, any Gold classification [6]
- Peripheral arterial disease: Claudication, carotid occlusion or >50% stenosis, amputation for arterial disease or previous or planned intervention on the abdominal aorta. limb arteries or carotids [7]
- Pulmonary hypertension: Systolic pulmonary artery pressure >50mmHg
- EuroSCORE II: European System for Cardiac Operative Risk Evaluation II proposing a risk assessment of cardiac surgical procedures which incorporates patient age, sex, diabetic status, pulmonary disease,

neurological function, renal function, presence of active endocarditis, pre-operative state, procedural urgency and procedure type[7]

- NYHA class: Functional class of dyspnoea according to the classification as proposed by the New York Heart Association
- Preoperative cardiogenic shock: Preoperative state with life-threatening hypotension despite rapidly escalating inotropic support. critical organ hypoperfusion, with worsening acidosis and/or lactate levels[8]
- Preoperative cardiac arrest: Preoperative cardiopulmonary resuscitation in the 24 hours prior to surgery
- Preoperative septic shock: Septic patients with vasopressor requirement to maintain mean arterial pressure (MAP) >65mmHg and serum lactate levels greater than 2mmol/L in the absence of hypovolemia[9]
- Preoperative right ventricular failure: Evidence of right-sided structural and/or functional abnormalities in combination with clinical symptoms and signs of right ventricular (RV) failure[10]
- Preoperative biventricular failure: Biventricular dysfunction accompanied by both signs and symptoms of right-sided and left-sided heart failure[11]
- Emergency surgery: Surgery before the beginning of the next working day after the decision to operate is made[7]
- 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 [7]
- 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 [7]
- Post LVAD right ventricular failure: RV 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 (either epicardial or endo-epicardial) ablation performed for atrial or ventricular arrhythmia
- Failure to wean: Failure to wean from cardio-pulmonary 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 and/or lactate levels [8]
- Right ventricular failure: Evidence of right-sided structural and/or functional abnormalities in combination with clinical symptoms and signs of RV failure [10]
- Respiratory failure: Reversible pulmonary disease which cannot anymore be managed by conventional mechanical ventilation, despite optimization of pharmacological interventions with or without prone positioning
- Biventricular failure: Biventricular dysfunction accompanied by both signs and symptoms of right-sided and left-sided heart failure [11]
- 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 one hour, without evidence of acute brain infarction [12]
- Arrhythmia: Any atrial or ventricular arrhythmia lasting more than 30 seconds
- Leg ischemia: Clinical signs of lower extremity ischemia requiring intervention (either by vascular surgery or cannula removal)
- Bowel ischemia: Intestinal ischemia with elevated lactate levels requiring abdominal surgical intervention
- Acute kidney injury: Postoperative requirement for dialysis while not on dialysis before or duplication of preoperative creatinine levels (and absolute creatinine level >177µmol/L)
- Pneumonia: Any (suspected) pulmonary infection treated with antibiotics
- Septic shock: Sepsis with vasopressor requirement to maintain MAP >65mmHg and serum lactate levels greater than 2mmol/L in the absence of hypovolemia[9]
- Distributive shock syndrome: MAP <50mmHg with cardiac index >2,5L/min/m^2, right atrial pressure <5mmHg, left atrial pressure <10mmHg an low systemic vascular resistance (<800 dyne/s/cm^{-5}) during intravenous norepinephrine infusion (>0,5µg/kg/min)[13]
- ARDS: Acute diffuse inflammatory lung injury requiring invasive mechanical ventilation of extracorporeal membrane oxygenation
- Multi-organ failure: Hypometabolic state with involvement of more than one organ as established by biochemical and/or radiological analysis

Statistical Analysis

Data were merged and analysed using SPSS 26.0 (IBM. New York. USA), and R 4.1.2 (R Foundation for Statistical Computing. Vienna. Austria) (Supplemental methods). The full cohort was categorized into two study groups (females and males) for comparisons. Missing data analysis was conducted with the *mice: Multivariate Imputation by Chained Equations* R package[14]. The percentage of missing values was

calculated for each variable and reported in Supplementary Table 1. Missing data patterns were investigated and were identified as missing completely at random (MCAR).

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: IQR) or mean and standard deviation for continuous variables. Categorical data were compared between groups with Pearson's chi-Square, or Fisher's exact test. Continuous variables were analysed 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 extracorporeal life support (ECLS) and post-operative complications stratified for males and females.

To estimate the associations between sex and post-operative 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 [15]. The random effect was used to account for dependency of observations due to clustering in centres and in years. For both outcomes, we first estimated a crude model, which was subsequently first adjusted for sets of variables (Supplemental methods) deemed potential confounders for the association with the outcome. For the association with right ventricular failure, we used:

1) Model 1: crude model with variable "Sex".
2) Model 2: sex, pulmonary hypertension.
3) Model 3: sex, pulmonary hypertension, left ventricular unloading.
4) 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.

5) 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, post-operative ECLS implantation, post-operative bleeding requiring re-thoracotomy, post-operative acute kidney injury, left ventricular unloading.

For the association with lower limb ischemia. we used:

1) Model 1: crude model with variable “Sex”.

2) Model 2: sex. body surface area.

3) Model 3: sex. body surface area, distal perfusion.

4) Model 4: sex. body surface area, distal perfusion, age, history of peripheral vessel disease, pre-operative 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 centres and in years. The proportional hazards assumption was tested with Schoenfeld residuals and non-linearity 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 (Supplemental methods) deemed potential confounders for the association with mortality at patient selection, intraoperative decisions, and for ECMO management, based on clinical practice and literature[16-20]. For the association with in-hospital mortality, we used:

1) Model 1: age;

2) 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 intra-aortic balloon pump, right ventricular failure.

3) 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)

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

5) Model 5: demographic data, pre-operative, intra-operative, ECMO variables, and postoperative complications. Model 4 + bleeding requiring re-thoracotomy, post-operative cerebral haemorrhage, post-operative stroke, leg ischemia, post-operative cardiac arrest, post-operative bowel ischemia, post-operative acute kidney injury, post-operative septic shock, post-operative right ventricular failure.

The mixed-effects Cox proportional hazards and logistic regression models were developed on five imputed datasets after imputation of variables with <20% missing data. Variables with more missing data were omitted from the models. We used the *mice: Multivariate Imputation by Chained Equations* R package[14] 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 hazard ratios (HRs) with their 95% confidence intervals (CIs) and p-values. Based on the hormonal variation in females' different ages, 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 were included in survival analyses and were 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 [21] was performed after exclusion of patients who received a post-cardiotomy ECLS before 2011. A further sensitivity analysis was performed to include only patients who underwent coronary artery bypass graft 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.

A two-sided p-value of < 0.05 and a p-interaction of < 0.1 were considered statistically significant.

Supplemental Tables

Supplemental Table 1 - Complete and missing cases for each study variable.

	Complete cases		Missing cases	
Age (years)	1822	(99.9%)	1	(0.1%)
Ethnicity	1823	(100%)	0	(0%)
Body mass index (kg/m2)	1812	(99.4%)	11	(0.6%)
Body surface area (m2)	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 days)	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 mmHg)	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 oedema	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				
Coronary artery disease	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%)
Post-acute 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%)
Coronary artery bypass graft	1823	(100%)	0	(0%)
Aortic valve surgery	1823	(100%)	0	(0%)
Mitral valve surgery	1822	(99.9%)	1	(0.1%)
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%)
Extracorporeal life support 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%)
Intra-aortic balloon pump	1801	(98.8%)	22	(1.2%)
Left ventricular vent	1479	(81.1%)	344	(18.9%)
Extracorporeal membrane oxygenation duration (hours)	1791	(98.2%)	32	(1.8%)
Intensive care unit stay (days)	1753	(96.2%)	70	(3.8%)
Hospital stay (days)	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 haemorrhage	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%)
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

Supplemental Table 2 - Pre-operative characteristics of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		P-value
Age (years)	66.27	(57-74)	66.00	(56-72)	0.073
Race					0.029
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/m2)	26.03	(23.3-30.1)	26.60	(24.2-29.8)	0.089
Body surface area (m2)	1.79	(1.6-1.9)	1.95	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	371	(69%)	589	(70%)	0.719
Smoking	93	(19.7%)	243	(30.1%)	<0.001
Diabetes mellitus	**128**	**(22.6%)**	**241**	**(27.5%)**	**0.036**
Previous myocardial infarction	120	(21.2%)	252	(28.8%)	0.001
Myocardial infarction (last 30 days)	**53**	**(9.9%)**	**120**	**(14.3%)**	**0.016**
Previous percutaneous coronary intervention	76	(13.5%)	162	(18.5%)	0.013
Previous stroke	86	(15.2%)	108	(12.3%)	0.133
Peripheral artery disease	78	(13.8%)	132	(15.1%)	0.541
Atrial fibrillation	156	(27.5%)	208	(23.8%)	0.121
Chronic obstructive pulmonary disease	52	(9.7%)	82	(9.5%)	0.926
Pulmonary hypertension (>50 mmHg)	132	(23.6%)	152	(17.4%)	0.004
Previous cardiac surgery	123	(21.7%)	204	(23.3%)	0.520
Preoperative creatinine (umol/L)	92.0	(71-123.8)	104.00	(80.4-141)	<0.001
Dialysis	40	(7.3%)	78	(9%)	0.278
Left ventricular ejection fraction (%)	52.5	(40-60)	48.00	(34-60)	0.001
Euroscore II	6.99	(2.8-18.2)	6.95	(2.7-17.3)	0.538
Preoperative condition					
NYHA class					0.882
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%)	0.008
Preoperative intubation	62	(11%)	116	(13.2%)	0.219
Preoperative cardiac arrest	45	(8.1%)	72	(8.3%)	0.921
Preoperative septic shock	14	(2.6%)	30	(3.6%)	0.350
Preoperative vasopressors	72	(12.8%)	153	(17.5%)	0.017
Preoperative acute pulmonary oedema	37	(6.9%)	64	(7.6%)	0.672
Preoperative right ventricular failure	50	(10.2%)	67	(8.3%)	0.232
Emergency surgery	131	(23.7%)	250	(28.7%)	0.043
Urgent surgery	113	(20.3%)	159	(18.2%)	0.334
Diagnosis					
Coronary artery disease	252	(44.4%)	489	(55.8%)	<0.001
Aortic vessel disease	106	(18.7%)	178	(20.3%)	0.457
Aortic valve disease	209	(36.9%)	322	(36.8%)	1.000
Mitral valve disease	233	(41.1%)	303	(34.6%)	0.014
Tricuspid valve disease	118	(20.8%)	145	(16.6%)	0.043
Pulmonary valve disease	5	(0.9%)	9	(1%)	1.000
Post-AMI ventricular septal rupture	13	(2.3%)	31	(3.5%)	0.211
Free wall/Papillary muscle rupture	8	(1.4%)	17	(1.9%)	0.539
Active endocarditis	**40**	**(7.1%)**	**88**	**(10%)**	**0.058**

Atrial septal defect	13	(2.3%)	13	(1.5%)	0.312
Other diagnosis	57	(10.1%)	90	(10.3%)	0.929

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. AMI. Acute Myocardial Infarction. NYHA. New York Heart Association.

Supplemental Table 3 - Procedural characteristics of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		p-value
CABG	255	(45%)	458	(52.3%)	0.007
Aortic valve surgery	230	(40.6%)	327	(37.3%)	0.224
Mitral valve surgery	222	(39.2%)	287	(32.8%)	0.013
Tricuspid valve surgery	109	(19.2%)	114	(13%)	0.002
Aortic surgery	118	(20.8%)	201	(22.9%)	0.363
Pulmonary valve surgery	4	(0.7%)	7	(0.8%)	1
Atrial septal defect repair	14	(2.5%)	15	(1.7%)	0.34
Ventricular septal defect repair	18	(3.2%)	33	(3.8%)	0.662
Ventricular surgery	26	(4.6%)	40	(4.6%)	1
Rhythm surgery	25	(4.4%)	32	(3.7%)	0.491
Pulmonary embolectomy	8	(1.4%)	8	(0.9%)	0.443
Pulmonary endarterectomy	**17**	**(3%)**	**12**	**(1.4%)**	**0.035**
Off-pump surgery	15	(2.7%)	56	(6.5%)	0.001
Conversion to cardiopulmonary bypass	7	(43.8%)	15	(25.9%)	0.218
Cardiopulmonary bypass time (min)	201	(135-297)	195	(134-280)	0.431
Crossclamp time (min)	103	(68-152)	103	(63-153)	0.455

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. CABG. Coronary Artery Bypass Graft. .

Supplemental Table 4 - Details on Extracorporeal Life Support of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		P-value
ECLS implantation timing					**0.078**
Intraoperative	**358**	**(63.1%)**	**512**	**(54.8%)**	
Postoperative	**209**	**(36.9%)**	**364**	**(41.6%)**	
Cannulation approach					0.075
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%)	0.002
IABP during any time of hospitalization	125	(22.6%)	286	(32.9%)	<0.001
IABP implantation timing					**0.033**
Pre-operative	**27**	**(21.6%)**	**92**	**(32.2%)**	
Intra-operative	**98**	**(78.4%)**	**194**	**(67.8%)**	
Distal femoral perfusion in patients with peripheral cannulation	158	(69.3%)	313	(77.9%)	0.022
ECLS duration (hours)	120	(64-204.4)	120.00	(60-199)	0.935

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. ECLS. Extracorporeal life support. IABP. Intra-Aortic Balloon Pump. LV. Left Ventricular.

Supplemental Table 5 - Postoperative outcomes of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		P-value
Intensive care unit stay (days)	14	(6-28)	13.00	(5-23)	0.082
Hospital stay (days)	19	(7-37)	19.00	(9-36)	0.997
Postoperative bleeding	307	(55.4%)	480	(55.7%)	0.913
Requiring rethoracotomy	213	(40.7%)	302	(36.2%)	0.096
Cannulation site bleeding	66	(12%)	104	(12.1%)	1
Diffuse no-surgical related bleeding	114	(23.4%)	193	(24%)	0.84
Neurological complications					
Cerebral haemorrhage	18	(3.4%)	24	(2.9%)	0.63
Stroke	66	(11.7%)	88	(10.1%)	0.383
Arrhythmia	172	(33.7%)	262	(31.9%)	0.509
Leg ischemia	**50**	**(9.5%)**	**71**	**(8.5%)**	**0.558**
Cardiac arrest	85	(16.7%)	126	(15.3%)	0.537
Pacemaker implantation	19	(3.7%)	23	(2.8%)	0.42
Bowel ischemia	27	(5.3%)	54	(6.6%)	0.409
Right ventricular failure	116	(23.7%)	145	(17.9%)	0.012
Acute kidney injury	266	(52.6%)	417	(50.9%)	0.572
Pneumonia	102	(20.8%)	178	(22%)	0.627
Septic shock	68	(13.9%)	148	(18.3%)	0.038
Distributive syndrome	45	(9.2%)	91	(11.3%)	0.262
Acute respiratory distress syndrome	25	(4.9%)	35	(4.3%)	0.59
Embolism	29	(5.9%)	38	(4.7%)	0.365
Postoperative procedures					
Percutaneous coronary intervention	14	(2.9%)	29	(3.6%)	0.526
Cardiac surgery	127	(24.9%)	203	(24.7%)	1
Abdominal surgery	18	(3.7%)	39	(4.8%)	0.402
Vascular surgery	37	(7.6%)	89	(11%)	0.053
In-hospital mortality	364	(64.2%)	530	(60.5%)	0.165
In-hospital mortality timing					0.520
Deceased on support	222	(61.0%)	341	(64.3%)	
Deceased after weaning	133	(36.6%)	185	(34.9%)	
Main cause of death					0.388
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 (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis.

Supplemental Table 6 - Odds ratios for variables associated with post-operative right ventricular failure.

	Full cohort (n=1823)			
	Odds Ratio	95% Confidence Interval		P-value
		Lower Limit	Upper Limit	
Model 1: crude model with a random intercept for hospital and year				
Sex (Reference: Males)	1.38	1.06	1.80	0.0160
Model 2: Model 1 + Pre-operative Pulmonary Hypertension				
Sex (Reference: Males)	1.37	1.08	1.74	0.0090
Pulmonary Hypertension (> 50 mmHg)	1.63	1.19	2.24	0.0032
Model 3: Model 2 + Left Ventricular Unloading				
Sex (Reference: Males)	1.36	1.07	1.73	0.0115
Pulmonary Hypertension (> 50 mmHg)	1.62	1.18	2.22	0.0036
Left Ventricular Unloading	0.64	0.41	1.00	0.0486
Model 4 : Model 1 + demographic data and pre-operative variables				
Sex (Reference: Males)	1.32	1.00	1.75	0.0464
Age (years)	1.00	0.99	1.01	0.8609
Body Mass Index	1.01	0.98	1.04	0.4587
Dialysis	1.17	0.72	1.89	0.5295
Myocardial Infarction	0.88	0.62	1.25	0.4752
Atrial Fibrillation	0.83	0.60	1.13	0.2349
Chronic Obstructive Pulmonary Disease	0.78	0.48	1.25	0.2984
Pulmonary Hypertension (> 50 mmHg)	1.50	1.04	2.17	0.0308
Previous Cardiac Surgery	1.00	0.73	1.38	0.9784
Left Ventricular Ejection Fraction	1.01	1.00	1.02	0.0358
Cardiogenic Shock	0.86	0.58	1.28	0.4639
Urgent Surgery	1.04	0.72	1.51	0.8334
Emergency Surgery	0.90	0.59	1.38	0.6241
Cardiac Arrest	1.27	0.78	2.07	0.3238
Acute Pulmonary Edema	0.93	0.54	1.61	0.8014
Preoperative Right Ventricular Failure	4.34	2.84	6.63	<0.001
Model 5: Variables Influencing Right Ventricular Function				
Sex (Reference: Males)	1.32	1.00	1.74	0.0521
Age (years)	1.00	0.98	1.01	0.5143
Pulmonary Hypertension (> 50 mmHg)	1.40	0.97	2.03	0.0752
Previous Cardiac Surgery	1.01	0.74	1.40	0.9290
Left Ventricular Ejection Fraction	1.01	1.00	1.02	0.0168
Acute Pulmonary Edema	0.88	0.52	1.46	0.6109
Preoperative Right Ventricular Failure	4.04	2.67	6.12	0.0000
Cardiopulmonary Bypass Time (min)	1.00	1.00	1.00	0.81
Mitral Valve Surgery	1.15	0.85	1.57	0.3674
Tricuspid Valve Surgery	1.13	0.74	1.71	0.5716
Post-operative ECLS Implantation	1.15	0.85	1.57	0.3708
Post-operative Bleeding Requiring Re-thoracotomy	1.17	0.89	1.56	0.2611
Post-operative Acute Kidney Injury	1.39	1.03	1.87	0.0309
Left Ventricular Unloading	0.72	0.43	1.19	0.1991

ECLS. Extracorporeal Life Support.

Supplemental Table 7 - Odds ratios for variables associated with post-operative lower ischemia.

	Full cohort (n=1823)			
	Odds Ratio	95% Confidence Interval		P-value
		Lower Limit	Upper Limit	
Model 1: crude model with a random intercept for hospital and year				
Sex (Reference: Males)	1.42	0.95	2.12	0.0838
Model 2: Model 1 + Body Surface Area				
Sex (Reference: Males)	1.40	0.93	2.13	0.1095
Body Surface Area (m2)	0.91	0.37	2.29	0.8474
Model 3: Model 2 + Distal Perfusion				
Sex (Reference: Males)	1.41	0.93	2.13	0.1082
Body Surface Area (m2)	0.91	0.37	2.29	0.8484
Distal Perfusion	1.03	0.64	1.65	0.8985
Model 4 : Model 1 + Variables Influencing Limb Ischemia				
Sex (Reference: Males)	1.53	1.00	2.36	0.0517
Body Surface Area (m2)	0.80	0.31	2.10	0.6538
Distal Perfusion	1.12	0.69	1.81	0.6488
Age (years)	0.98	0.97	1.00	0.0485
History of Peripheral Vessel Disease	1.34	0.72	2.50	0.3499
Pre-operative Vasopressors	2.04	1.27	3.29	0.0033
Bleeding at Cannulation Site	2.09	1.24	3.52	0.0058
Extracorporeal Cardiopulmonary Resuscitation	1.41	0.75	2.64	0.2836

Supplemental Table 8 - Postoperative transfusions

	Females (n=743)		Males (n=1080)		P-value
		Missing values		Missing values	
Postoperative transfusions (number of packed red blood cells)	11 (4-21)	407 (54.8%)	10 (4-21)	494 (45.7%)	0.434
Data are reported as n(%) or median (1st and 3rd quartile).					

Sensitivity analysis after excluding patients who did not receive a coronary artery bypass or valvular surgery

Supplemental Table 9 - Pre-operative characteristics of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		P-value
Age (years)	67.00	(58-74)	67.00	(57-72.1)	0.157
Race					<0.001
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)	0.685
Bodi surface area (m^2)	1.80	(1.7-2)	1.93	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	425	(68.5%)	660	(71.5%)	0.233
Smoking	97	(19.2%)	277	(32.4%)	<0.001
Diabetes mellitus	169	(26%)	283	(29.7%)	0.109
Previous myocardial infarction	149	(22.9%)	294	(30.8%)	<0.001
Myocardial infarction (last 30 days)	76	(12.3%)	132	(14.3%)	0.249
Previous percutaneous coronary intervention	94	(14.6%)	175	(18.4%)	0.044
Previous stroke	96	(14.8%)	125	(13.1%)	0.342
Peripheral artery disease	96	(14.8%)	158	(16.6%)	0.334
Atrial fibrillation	**195**	**(30%)**	**243**	**(25.5%)**	**0.047**
Chronic obstructive pulmonary disease	73	(11.9%)	100	(10.7%)	0.463
Pulmonary hypertension (>50 mmHg)	**144**	**(22.4%)**	**181**	**(19%)**	**0.103**
Previous cardiac surgery	151	(23.2%)	228	(23.9%)	0.757
Preoperative creatinine (umol/L)	**79.0**	**(48-169)**	**92.00**	**(57-189.9)**	**0.103**
Dialysis	44	(7.1%)	88	(9.4%)	0.111
Left ventricular ejection fraction (%)	50.0	(38.5-60)	47.02	(32-60)	0.006
Euroscore II*	7.60	(2.9-20.7)	7.28	(2.8-19)	0.430
Preoperative condition					
New York Heart Association class					0.714
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%)	0.006
Preoperative cardiac arrest	69	(10.8%)	97	(10.3%)	0.755
Preoperative intubation	65	(10%)	121	(12.7%)	0.102
Preoperative septic shock	15	(2.4%)	31	(3.4%)	0.293
Preoperative vasopressors	**87**	**(13.6%)**	**162**	**(17.1%)**	**0.059**
Preoperative right ventricular failure	53	(9.9%)	69	(7.9%)	0.206
Emergency surgery	**147**	**(23.1%)**	**268**	**(28.2%)**	**0.025**
Urgent surgery	129	(20.2%)	171	(18%)	0.268
Diagnosis					
Coronary artery disease	319	(49.1%)	582	(61%)	<0.001
Aortic vessel disease	94	(14.5%)	150	(15.7%)	0.490
Aortic valve disease	280	(43.1%)	391	(41%)	0.404
Mitral valve disease	295	(45.4%)	375	(39.3%)	0.015
Tricuspid valve disease	138	(21.2%)	162	(17%)	0.032
Pulmonary valve disease	5	(0.8%)	8	(0.8%)	0.879
Post-AMI ventricular septal rupture	8	(1.2%)	18	(1.9%)	0.307
Free wall/Papillary mucle rupture	11	(1.7%)	23	(2.4%)	0.327
Active endocarditis	45	(6.9%)	99	(10.4%)	0.018
Atrial septal defect	13	(2%)	9	(0.9%)	0.074

Other diagnosis	30	(4.6%)	71	(7.4%)	0.022

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).
Text in bold indicates differences compared to the main analysis. AMI. Acute Myocardial Infarction.

Supplemental Table 10 - Intra-operative characteristics of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		p-value
Coronary artery bypass graft	341	(52.5%)	566	(59.3%)	0.006
Aortic valve surgery	305	(46.9%)	402	(42.1%)	0.058
Mitral valve surgery	285	(43.8%)	357	(37.4%)	0.010
Tricuspid valve surgery	134	(20.6%)	134	(14%)	<0.001
Aortic surgery	111	(17.1%)	173	(18.1%)	0.586
Pulmonary valve surgery	5	(0.8%)	7	(0.7%)	0.935
Atrial septal defect repair	14	(2.2%)	12	(1.3%)	0.163
Ventricular septal defect repair	12	(1.8%)	21	(2.2%)	0.623
Ventricular surgery	14	(2.2%)	25	(2.6%)	0.551
Rhythm surgery	24	(3.7%)	32	(3.4%)	0.717
Pulmonary embolectomy	3	(0.5%)	3	(0.3%)	0.691
Pulmonary endoarterectomy	4	(0.6%)	4	(0.4%)	0.722
Off-pump surgery	15	(2.4%)	58	(6.1%)	<0.001
Conversion to Cardiopulmonary bypass	6	(40%)	16	(27.1%)	0.355
Cardiopulmonary bypass time (min)	198	(135-288)	195	(132-277)	0.452
Crossclamp time (min)	102	(68-150)	102	(62-152)	0.265

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis.

Supplemental Table 11 - Details on Extracorporeal Life Support of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		P-value
ECLS implantation timing					0.049
Intraoperative	410	(63.1%)	555	(58.2%)	
Postoperative	240	(36.9%)	399	(41.8%)	
Cannulation approach					0.454
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%)	<0.001
IABP during any time of hospitalization	176	(27.7%)	363	(38.3%)	<0.001
IABP implantation timing					0.699
Pre-operative	50	(28.4%)	109	(30%)	
Intra-operative	126	(71.6%)	254	(70%)	
ECLS duration (hours)	117	(62-192)	120.00	(60-195)	0.734

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. ECLS, Extracorporeal Life Support. IABP, Intra-Aortic Balloon Pump.

Supplemental Table 12 - Postoperative outcomes of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		P-value
Intensive care unit stay (days)	14	(6-27)	13.00	(6-24)	0.339
Hospital stay (days)	18	(7-36)	19.00	(8-36)	0.479
Postoperative bleeding	366	(57.4%)	543	(57.6%)	0.913
Requiring re-thoracotomy	245	(41%)	350	(38.4%)	0.313
Cannulation site bleeding	89	(14%)	107	(11.4%)	0.121
Diffuse no-surgical related bleeding	143	(25.4%)	248	(28%)	0.282
Neurological complications					
Cerebral hemorrhage	21	(3.5%)	28	(3.1%)	0.684
Stroke	69	(10.7%)	94	(9.9%)	0.620
Arrhythmia	198	(34.1%)	304	(34%)	0.964
Leg ischemia	75	(12.4%)	81	(9%)	0.031
Cardiac arrest	112	(19.3%)	151	(16.9%)	0.234
Pacemaker implantation	18	(3.1%)	28	(3.1%)	0.974
Bowel ischemia	29	(5%)	53	(5.9%)	0.446
Right ventricular failure	136	(24.3%)	169	(19.1%)	0.019
Acute kidney injury	327	(56.8%)	482	(53.9%)	0.283
Pneumonia	119	(21.3%)	199	(22.5%)	0.566
Septic shock	75	(13.4%)	159	(18%)	0.021
Distributive shock syndrome	44	(7.9%)	91	(10.3%)	0.123
Acute respiratory distress syndrome	33	(5.7%)	45	(5%)	0.584
Embolism	34	(6.1%)	43	(4.9%)	0.321
Postoperative procedures					
Percutaneous coronary intervention	14	(2.6%)	28	(3.2%)	0.497
Cardiac surgery	142	(24.4%)	211	(23.6%)	0.712
Abdominal surgery	21	(3.9%)	44	(5%)	0.305
Vascular surgery	59	(10.8%)	86	(9.8%)	0.560
In-hospital mortality	425	(65.4%)	587	(61.5%)	0.116
In-hospital mortality timing					0.351
Deceased on support	256	(39.9%)	363	(38.2%)	
Deceased after weaning	160	(25.0%)	220	(23.2%)	
Main cause of death					0.249
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%)	

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis.

Sub-group analysis of patients who underwent coronary artery bypass surgery

Supplemental Table 13 - Pre-operative characteristics of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		P-value
Age (years)	68.00	(60-74.2)	67.00	(59-72.4)	0.050
Race					<0.001
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)	0.506
Bodi surface area (m^2)	1.83	(1.7-2)	1.94	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	252	(75.7%)	417	(75.5%)	0.965
Smoking	56	(21.6%)	179	(34.6%)	<0.001
Diabetes mellitus	110	(32.3%)	199	(35.2%)	0.372
Previous myocardial infarction	126	(37%)	241	(42.6%)	0.094
Myocardial infarction (last 30 days)	66	(19.8%)	116	(21%)	0.670
Previous percutaneous coronary intervention	73	(21.7%)	126	(22.3%)	0.823
Previous stroke	43	(12.6%)	67	(11.8%)	0.730
Peripheral artery disease	68	(19.9%)	117	(20.7%)	0.792
Atrial fibrillation	71	(20.8%)	117	(20.7%)	0.968
Chronic obstructive pulmonary disease	48	(15.2%)	64	(11.6%)	0.123
Pulmonary hypertension (>50 mmHg)	64	(19%)	89	(15.8%)	0.210
Previous cardiac surgery	61	(17.9%)	82	(14.5%)	0.173
Preoperative creatinine (umol/L)	97.3	(76.9-132)	102.00	(81.3-132.7)	0.023
Dialysis	21	(6.6%)	57	(10.3%)	0.066
Left ventricular ejection fraction (%)	45.0	(30-60)	43.00	(30-55)	0.121
Euroscore II*	8.70	(3.6-21.7)	7.81	(2.9-19)	0.102
Preoperative condition					
New York Heart Association class					0.502
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%)	0.005
Preoperative cardiac arrest	50	(14.8%)	64	(11.4%)	0.138
Preoperative intubation	30	(8.8%)	80	(14.1%)	0.018
Preoperative septic shock	7	(2.1%)	12	(2.2%)	0.957
Preoperative vasopressors	43	(12.8%)	110	(19.5%)	0.010
Preoperative right ventricular failure	23	(8.3%)	27	(5.2%)	0.087
Emergency surgery	94	(28.7%)	191	(33.9%)	0.108
Urgent surgery	63	(19%)	96	(17%)	0.447
Diagnosis					
Aortic vessel disease	52	(15.2%)	73	(12.9%)	0.320
Aortic valve disease	124	(36.4%)	178	(31.4%)	0.128
Mitral valve disease	114	(33.4%)	164	(29%)	0.159
Tricuspid valve disease	48	(14.1%)	60	(10.6%)	0.117
Pulmonary valve disease	3	(0.9%)	0	(0%)	0.025
Post-AMI ventricular septal rupture	4	(1.2%)	13	(2.3%)	0.227
Free wall/Papillary mucle rupture	4	(1.2%)	11	(1.9%)	0.378
Active endocarditis	14	(4.1%)	29	(5.1%)	0.485
Atrial septal defect	5	(1.5%)	3	(0.5%)	0.160
Other diagnosis	11	(3.2%)	33	(5.8%)	0.077

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).
AMI. Acute Myocardial Infarction.

Supplemental Table 14 - Procedural characteristics of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		p-value
Aortic valve surgery	139	(40.8%)	169	(29.9%)	<0.001
Mitral valve surgery	100	(29.3%)	145	(25.6%)	0.223
Tricuspid valve surgery	45	(13.2%)	36	(6.4%)	<0.001
Aortic surgery	65	(19.1%)	80	(14.1%)	0.050
Pulmonary valve surgery	3	(0.9%)	0	(0%)	0.053
Atrial septal defect repair	5	(1.5%)	3	(0.5%)	0.160
Ventricular septal defect repair	6	(1.8%)	12	(2.1%)	0.706
Ventricular surgery	2	(0.6%)	18	(3.2%)	0.010
Rhythm surgery	9	(2.6%)	16	(2.8%)	0.867
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%)	0.003
Conversion to Cardiopulmonary bypass	6	(40%)	14	(24.6%)	0.331
Cardiopulmonary bypass time (min)	216	(147-316)	190	(124-267)	<0.001
Crossclamp time (min)	103	(70-156)	92	(56-142)	0.002

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Supplemental Table 15 - Details on Extracorporeal Life Support of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		P-value
ECLS implantation timing					0.003
Intraoperative	230	(67.4%)	325	(57.4%)	
Postoperative	111	(32.6%)	241	(42.6%)	
Cannulation approach					0.050
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%)	<0.001
IABP during any time of hospitalization	108	(32.4%)	272	(48.1%)	<0.001
IABP implantation timing					0.464
Pre-operative	40	(37%)	90	(33.1%)	
Intra-operative	68	(63%)	182	(66.9%)	
ECLS duration (hours)	115	(64-192)	120.00	(61.4-207.5)	0.215

DData are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

Supplemental Table 16 - Postoperative outcomes of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		P-value
Intensive care unit stay (days)	13	(6-28)	13.00	(6-23)	0.425
Hospital stay (days)	19	(7-37)	19.00	(8-34)	0.868
Postoperative bleeding	190	(56.9%)	313	(55.9%)	0.722
Requiring re-thoracotomy	130	(41.8%)	206	(38.0%)	0.275
Cannulation site bleeding	50	(15%)	63	(11.3%)	0.102
Diffuse no-surgical related bleeding	61	(20.5%)	142	(26.6%)	0.049
Neurological complications					
Cerebral hemorrhage	9	(2.8%)	16	(2.9%)	0.895
Stroke	39	(11.5%)	63	(11.2%)	0.866
Arrhythmia	111	(35.7%)	190	(35.4%)	0.928
Leg ischemia	46	(14.3%)	50	(9.2%)	0.022
Cardiac arrest	64	(20.6%)	93	(17.3%)	0.239
Pacemaker implantation	7	(2.3%)	13	(2.4%)	0.875
Bowel ischemia	17	(5.5%)	33	(6.1%)	0.686
Right ventricular failure	62	(21%)	96	(18.1%)	0.304
Acute kidney injury	176	(57.9%)	293	(54.6%)	0.35
Pneumonia	60	(20.3%)	115	(21.7%)	o.630
Septic shock	36	(12.2%)	84	(15.8%)	0.155
Distributive shock syndrome	21	(7.1%)	47	(8.9%)	0.389
Acute respiratory distress syndrome	18	(5.8%)	25	(4.7%)	0.469
Embolism	21	(7.1%)	25	(4.7%)	0.149
Postoperative procedures					
Percutaneous coronary intervention	3	(1.1%)	18	(3.4%)	0.043
Cardiac surgery	73	(23.5%)	132	(24.6%)	0.716
Abdominal surgery	9	(3.2%)	26	(4.9%)	0.236
Vascular surgery	39	(13.6%)	52	(9.8%)	0.103
In-hospital mortality	213	(62.5%)	345	(61.0%)	0.651
In-hospital mortality timing					0.956
Deceased on support	125	(37.4%)	206	(36.5%)	
Deceased after weaning	81	(24.3%)	138	(24.4%)	
Main cause of death					0.550
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%)	

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Sub-group analysis of patients who underwent mitral valve surgery

Supplemental Table 17 - Pre-operative characteristics of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		P-value
Age (years)	66.00	(58-74)	67.00	(56.5-72)	0.836
Race					0.122
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)	0.552
Bodi surface area (m^2)	1.80	(1.7-2)	1.93	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	177	(65.1%)	237	(69.5%)	0.245
Smoking	48	(21%)	88	(29%)	0.034
Diabetes mellitus	72	(25.3%)	96	(26.9%)	0.641
Previous myocardial infarction	45	(15.8%)	85	(23.8%)	0.012
Myocardial infarction (last 30 days)	23	(8.5%)	35	(10.3%)	0.447
Previous percutaneous coronary intervention	42	(14.8%)	65	(18.3%)	0.224
Previous stroke	47	(16.5%)	59	(16.5%)	0.990
Peripheral artery disease	33	(11.6%)	49	(13.7%)	0.418
Atrial fibrillation	124	(43.5%)	136	(38.1%)	0.165
Chronic obstructive pulmonary disease	35	(12.9%)	37	(10.7%)	0.403
Pulmonary hypertension (>50 mmHg)	90	(32%)	104	(29.2%)	0.443
Previous cardiac surgery	80	(28.1%)	111	(31.1%)	0.405
Preoperative creatinine (umol/L)	98.15	(79.6-133.5)	109.62	(87.4-153.9)	<0.001
Dialysis	18	(6.6%)	44	(12.8%)	0.012
Left ventricular ejection fraction (%)	50.00	(37-60)	50.00	(37.5-60)	0.608
Euroscore II*	8.32	(3.7-21.9)	8.03	(3.1-22.9)	0.820
Preoperative condition					
New York Heart Association class					0.535
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%)	0.135
Preoperative cardiac arrest	21	(7.6%)	28	(8%)	0.830
Preoperative intubation	38	(13.4%)	45	(12.6%)	0.772
Preoperative septic shock	8	(3%)	17	(5%)	0.204
Preoperative vasopressors	42	(14.8%)	66	(18.5%)	0.208
Preoperative right ventricular failure	26	(10.6%)	37	(11.6%)	0.722
Emergency surgery	48	(17.4%)	79	(22.3%)	0.126
Urgent surgery	60	(21.5%)	74	(20.9%)	0.854
Diagnosis					
Coronary artery disease	110	(38.6%)	182	(51%)	0.002
Aortic vessel disease	16	(5.6%)	27	(7.6%)	0.326
Aortic valve disease	96	(33.7%)	133	(37.3%)	0.348
Tricuspid valve disease	100	(35.1%)	107	(30%)	0.168
Pulmonary valve disease	1	(0.4%)	0	(0%)	0.444
Post-AMI ventricular septal rupture	6	(2.1%)	3	(0.8%)	0.195
Free wall/Papillary mucle rupture	10	(3.5%)	22	(6.2%)	0.125
Active endocarditis	19	(6.7%)	52	(14.6%)	0.001
Atrial septal defect	8	(2.8%)	3	(0.8%)	0.069
Other diagnosis	17	(6%)	22	(6.2%)	0.917

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).
AMI. Acute Myocardial Infarction.

Supplemental Table 18 - Procedural characteristics of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		p-value
Coronary Artery Bypass Graft	100	(35.1%)	145	(40.6%)	0.152
Aortic valve surgery	101	(35.4%)	130	(36.4%)	0.798
Tricuspid valve surgery	101	(35.4%)	102	(28.6%)	0.063
Aortic surgery	19	(6.7%)	41	(11.5%)	0.037
Pulmonary valve surgery	1	(0.4%)	0	(0%)	0.444
Atrial septal defect repair	9	(3.2%)	5	(1.4%)	0.130
Ventricular septal defect repair	6	(2.1%)	4	(1.1%)	0.317
Ventricular surgery	10	(3.5%)	10	(2.8%)	0.608
Rhythm surgery	21	(7.4%)	21	(5.9%)	0.449
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)	0.224
Crossclamp time (min)	119.00	(86-160)	128.00	(86-175)	0.095

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Supplemental Table 19 - Details on Extracorporeal Life Support of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		P-value
ECLS implantation timing					0.003
Intraoperative	183	(64.2%)	223	(62.5%)	
Postoperative	102	(35.8%)	134	(37.5%)	
Cannulation approach					0.178
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%)	0.141
IABP during any time of hospitalization	75	(26.8%)	124	(35%)	0.591
IABP implantation timing					0.588
Pre-operative	22	(29.3%)	32	(25.8%)	
Intra-operative	53	(70.7%)	92	(74.2%)	
ECLS duration (hours)	119.13	(72-194.3)	120.00	(62.4-191.8)	0.448

DData are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

Supplemental Table 20 - Postoperative outcomes of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		P-value
Intensive care unit stay (days)	14.50	(7-29)	12.00	(5-24)	0.117
Hospital stay (days)	21.00	(8-40)	18.00	(7-39)	0.595
Postoperative bleeding	164	(58.6%)	211	(59.4%)	0.826
Requiring re-thoracotomy	105	(39.3%)	137	(39.9%)	0.877
Cannulation site bleeding	46	(16.4%)	39	(11%)	0.047
Diffuse no-surgical related bleeding	65	(26.4%)	90	(28%)	0.685
Neurological complications					
Cerebral hemorrhage	9	(3.4%)	10	(3%)	0.783
Stroke	25	(8.8%)	34	(9.6%)	0.756
Arrhythmia	87	(33.3%)	100	(30.1%)	0.403
Leg ischemia	32	(12%)	27	(8.2%)	0.118
Cardiac arrest	45	(17.3%)	42	(12.7%)	0.112
Pacemaker implantation	8	(3.1%)	13	(3.9%)	0.578
Bowel ischemia	12	(4.6%)	26	(7.8%)	0.11
Right ventricular failure	62	(24.8%)	77	(23.8%)	0.774
Acute kidney injury	150	(57.3%)	191	(58.1%)	0.844
Pneumonia	65	(25.9%)	76	(23.5%)	0.5
Septic shock	39	(15.6%)	69	(21.4%)	0.08
Distributive shock syndrome	23	(9.2%)	42	(13%)	0.163
Acute respiratory distress syndrome	17	(6.5%)	12	(3.6%)	0.104
Embolism	15	(6%)	23	(7.1%)	0.6
Postoperative procedures					
Percutaneous coronary intervention	6	(2.5%)	5	(1.6%)	0.439
Cardiac surgery	63	(24.2%)	76	(23%)	0.718
Abdominal surgery	12	(5%)	17	(5.3%)	0.847
Vascular surgery	23	(9.5%)	25	(7.8%)	0.484
In-hospital mortality	187	(65.6%)	234	(65.5%)	0.986
In-hospital mortality timing					0.847
Deceased on support	109	(38.4%)	143	(40.2%)	
Deceased after weaning	77	(27.1%)	90	(25.3%)	
Main cause of death					0.780
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 (1st and 3rd quartile).

Sub-group analysis of patients who underwent tricuspid valve surgery

Supplemental Table 21 - Pre-operative characteristics of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		P-value
Age (years)	67.50	(59-74)	68.02	(58.9-73.8)	0.601
Race					0.365
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)	0.460
Bodi surface area (m^2)	1.83	(1.7-2)	1.90	(1.8-2)	0.009
Comorbidities					
Hypertension	83	(65.4%)	81	(63.3%)	0.730
Smoking	16	(14.7%)	31	(28.4%)	0.013
Diabetes mellitus	32	(23.9%)	31	(23.1%)	0.885
Previous myocardial infarction	14	(10.4%)	25	(18.7%)	0.057
Myocardial infarction (last 30 days)	4	(3.1%)	4	(3.1%)	1.000
Previous percutaneous coronary intervention	15	(11.3%)	26	(19.5%)	0.062
Previous stroke	16	(11.9%)	22	(16.4%)	0.293
Peripheral artery disease	10	(7.5%)	16	(11.9%)	0.216
Atrial fibrillation	74	(55.2%)	70	(52.2%)	0.624
Chronic obstructive pulmonary disease	16	(12.5%)	18	(13.8%)	0.749
Pulmonary hypertension (>50 mmHg)	48	(36.4%)	57	(42.5%)	0.303
Previous cardiac surgery	42	(31.3%)	47	(35.1%)	0.517
Preoperative creatinine (umol/L)	107.42	(85.6-141)	109.18	(85.7-152.1)	0.476
Dialysis	9	(7.1%)	15	(11.5%)	0.220
Left ventricular ejection fraction (%)	55.00	(40-60)	50.00	(40-60)	0.159
Euroscore II*	9.01	(4.4-20.7)	9.80	(3.7-21.1)	0.698
Preoperative condition					
New York Heart Association class					0.071
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%)	0.726
Preoperative cardiac arrest	6	(4.5%)	6	(4.5%)	1.000
Preoperative intubation	13	(9.7%)	8	(6%)	0.256
Preoperative septic shock	2	(1.6%)	4	(3.1%)	0.684
Preoperative vasopressors	15	(11.2%)	17	(12.8%)	0.690
Preoperative right ventricular failure	22	(19.5%)	23	(18.9%)	0.904
Emergency surgery	11	(8.5%)	23	(17.3%)	0.033
Urgent surgery	35	(26.5%)	22	(16.5%)	0.048
Diagnosis					
Coronary artery disease	46	(34.3%)	53	(39.6%)	0.376
Aortic vessel disease	12	(9%)	12	(9%)	1.000
Aortic valve disease	50	(37.3%)	53	(39.6%)	0.706
Mitral valve disease	100	(74.6%)	104	(77.6%)	0.567
Tricuspid valve disease	117	(87.3%)	120	(89.6%)	0.567
Pulmonary valve disease	2	(1.5%)	0	(0%)	0.498
Post-AMI ventricular septal rupture	2	(1.5%)	1	(0.7%)	1.000
Free wall/Papillary mucle rupture	0	(0%)	0	(0%)	n.a.
Active endocarditis	7	(5.2%)	9	(6.7%)	0.606

Atrial septal defect	5	(3.7%)	4	(3%)	1.000
Other diagnosis	6	(4.5%)	16	(11.9%)	0.026

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). AMI. Acute Myocardial Infarction.

Supplemental Table 22 - Procedural characteristics of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		p-value
Coronary Artery Bypass Graft	45	(33.6%)	36	(26.9%)	0.231
Aortic valve surgery	52	(38.8%)	47	(35.1%)	0.527
Mitral valve surgery	101	(75.4%)	102	(76.1%)	0.887
Aortic surgery	15	(11.2%)	15	(11.2%)	1.000
Pulmonary valve surgery	2	(1.5%)	0	(0%)	0.498
Atrial septal defect repair	5	(3.7%)	6	(4.5%)	0.758
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%)	0.051
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)	0.801
Crossclamp time (min)	121.00	(88-160)	118.00	(84-161)	0.669

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Supplemental Table 23 - Details on Extracorporeal Life Support of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		P-value
ECLS implantation timing					0,543
Intraoperative	82	(61.2%)	77	(57.5%)	
Postoperative	52	(38.8%)	57	(42.5%)	
Cannulation approach					0.235
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%)	0.387
IABP during any time of hospitalization	25	(19.7%)	36	(27.1%)	0.16
IABP implantation timing					0.727
Pre-operative	5	(20%)	5	(13.9%)	
Intra-operative	20	(80%)	31	(86.1%)	
ECLS duration (hours)	123.00	(56.2-195.8)	131.27	(72-192)	0.822

DData are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

Supplemental Table 24 - Postoperative outcomes of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		P-value
Intensive care unit stay (days)	14.00	(6-31)	12.00	(6-20.5)	0.188
Hospital stay (days)	21.00	(7-39)	18.00	(9-33)	0.613
Postoperative bleeding	69	(52.3%)	84	(63.2%)	0.073
Requiring re-thoracotomy	56	(44.8%)	50	(38.5%)	0.305
Cannulation site bleeding	16	(12.1%)	18	(13.5%)	0.731
Diffuse no-surgical related bleeding	26	(23%)	43	(36.4%)	0.026
Neurological complications					
Cerebral hemorrhage	1	(0.8%)	3	(2.4%)	0.37
Stroke	5	(3.7%)	6	(4.5%)	0.739
Arrhythmia	37	(31.4%)	41	(33.1%)	0.776
Leg ischemia	10	(7.9%)	8	(6.4%)	0.65
Cardiac arrest	19	(16.2%)	13	(10.5%)	0.188
Pacemaker implantation	5	(4.2%)	6	(4.8%)	0.822
Bowel ischemia	3	(2.5%)	9	(7.3%)	0.091
Right ventricular failure	32	(28.1%)	35	(28.7%)	0.916
Acute kidney injury	79	(64.2%)	69	(57%)	0.25
Pneumonia	33	(28.7%)	34	(28.3%)	0.951
Septic shock	18	(15.8%)	32	(26.9%)	0.039
Distributive shock syndrome	10	(8.8%)	14	(11.7%)	0.466
Acute respiratory distress syndrome	9	(7.6%)	3	(2.4%)	0.062
Embolism	6	(5.3%)	8	(6.6%)	0.674
Postoperative procedures					
Percutaneous coronary intervention	3	(2.7%)	1	(0.9%)	0.361
Cardiac surgery	21	(17.8%)	31	(25.2%)	0.162
Abdominal surgery	3	(2.7%)	3	(2.6%)	1
Vascular surgery	5	(4.5%)	7	(5.9%)	0.617
In-hospital mortality	95	(70.9%)	92	(68.7%)	0.690
In-hospital mortality timing					0.720
Deceased on support	55	(42%)	60	(44.8%)	
Deceased after weaning	37	(28.2%)	32	(23.9%)	
Main cause of death					0.285
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 (1st and 3rd quartile).

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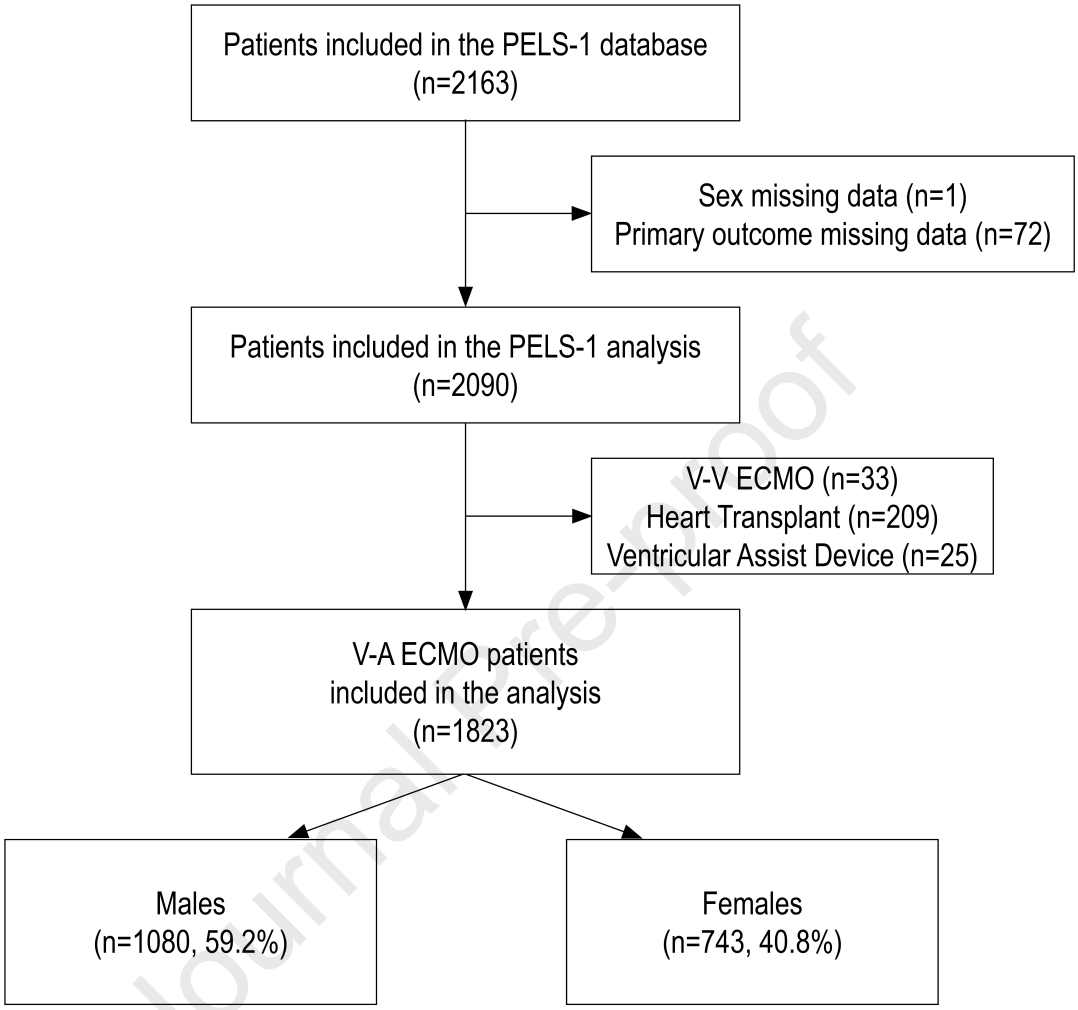
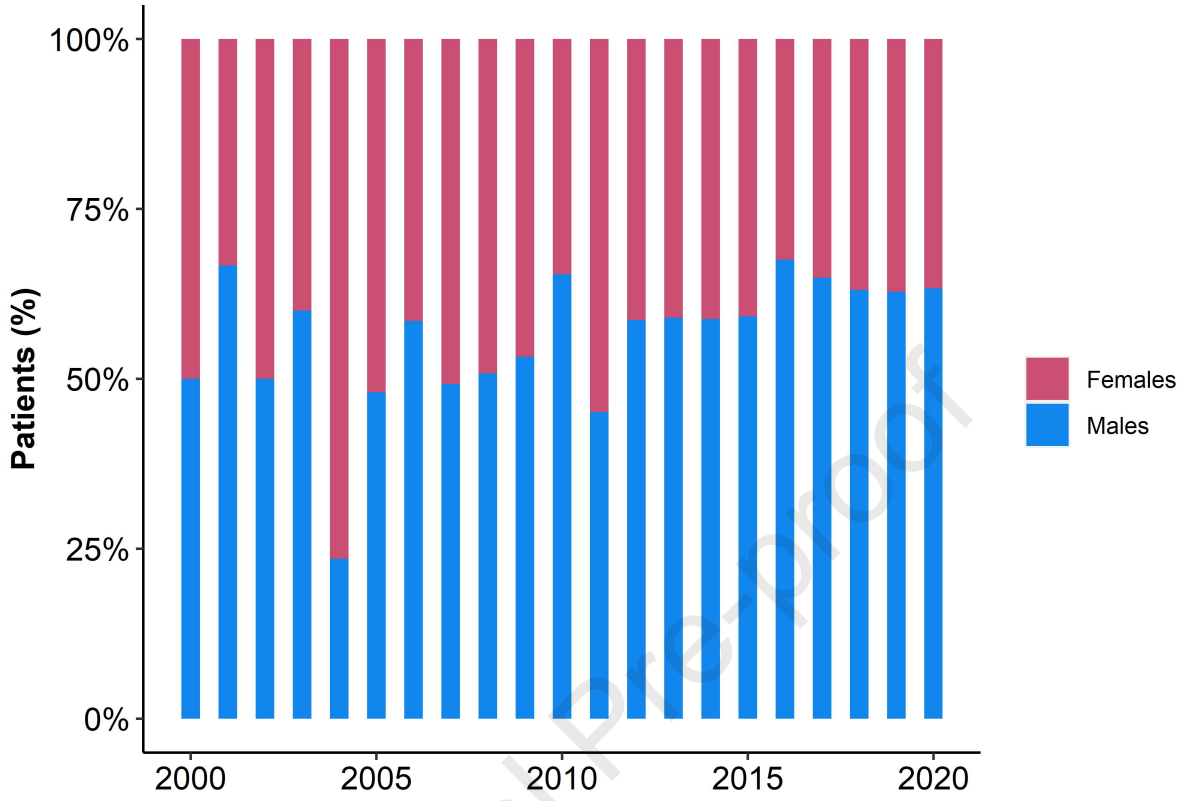
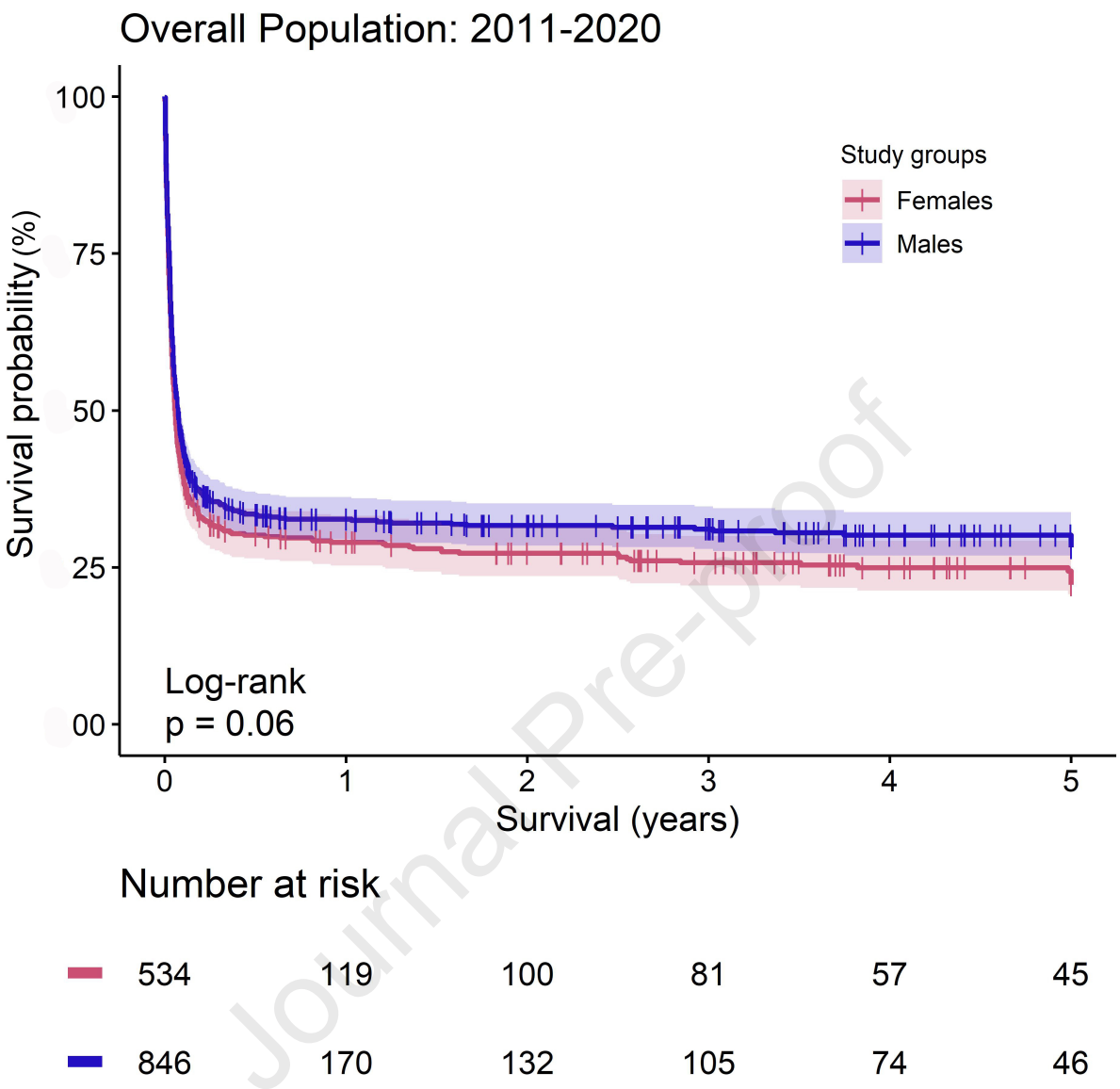
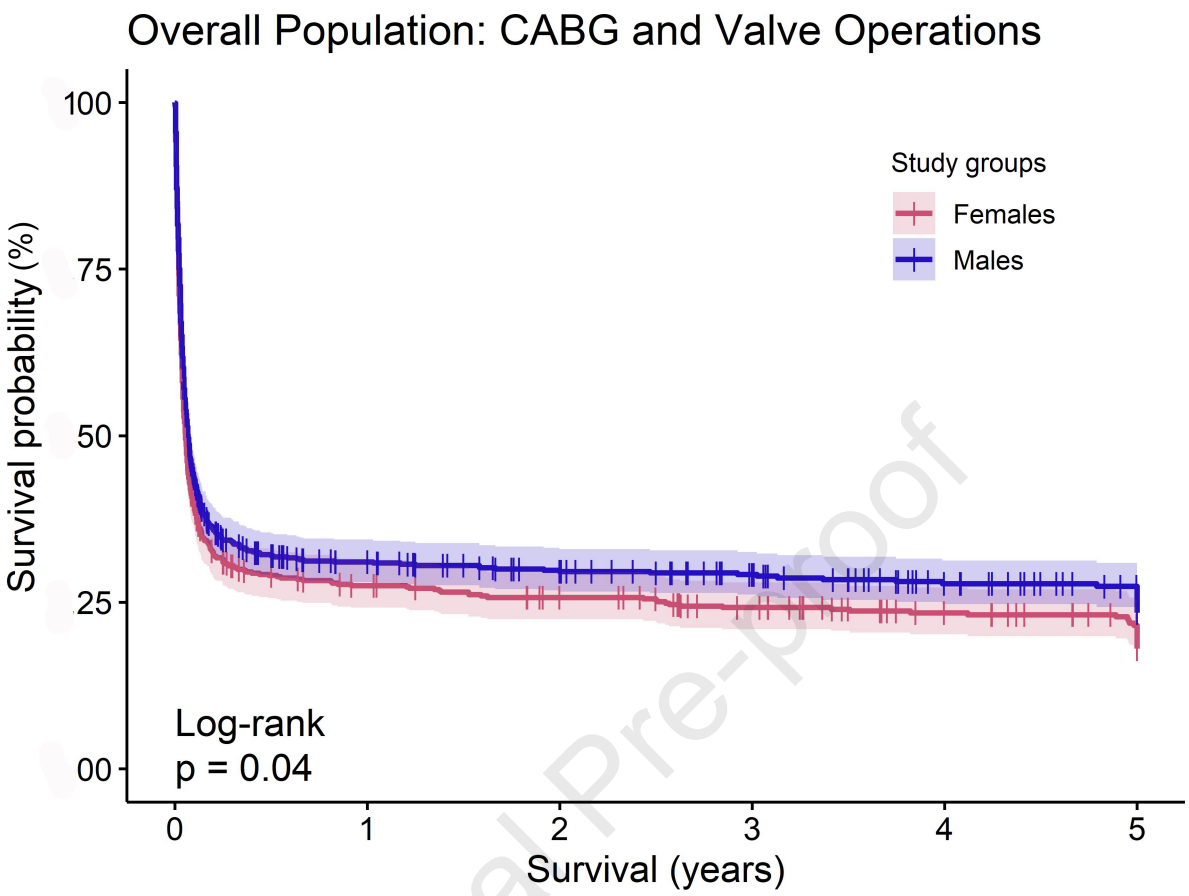


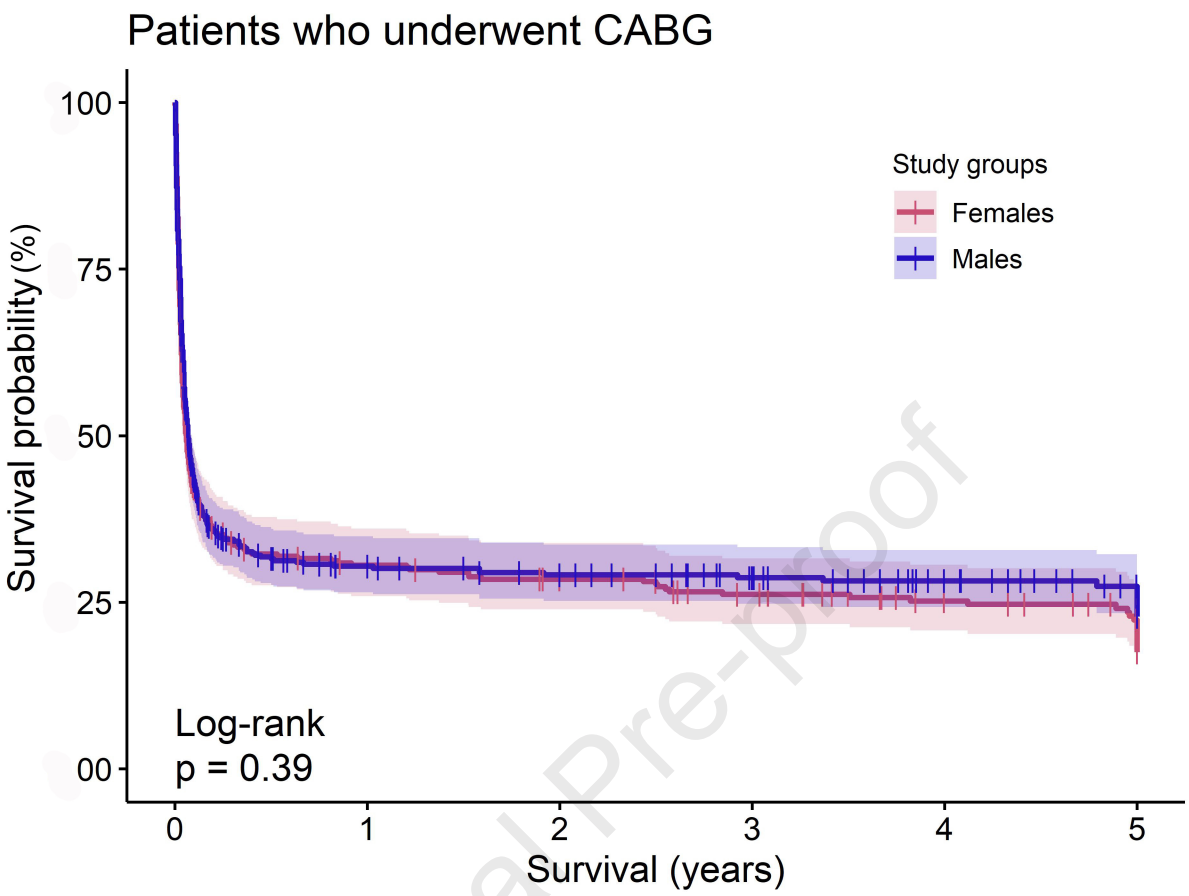






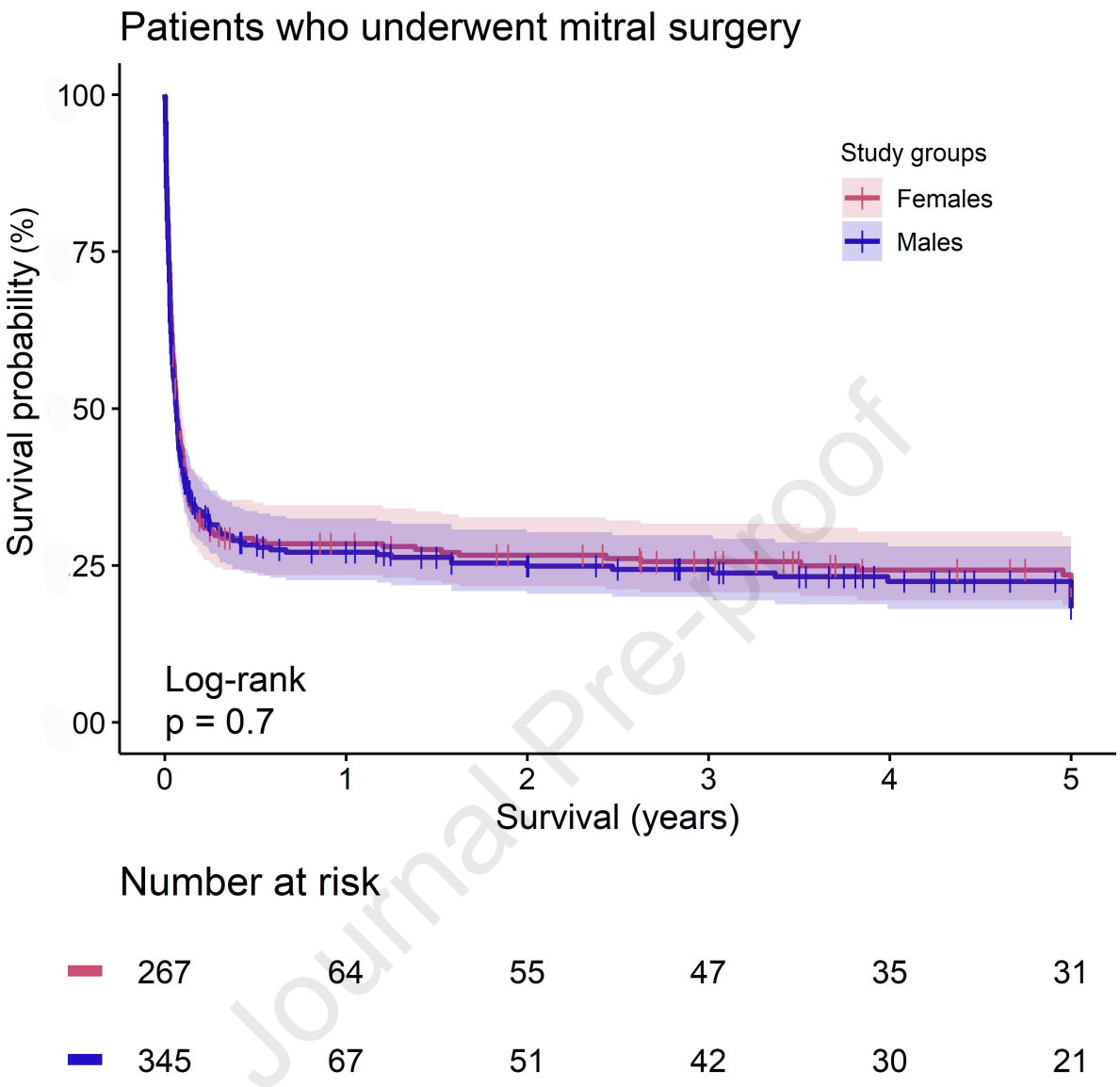
Number at risk

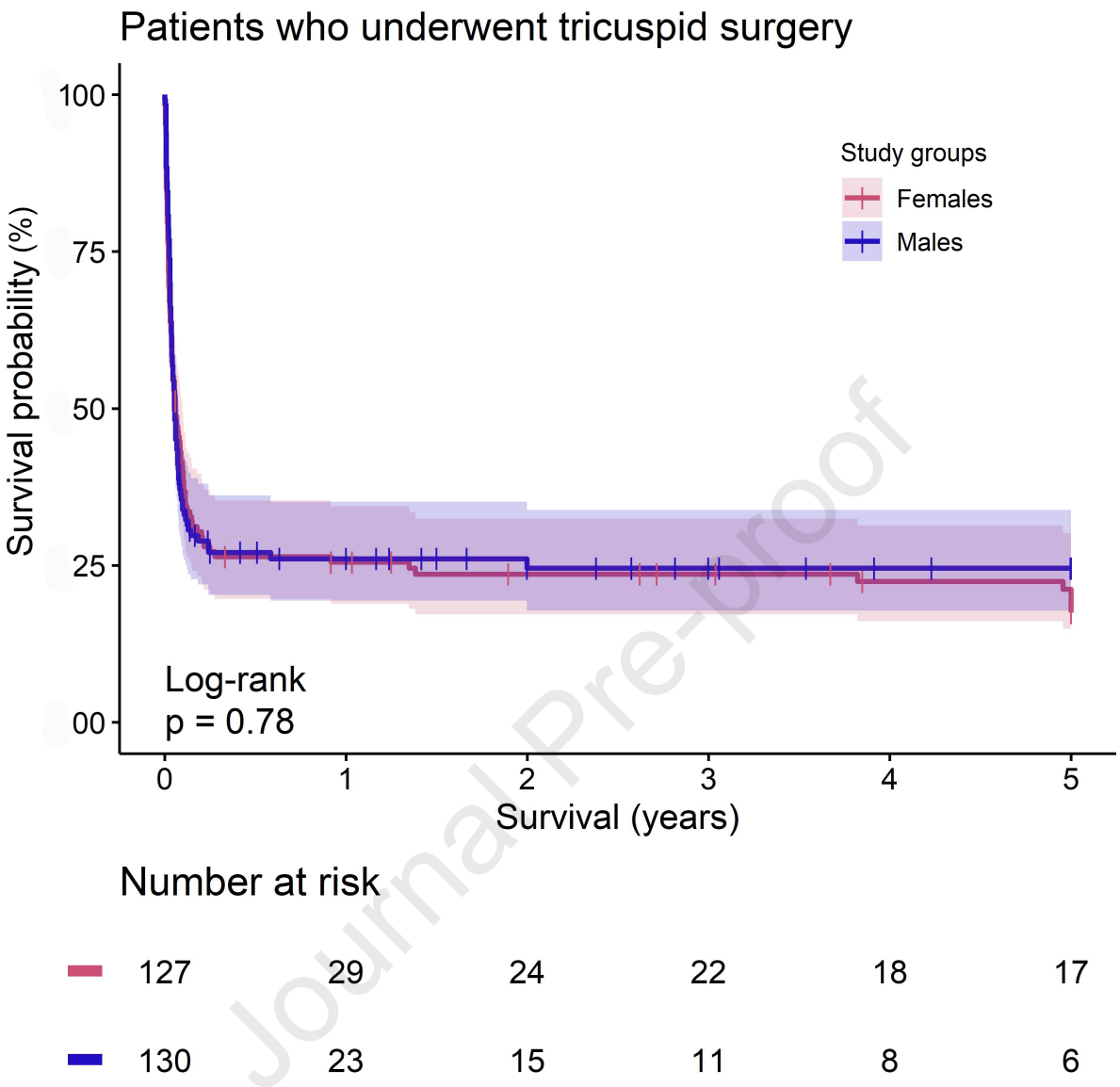
Females	622	143	123	105	83	67
Males	919	184	147	119	88	62

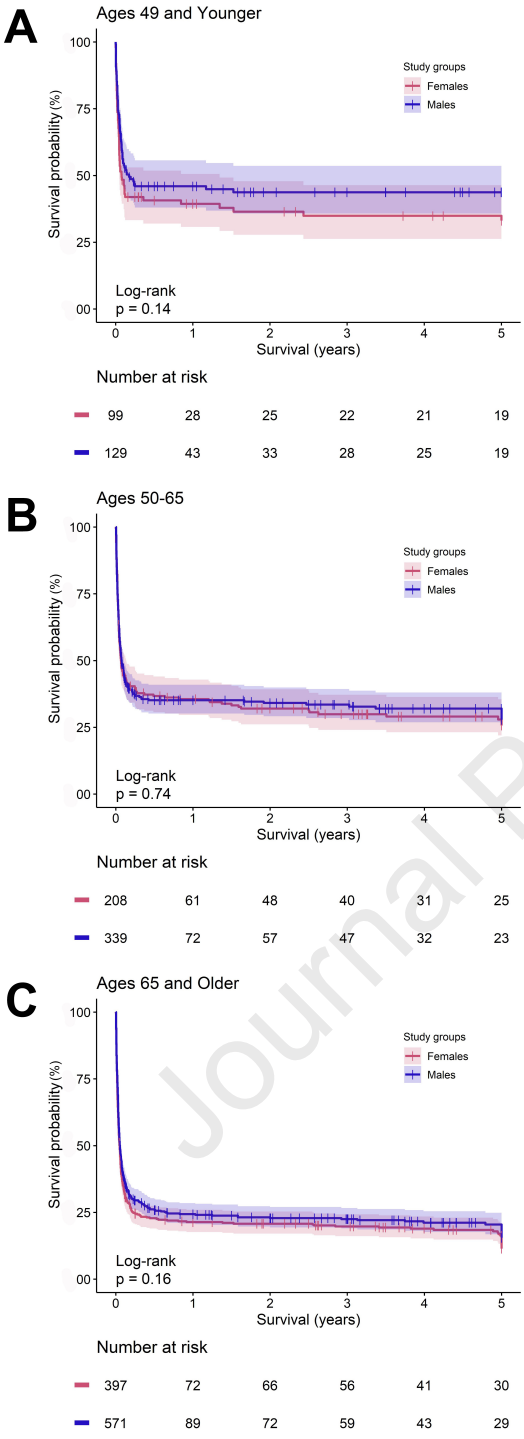


Number at risk

Females	331	88	77	65	48	37
Males	543	97	80	65	47	30







Supplemental Tables

Supplemental Table 1 - Complete and missing cases for each study variable.

	Complete cases		Missing cases	
Age (years)	1822	(99.9%)	1	(0.1%)
Ethnicity	1823	(100%)	0	(0%)
Body mass index (kg/m2)	1812	(99.4%)	11	(0.6%)
Body surface area (m2)	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 days)	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 mmHg)	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 oedema	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				
Coronary artery disease	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%)
Post-acute 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%)
Coronary artery bypass graft	1823	(100%)	0	(0%)
Aortic valve surgery	1823	(100%)	0	(0%)
Mitral valve surgery	1822	(99.9%)	1	(0.1%)
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%)
Extracorporeal life support 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%)
Intra-aortic balloon pump	1801	(98.8%)	22	(1.2%)
Left ventricular vent	1479	(81.1%)	344	(18.9%)
Extracorporeal membrane oxygenation duration (hours)	1791	(98.2%)	32	(1.8%)
Intensive care unit stay (days)	1753	(96.2%)	70	(3.8%)
Hospital stay (days)	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 haemorrhage	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%)
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

Supplemental Table 2 - Pre-operative characteristics of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		P-value
Age (years)	66.27	(57-74)	66.00	(56-72)	0.073
Race					0.029
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/m2)	26.03	(23.3-30.1)	26.60	(24.2-29.8)	0.089
Body surface area (m2)	1.79	(1.6-1.9)	1.95	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	371	(69%)	589	(70%)	0.719
Smoking	93	(19.7%)	243	(30.1%)	<0.001
Diabetes mellitus	**128**	**(22.6%)**	**241**	**(27.5%)**	**0.036**
Previous myocardial infarction	120	(21.2%)	252	(28.8%)	0.001
Myocardial infarction (last 30 days)	**53**	**(9.9%)**	**120**	**(14.3%)**	**0.016**
Previous percutaneous coronary intervention	76	(13.5%)	162	(18.5%)	0.013
Previous stroke	86	(15.2%)	108	(12.3%)	0.133
Peripheral artery disease	78	(13.8%)	132	(15.1%)	0.541
Atrial fibrillation	156	(27.5%)	208	(23.8%)	0.121
Chronic obstructive pulmonary disease	52	(9.7%)	82	(9.5%)	0.926
Pulmonary hypertension (>50 mmHg)	132	(23.6%)	152	(17.4%)	0.004
Previous cardiac surgery	123	(21.7%)	204	(23.3%)	0.520
Preoperative creatinine (umol/L)	92.0	(71-123.8)	104.00	(80.4-141)	<0.001
Dialysis	40	(7.3%)	78	(9%)	0.278
Left ventricular ejection fraction (%)	52.5	(40-60)	48.00	(34-60)	0.001
Euroscore II	6.99	(2.8-18.2)	6.95	(2.7-17.3)	0.538
Preoperative condition					
NYHA class					0.882
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%)	0.008
Preoperative intubation	62	(11%)	116	(13.2%)	0.219
Preoperative cardiac arrest	45	(8.1%)	72	(8.3%)	0.921
Preoperative septic shock	14	(2.6%)	30	(3.6%)	0.350
Preoperative vasopressors	72	(12.8%)	153	(17.5%)	0.017
Preoperative acute pulmonary oedema	37	(6.9%)	64	(7.6%)	0.672
Preoperative right ventricular failure	50	(10.2%)	67	(8.3%)	0.232
Emergency surgery	131	(23.7%)	250	(28.7%)	0.043
Urgent surgery	113	(20.3%)	159	(18.2%)	0.334
Diagnosis					
Coronary artery disease	252	(44.4%)	489	(55.8%)	<0.001
Aortic vessel disease	106	(18.7%)	178	(20.3%)	0.457
Aortic valve disease	209	(36.9%)	322	(36.8%)	1.000
Mitral valve disease	233	(41.1%)	303	(34.6%)	0.014
Tricuspid valve disease	118	(20.8%)	145	(16.6%)	0.043
Pulmonary valve disease	5	(0.9%)	9	(1%)	1.000
Post-AMI ventricular septal rupture	13	(2.3%)	31	(3.5%)	0.211
Free wall/Papillary muscle rupture	8	(1.4%)	17	(1.9%)	0.539
Active endocarditis	**40**	**(7.1%)**	**88**	**(10%)**	**0.058**

Atrial septal defect	13	(2.3%)	13	(1.5%)	0.312
Other diagnosis	57	(10.1%)	90	(10.3%)	0.929

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. AMI. Acute Myocardial Infarction. NYHA. New York Heart Association.

Supplemental Table 3 - Procedural characteristics of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		p-value
CABG	255	(45%)	458	(52.3%)	0.007
Aortic valve surgery	230	(40.6%)	327	(37.3%)	0.224
Mitral valve surgery	222	(39.2%)	287	(32.8%)	0.013
Tricuspid valve surgery	109	(19.2%)	114	(13%)	0.002
Aortic surgery	118	(20.8%)	201	(22.9%)	0.363
Pulmonary valve surgery	4	(0.7%)	7	(0.8%)	1
Atrial septal defect repair	14	(2.5%)	15	(1.7%)	0.34
Ventricular septal defect repair	18	(3.2%)	33	(3.8%)	0.662
Ventricular surgery	26	(4.6%)	40	(4.6%)	1
Rhythm surgery	25	(4.4%)	32	(3.7%)	0.491
Pulmonary embolectomy	8	(1.4%)	8	(0.9%)	0.443
Pulmonary endarterectomy	**17**	**(3%)**	**12**	**(1.4%)**	**0.035**
Off-pump surgery	15	(2.7%)	56	(6.5%)	0.001
Conversion to cardiopulmonary bypass	7	(43.8%)	15	(25.9%)	0.218
Cardiopulmonary bypass time (min)	201	(135-297)	195	(134-280)	0.431
Crossclamp time (min)	103	(68-152)	103	(63-153)	0.455

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. CABG. Coronary Artery Bypass Graft. .

Supplemental Table 4 - Details on Extracorporeal Life Support of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		P-value
ECLS implantation timing					**0.078**
Intraoperative	**358**	**(63.1%)**	**512**	**(54.8%)**	
Postoperative	**209**	**(36.9%)**	**364**	**(41.6%)**	
Cannulation approach					0.075
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%)	0.002
IABP during any time of hospitalization	125	(22.6%)	286	(32.9%)	<0.001
IABP implantation timing					**0.033**
Pre-operative	**27**	**(21.6%)**	**92**	**(32.2%)**	
Intra-operative	**98**	**(78.4%)**	**194**	**(67.8%)**	
Distal femoral perfusion in patients with peripheral cannulation	158	(69.3%)	313	(77.9%)	0.022
ECLS duration (hours)	120	(64-204.4)	120.00	(60-199)	0.935

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. ECLS. Extracorporeal life support. IABP. Intra-Aortic Balloon Pump. LV. Left Ventricular.

Supplemental Table 5 - Postoperative outcomes of patients who received treatment in the decade 2011-2020.

	Females (n=567)		Males (n=876)		P-value
Intensive care unit stay (days)	14	(6-28)	13.00	(5-23)	0.082
Hospital stay (days)	19	(7-37)	19.00	(9-36)	0.997
Postoperative bleeding	307	(55.4%)	480	(55.7%)	0.913
Requiring rethoracotomy	213	(40.7%)	302	(36.2%)	0.096
Cannulation site bleeding	66	(12%)	104	(12.1%)	1
Diffuse no-surgical related bleeding	114	(23.4%)	193	(24%)	0.84
Neurological complications					
Cerebral haemorrhage	18	(3.4%)	24	(2.9%)	0.63
Stroke	66	(11.7%)	88	(10.1%)	0.383
Arrhythmia	172	(33.7%)	262	(31.9%)	0.509
Leg ischemia	**50**	**(9.5%)**	**71**	**(8.5%)**	**0.558**
Cardiac arrest	85	(16.7%)	126	(15.3%)	0.537
Pacemaker implantation	19	(3.7%)	23	(2.8%)	0.42
Bowel ischemia	27	(5.3%)	54	(6.6%)	0.409
Right ventricular failure	116	(23.7%)	145	(17.9%)	0.012
Acute kidney injury	266	(52.6%)	417	(50.9%)	0.572
Pneumonia	102	(20.8%)	178	(22%)	0.627
Septic shock	68	(13.9%)	148	(18.3%)	0.038
Distributive syndrome	45	(9.2%)	91	(11.3%)	0.262
Acute respiratory distress syndrome	25	(4.9%)	35	(4.3%)	0.59
Embolism	29	(5.9%)	38	(4.7%)	0.365
Postoperative procedures					
Percutaneous coronary intervention	14	(2.9%)	29	(3.6%)	0.526
Cardiac surgery	127	(24.9%)	203	(24.7%)	1
Abdominal surgery	18	(3.7%)	39	(4.8%)	0.402
Vascular surgery	37	(7.6%)	89	(11%)	0.053
In-hospital mortality	364	(64.2%)	530	(60.5%)	0.165
In-hospital mortality timing					0.520
Deceased on support	222	(61.0%)	341	(64.3%)	
Deceased after weaning	133	(36.6%)	185	(34.9%)	
Main cause of death					0.388
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 (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis.

Supplemental Table 6 - Odds ratios for variables associated with post-operative right ventricular failure.

	Full cohort (n=1823)			
	Odds Ratio	95% Confidence Interval		P-value
		Lower Limit	Upper Limit	
Model 1: crude model with a random intercept for hospital and year				
Sex (Reference: Males)	1.38	1.06	1.80	0.0160
Model 2: Model 1 + Pre-operative Pulmonary Hypertension				
Sex (Reference: Males)	1.37	1.08	1.74	0.0090
Pulmonary Hypertension (> 50 mmHg)	1.63	1.19	2.24	0.0032
Model 3: Model 2 + Left Ventricular Unloading				
Sex (Reference: Males)	1.36	1.07	1.73	0.0115
Pulmonary Hypertension (> 50 mmHg)	1.62	1.18	2.22	0.0036
Left Ventricular Unloading	0.64	0.41	1.00	0.0486
Model 4 : Model 1 + demographic data and pre-operative variables				
Sex (Reference: Males)	1.32	1.00	1.75	0.0464
Age (years)	1.00	0.99	1.01	0.8609
Body Mass Index	1.01	0.98	1.04	0.4587
Dialysis	1.17	0.72	1.89	0.5295
Myocardial Infarction	0.88	0.62	1.25	0.4752
Atrial Fibrillation	0.83	0.60	1.13	0.2349
Chronic Obstructive Pulmonary Disease	0.78	0.48	1.25	0.2984
Pulmonary Hypertension (> 50 mmHg)	1.50	1.04	2.17	0.0308
Previous Cardiac Surgery	1.00	0.73	1.38	0.9784
Left Ventricular Ejection Fraction	1.01	1.00	1.02	0.0358
Cardiogenic Shock	0.86	0.58	1.28	0.4639
Urgent Surgery	1.04	0.72	1.51	0.8334
Emergency Surgery	0.90	0.59	1.38	0.6241
Cardiac Arrest	1.27	0.78	2.07	0.3238
Acute Pulmonary Edema	0.93	0.54	1.61	0.8014
Preoperative Right Ventricular Failure	4.34	2.84	6.63	<0.001
Model 5: Variables Influencing Right Ventricular Function				
Sex (Reference: Males)	1.32	1.00	1.74	0.0521
Age (years)	1.00	0.98	1.01	0.5143
Pulmonary Hypertension (> 50 mmHg)	1.40	0.97	2.03	0.0752
Previous Cardiac Surgery	1.01	0.74	1.40	0.9290
Left Ventricular Ejection Fraction	1.01	1.00	1.02	0.0168
Acute Pulmonary Edema	0.88	0.52	1.46	0.6109
Preoperative Right Ventricular Failure	4.04	2.67	6.12	0.0000
Cardiopulmonary Bypass Time (min)	1.00	1.00	1.00	0.81
Mitral Valve Surgery	1.15	0.85	1.57	0.3674
Tricuspid Valve Surgery	1.13	0.74	1.71	0.5716
Post-operative ECLS Implantation	1.15	0.85	1.57	0.3708
Post-operative Bleeding Requiring Re-thoracotomy	1.17	0.89	1.56	0.2611
Post-operative Acute Kidney Injury	1.39	1.03	1.87	0.0309
Left Ventricular Unloading	0.72	0.43	1.19	0.1991

ECLS. Extracorporeal Life Support.

Supplemental Table 7 - Odds ratios for variables associated with post-operative lower ischemia.

	Full cohort (n=1823)			
	Odds Ratio	95% Confidence Interval		P-value
		Lower Limit	Upper Limit	
Model 1: crude model with a random intercept for hospital and year				
Sex (Reference: Males)	1.42	0.95	2.12	0.0838
Model 2: Model 1 + Body Surface Area				
Sex (Reference: Males)	1.40	0.93	2.13	0.1095
Body Surface Area (m2)	0.91	0.37	2.29	0.8474
Model 3: Model 2 + Distal Perfusion				
Sex (Reference: Males)	1.41	0.93	2.13	0.1082
Body Surface Area (m2)	0.91	0.37	2.29	0.8484
Distal Perfusion	1.03	0.64	1.65	0.8985
Model 4 : Model 1 + Variables Influencing Limb Ischemia				
Sex (Reference: Males)	1.53	1.00	2.36	0.0517
Body Surface Area (m2)	0.80	0.31	2.10	0.6538
Distal Perfusion	1.12	0.69	1.81	0.6488
Age (years)	0.98	0.97	1.00	0.0485
History of Peripheral Vessel Disease	1.34	0.72	2.50	0.3499
Pre-operative Vasopressors	2.04	1.27	3.29	0.0033
Bleeding at Cannulation Site	2.09	1.24	3.52	0.0058
Extracorporeal Cardiopulmonary Resuscitation	1.41	0.75	2.64	0.2836

Supplemental Table 8 - Postoperative transfusions

	Females (n=743)		Males (n=1080)		P-value
		Missing values		Missing values	
Postoperative transfusions (number of packed red blood cells)	11 (4-21)	407 (54.8%)	10 (4-21)	494 (45.7%)	0.434
Data are reported as n(%) or median (1st and 3rd quartile).					

Sensitivity analysis after excluding patients who did not receive a coronary artery bypass or valvular surgery

Supplemental Table 9 - Pre-operative characteristics of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		P-value
Age (years)	67.00	(58-74)	67.00	(57-72.1)	0.157
Race					<0.001
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)	0.685
Bodi surface area (m^2)	1.80	(1.7-2)	1.93	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	425	(68.5%)	660	(71.5%)	0.233
Smoking	97	(19.2%)	277	(32.4%)	<0.001
Diabetes mellitus	169	(26%)	283	(29.7%)	0.109
Previous myocardial infarction	149	(22.9%)	294	(30.8%)	<0.001
Myocardial infarction (last 30 days)	76	(12.3%)	132	(14.3%)	0.249
Previous percutaneous coronary intervention	94	(14.6%)	175	(18.4%)	0.044
Previous stroke	96	(14.8%)	125	(13.1%)	0.342
Peripheral artery disease	96	(14.8%)	158	(16.6%)	0.334
Atrial fibrillation	**195**	**(30%)**	**243**	**(25.5%)**	**0.047**
Chronic obstructive pulmonary disease	73	(11.9%)	100	(10.7%)	0.463
Pulmonary hypertension (>50 mmHg)	**144**	**(22.4%)**	**181**	**(19%)**	**0.103**
Previous cardiac surgery	151	(23.2%)	228	(23.9%)	0.757
Preoperative creatinine (umol/L)	**79.0**	**(48-169)**	**92.00**	**(57-189.9)**	**0.103**
Dialysis	44	(7.1%)	88	(9.4%)	0.111
Left ventricular ejection fraction (%)	50.0	(38.5-60)	47.02	(32-60)	0.006
Euroscore II*	7.60	(2.9-20.7)	7.28	(2.8-19)	0.430
Preoperative condition					
New York Heart Association class					0.714
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%)	0.006
Preoperative cardiac arrest	69	(10.8%)	97	(10.3%)	0.755
Preoperative intubation	65	(10%)	121	(12.7%)	0.102
Preoperative septic shock	15	(2.4%)	31	(3.4%)	0.293
Preoperative vasopressors	**87**	**(13.6%)**	**162**	**(17.1%)**	**0.059**
Preoperative right ventricular failure	53	(9.9%)	69	(7.9%)	0.206
Emergency surgery	**147**	**(23.1%)**	**268**	**(28.2%)**	**0.025**
Urgent surgery	129	(20.2%)	171	(18%)	0.268
Diagnosis					
Coronary artery disease	319	(49.1%)	582	(61%)	<0.001
Aortic vessel disease	94	(14.5%)	150	(15.7%)	0.490
Aortic valve disease	280	(43.1%)	391	(41%)	0.404
Mitral valve disease	295	(45.4%)	375	(39.3%)	0.015
Tricuspid valve disease	138	(21.2%)	162	(17%)	0.032
Pulmonary valve disease	5	(0.8%)	8	(0.8%)	0.879
Post-AMI ventricular septal rupture	8	(1.2%)	18	(1.9%)	0.307

Free wall/Papillary mucle rupture	11	(1.7%)	23	(2.4%)	0.327
Active endocarditis	45	(6.9%)	99	(10.4%)	0.018
Atrial septal defect	13	(2%)	9	(0.9%)	0.074
Other diagnosis	30	(4.6%)	71	(7.4%)	0.022

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. AMI. Acute Myocardial Infarction.

Supplemental Table 10 - Intra-operative characteristics of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		p-value
Coronary artery bypass graft	341	(52.5%)	566	(59.3%)	0.006
Aortic valve surgery	305	(46.9%)	402	(42.1%)	0.058
Mitral valve surgery	285	(43.8%)	357	(37.4%)	0.010
Tricuspid valve surgery	134	(20.6%)	134	(14%)	<0.001
Aortic surgery	111	(17.1%)	173	(18.1%)	0.586
Pulmonary valve surgery	5	(0.8%)	7	(0.7%)	0.935
Atrial septal defect repair	14	(2.2%)	12	(1.3%)	0.163
Ventricular septal defect repair	12	(1.8%)	21	(2.2%)	0.623
Ventricular surgery	14	(2.2%)	25	(2.6%)	0.551
Rhythm surgery	24	(3.7%)	32	(3.4%)	0.717
Pulmonary embolectomy	3	(0.5%)	3	(0.3%)	0.691
Pulmonary endoarterectomy	4	(0.6%)	4	(0.4%)	0.722
Off-pump surgery	15	(2.4%)	58	(6.1%)	<0.001
Conversion to Cardiopulmonary bypass	6	(40%)	16	(27.1%)	0.355
Cardiopulmonary bypass time (min)	198	(135-288)	195	(132-277)	0.452
Crossclamp time (min)	102	(68-150)	102	(62-152)	0.265

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis.

Supplemental Table 11 - Details on Extracorporeal Life Support of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		P-value
ECLS implantation timing					0.049
Intraoperative	410	(63.1%)	555	(58.2%)	
Postoperative	240	(36.9%)	399	(41.8%)	
Cannulation approach					0.454
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%)	<0.001
IABP during any time of hospitalization	176	(27.7%)	363	(38.3%)	<0.001
IABP implantation timing					0.699
Pre-operative	50	(28.4%)	109	(30%)	
Intra-operative	126	(71.6%)	254	(70%)	
ECLS duration (hours)	117	(62-192)	120.00	(60-195)	0.734

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis. ECLS, Extracorporeal Life Support. IABP, Intra-Aortic Balloon Pump.

Supplemental Table 12 - Postoperative outcomes of patients who received a coronary artery bypass or valvular surgery.

	Females (n=649)		Males (n=952)		P-value
Intensive care unit stay (days)	14	(6-27)	13.00	(6-24)	0.339
Hospital stay (days)	18	(7-36)	19.00	(8-36)	0.479
Postoperative bleeding	366	(57.4%)	543	(57.6%)	0.913
Requiring re-thoracotomy	245	(41%)	350	(38.4%)	0.313
Cannulation site bleeding	89	(14%)	107	(11.4%)	0.121
Diffuse no-surgical related bleeding	143	(25.4%)	248	(28%)	0.282
Neurological complications					
Cerebral hemorrhage	21	(3.5%)	28	(3.1%)	0.684
Stroke	69	(10.7%)	94	(9.9%)	0.620
Arrhythmia	198	(34.1%)	304	(34%)	0.964
Leg ischemia	75	(12.4%)	81	(9%)	0.031
Cardiac arrest	112	(19.3%)	151	(16.9%)	0.234
Pacemaker implantation	18	(3.1%)	28	(3.1%)	0.974
Bowel ischemia	29	(5%)	53	(5.9%)	0.446
Right ventricular failure	136	(24.3%)	169	(19.1%)	0.019
Acute kidney injury	327	(56.8%)	482	(53.9%)	0.283
Pneumonia	119	(21.3%)	199	(22.5%)	0.566
Septic shock	75	(13.4%)	159	(18%)	0.021
Distributive shock syndrome	44	(7.9%)	91	(10.3%)	0.123
Acute respiratory distress syndrome	33	(5.7%)	45	(5%)	0.584
Embolism	34	(6.1%)	43	(4.9%)	0.321
Postoperative procedures					
Percutaneous coronary intervention	14	(2.6%)	28	(3.2%)	0.497
Cardiac surgery	142	(24.4%)	211	(23.6%)	0.712
Abdominal surgery	21	(3.9%)	44	(5%)	0.305
Vascular surgery	59	(10.8%)	86	(9.8%)	0.560
In-hospital mortality	425	(65.4%)	587	(61.5%)	0.116
In-hospital mortality timing					0.351
Deceased on support	256	(39.9%)	363	(38.2%)	
Deceased after weaning	160	(25.0%)	220	(23.2%)	
Main cause of death					0.249
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%)	

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). Text in bold indicates differences compared to the main analysis.

Sub-group analysis of patients who underwent coronary artery bypass surgery

Supplemental Table 13 - Pre-operative characteristics of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		P-value
Age (years)	68.00	(60-74.2)	67.00	(59-72.4)	0.050
Race					<0.001
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)	0.506
Bodi surface area (m^2)	1.83	(1.7-2)	1.94	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	252	(75.7%)	417	(75.5%)	0.965
Smoking	56	(21.6%)	179	(34.6%)	<0.001
Diabetes mellitus	110	(32.3%)	199	(35.2%)	0.372
Previous myocardial infarction	126	(37%)	241	(42.6%)	0.094
Myocardial infarction (last 30 days)	66	(19.8%)	116	(21%)	0.670
Previous percutaneous coronary intervention	73	(21.7%)	126	(22.3%)	0.823
Previous stroke	43	(12.6%)	67	(11.8%)	0.730
Peripheral artery disease	68	(19.9%)	117	(20.7%)	0.792
Atrial fibrillation	71	(20.8%)	117	(20.7%)	0.968
Chronic obstructive pulmonary disease	48	(15.2%)	64	(11.6%)	0.123
Pulmonary hypertension (>50 mmHg)	64	(19%)	89	(15.8%)	0.210
Previous cardiac surgery	61	(17.9%)	82	(14.5%)	0.173
Preoperative creatinine (umol/L)	97.3	(76.9-132)	102.00	(81.3-132.7)	0.023
Dialysis	21	(6.6%)	57	(10.3%)	0.066
Left ventricular ejection fraction (%)	45.0	(30-60)	43.00	(30-55)	0.121
Euroscore II*	8.70	(3.6-21.7)	7.81	(2.9-19)	0.102
Preoperative condition					
New York Heart Association class					0.502
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%)	0.005
Preoperative cardiac arrest	50	(14.8%)	64	(11.4%)	0.138
Preoperative intubation	30	(8.8%)	80	(14.1%)	0.018
Preoperative septic shock	7	(2.1%)	12	(2.2%)	0.957
Preoperative vasopressors	43	(12.8%)	110	(19.5%)	0.010
Preoperative right ventricular failure	23	(8.3%)	27	(5.2%)	0.087
Emergency surgery	94	(28.7%)	191	(33.9%)	0.108
Urgent surgery	63	(19%)	96	(17%)	0.447
Diagnosis					
Aortic vessel disease	52	(15.2%)	73	(12.9%)	0.320

Aortic valve disease	124	(36.4%)	178	(31.4%)	0.128
Mitral valve disease	114	(33.4%)	164	(29%)	0.159
Tricuspid valve disease	48	(14.1%)	60	(10.6%)	0.117
Pulmonary valve disease	3	(0.9%)	0	(0%)	0.025
Post-AMI ventricular septal rupture	4	(1.2%)	13	(2.3%)	0.227
Free wall/Papillary mucle rupture	4	(1.2%)	11	(1.9%)	0.378
Active endocarditis	14	(4.1%)	29	(5.1%)	0.485
Atrial septal defect	5	(1.5%)	3	(0.5%)	0.160
Other diagnosis	11	(3.2%)	33	(5.8%)	0.077

Data are reported as n (% as valid percentage excluding missing values) or median (1^{st} and 3^{rd} quartile).
AMI. Acute Myocardial Infarction.

Supplemental Table 14 - Procedural characteristics of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		p-value
Aortic valve surgery	139	(40.8%)	169	(29.9%)	<0.001
Mitral valve surgery	100	(29.3%)	145	(25.6%)	0.223
Tricuspid valve surgery	45	(13.2%)	36	(6.4%)	<0.001
Aortic surgery	65	(19.1%)	80	(14.1%)	0.050
Pulmonary valve surgery	3	(0.9%)	0	(0%)	0.053
Atrial septal defect repair	5	(1.5%)	3	(0.5%)	0.160
Ventricular septal defect repair	6	(1.8%)	12	(2.1%)	0.706
Ventricular surgery	2	(0.6%)	18	(3.2%)	0.010
Rhythm surgery	9	(2.6%)	16	(2.8%)	0.867
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%)	0.003
Conversion to Cardiopulmonary bypass	6	(40%)	14	(24.6%)	0.331
Cardiopulmonary bypass time (min)	216	(147-316)	190	(124-267)	<0.001
Crossclamp time (min)	103	(70-156)	92	(56-142)	0.002

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Supplemental Table 15 - Details on Extracorporeal Life Support of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		P-value
ECLS implantation timing					0.003
Intraoperative	230	(67.4%)	325	(57.4%)	
Postoperative	111	(32.6%)	241	(42.6%)	
Cannulation approach					0.050
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%)	<0.001
IABP during any time of hospitalization	108	(32.4%)	272	(48.1%)	<0.001
IABP implantation timing					0.464
Pre-operative	40	(37%)	90	(33.1%)	
Intra-operative	68	(63%)	182	(66.9%)	
ECLS duration (hours)	115	(64-192)	120.00	(61.4-207.5)	0.215

DData are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

Supplemental Table 16 - Postoperative outcomes of patients who underwent coronary artery bypass surgery

	Females (n=333)		Males (n=552)		P-value
Intensive care unit stay (days)	13	(6-28)	13.00	(6-23)	0.425
Hospital stay (days)	19	(7-37)	19.00	(8-34)	0.868
Postoperative bleeding	190	(56.9%)	313	(55.9%)	0.722
Requiring re-thoracotomy	130	(41.8%)	206	(38.0%)	0.275
Cannulation site bleeding	50	(15%)	63	(11.3%)	0.102
Diffuse no-surgical related bleeding	61	(20.5%)	142	(26.6%)	0.049
Neurological complications					
Cerebral hemorrhage	9	(2.8%)	16	(2.9%)	0.895
Stroke	39	(11.5%)	63	(11.2%)	0.866
Arrhythmia	111	(35.7%)	190	(35.4%)	0.928
Leg ischemia	46	(14.3%)	50	(9.2%)	0.022
Cardiac arrest	64	(20.6%)	93	(17.3%)	0.239
Pacemaker implantation	7	(2.3%)	13	(2.4%)	0.875
Bowel ischemia	17	(5.5%)	33	(6.1%)	0.686
Right ventricular failure	62	(21%)	96	(18.1%)	0.304
Acute kidney injury	176	(57.9%)	293	(54.6%)	0.35
Pneumonia	60	(20.3%)	115	(21.7%)	o.630
Septic shock	36	(12.2%)	84	(15.8%)	0.155
Distributive shock syndrome	21	(7.1%)	47	(8.9%)	0.389
Acute respiratory distress syndrome	18	(5.8%)	25	(4.7%)	0.469
Embolism	21	(7.1%)	25	(4.7%)	0.149
Postoperative procedures					
Percutaneous coronary intervention	3	(1.1%)	18	(3.4%)	0.043
Cardiac surgery	73	(23.5%)	132	(24.6%)	0.716
Abdominal surgery	9	(3.2%)	26	(4.9%)	0.236
Vascular surgery	39	(13.6%)	52	(9.8%)	0.103
In-hospital mortality	213	(62.5%)	345	(61.0%)	0.651
In-hospital mortality timing					0.956
Deceased on support	125	(37.4%)	206	(36.5%)	
Deceased after weaning	81	(24.3%)	138	(24.4%)	
Main cause of death					0.550
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%)	

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Sub-group analysis of patients who underwent mitral valve surgery

Supplemental Table 17 - Pre-operative characteristics of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		P-value
Age (years)	66.00	(58-74)	67.00	(56.5-72)	0.836
Race					0.122
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)	0.552
Bodi surface area (m^2)	1.80	(1.7-2)	1.93	(1.8-2.1)	<0.001
Comorbidities					
Hypertension	177	(65.1%)	237	(69.5%)	0.245
Smoking	48	(21%)	88	(29%)	0.034
Diabetes mellitus	72	(25.3%)	96	(26.9%)	0.641
Previous myocardial infarction	45	(15.8%)	85	(23.8%)	0.012
Myocardial infarction (last 30 days)	23	(8.5%)	35	(10.3%)	0.447
Previous percutaneous coronary intervention	42	(14.8%)	65	(18.3%)	0.224
Previous stroke	47	(16.5%)	59	(16.5%)	0.990
Peripheral artery disease	33	(11.6%)	49	(13.7%)	0.418
Atrial fibrillation	124	(43.5%)	136	(38.1%)	0.165
Chronic obstructive pulmonary disease	35	(12.9%)	37	(10.7%)	0.403
Pulmonary hypertension (>50 mmHg)	90	(32%)	104	(29.2%)	0.443
Previous cardiac surgery	80	(28.1%)	111	(31.1%)	0.405
Preoperative creatinine (umol/L)	98.15	(79.6-133.5)	109.62	(87.4-153.9)	<0.001
Dialysis	18	(6.6%)	44	(12.8%)	0.012
Left ventricular ejection fraction (%)	50.00	(37-60)	50.00	(37.5-60)	0.608
Euroscore II*	8.32	(3.7-21.9)	8.03	(3.1-22.9)	0.820
Preoperative condition					
New York Heart Association class					0.535
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%)	0.135
Preoperative cardiac arrest	21	(7.6%)	28	(8%)	0.830
Preoperative intubation	38	(13.4%)	45	(12.6%)	0.772
Preoperative septic shock	8	(3%)	17	(5%)	0.204
Preoperative vasopressors	42	(14.8%)	66	(18.5%)	0.208
Preoperative right ventricular failure	26	(10.6%)	37	(11.6%)	0.722
Emergency surgery	48	(17.4%)	79	(22.3%)	0.126
Urgent surgery	60	(21.5%)	74	(20.9%)	0.854
Diagnosis					
Coronary artery disease	110	(38.6%)	182	(51%)	0.002

Aortic vessel disease	16	(5.6%)	27	(7.6%)	0.326
Aortic valve disease	96	(33.7%)	133	(37.3%)	0.348
Tricuspid valve disease	100	(35.1%)	107	(30%)	0.168
Pulmonary valve disease	1	(0.4%)	0	(0%)	0.444
Post-AMI ventricular septal rupture	6	(2.1%)	3	(0.8%)	0.195
Free wall/Papillary mucle rupture	10	(3.5%)	22	(6.2%)	0.125
Active endocarditis	19	(6.7%)	52	(14.6%)	0.001
Atrial septal defect	8	(2.8%)	3	(0.8%)	0.069
Other diagnosis	17	(6%)	22	(6.2%)	0.917

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).
AMI. Acute Myocardial Infarction.

Supplemental Table 18 - Procedural characteristics of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		p-value
Coronary Artery Bypass Graft	100	(35.1%)	145	(40.6%)	0.152
Aortic valve surgery	101	(35.4%)	130	(36.4%)	0.798
Tricuspid valve surgery	101	(35.4%)	102	(28.6%)	0.063
Aortic surgery	19	(6.7%)	41	(11.5%)	0.037
Pulmonary valve surgery	1	(0.4%)	0	(0%)	0.444
Atrial septal defect repair	9	(3.2%)	5	(1.4%)	0.130
Ventricular septal defect repair	6	(2.1%)	4	(1.1%)	0.317
Ventricular surgery	10	(3.5%)	10	(2.8%)	0.608
Rhythm surgery	21	(7.4%)	21	(5.9%)	0.449
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)	0.224
Crossclamp time (min)	119.00	(86-160)	128.00	(86-175)	0.095

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Supplemental Table 19 - Details on Extracorporeal Life Support of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		P-value
ECLS implantation timing					0.003
Intraoperative	183	(64.2%)	223	(62.5%)	
Postoperative	102	(35.8%)	134	(37.5%)	
Cannulation approach					0.178
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%)	0.141
IABP during any time of hospitalization	75	(26.8%)	124	(35%)	0.591
IABP implantation timing					0.588
Pre-operative	22	(29.3%)	32	(25.8%)	
Intra-operative	53	(70.7%)	92	(74.2%)	
ECLS duration (hours)	119.13	(72-194.3)	120.00	(62.4-191.8)	0.448

DData are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

Supplemental Table 20 - Postoperative outcomes of patients who underwent mitral valve surgery.

	Females (n=285)		Males (n=356)		P-value
Intensive care unit stay (days)	14.50	(7-29)	12.00	(5-24)	0.117
Hospital stay (days)	21.00	(8-40)	18.00	(7-39)	0.595
Postoperative bleeding	164	(58.6%)	211	(59.4%)	0.826
Requiring re-thoracotomy	105	(39.3%)	137	(39.9%)	0.877
Cannulation site bleeding	46	(16.4%)	39	(11%)	0.047
Diffuse no-surgical related bleeding	65	(26.4%)	90	(28%)	0.685
Neurological complications					
Cerebral hemorrhage	9	(3.4%)	10	(3%)	0.783
Stroke	25	(8.8%)	34	(9.6%)	0.756
Arrhythmia	87	(33.3%)	100	(30.1%)	0.403
Leg ischemia	32	(12%)	27	(8.2%)	0.118
Cardiac arrest	45	(17.3%)	42	(12.7%)	0.112
Pacemaker implantation	8	(3.1%)	13	(3.9%)	0.578
Bowel ischemia	12	(4.6%)	26	(7.8%)	0.11
Right ventricular failure	62	(24.8%)	77	(23.8%)	0.774
Acute kidney injury	150	(57.3%)	191	(58.1%)	0.844
Pneumonia	65	(25.9%)	76	(23.5%)	0.5
Septic shock	39	(15.6%)	69	(21.4%)	0.08
Distributive shock syndrome	23	(9.2%)	42	(13%)	0.163
Acute respiratory distress syndrome	17	(6.5%)	12	(3.6%)	0.104
Embolism	15	(6%)	23	(7.1%)	0.6
Postoperative procedures					
Percutaneous coronary intervention	6	(2.5%)	5	(1.6%)	0.439
Cardiac surgery	63	(24.2%)	76	(23%)	0.718
Abdominal surgery	12	(5%)	17	(5.3%)	0.847
Vascular surgery	23	(9.5%)	25	(7.8%)	0.484
In-hospital mortality	187	(65.6%)	234	(65.5%)	0.986
In-hospital mortality timing					0.847
Deceased on support	109	(38.4%)	143	(40.2%)	
Deceased after weaning	77	(27.1%)	90	(25.3%)	
Main cause of death					0.780
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 (1st and 3rd quartile).

Sub-group analysis of patients who underwent tricuspid valve surgery

Supplemental Table 21 - Pre-operative characteristics of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		P-value
Age (years)	67.50	(59-74)	68.02	(58.9-73.8)	0.601
Race					0.365
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)	0.460
Bodi surface area (m^2)	1.83	(1.7-2)	1.90	(1.8-2)	0.009
Comorbidities					
Hypertension	83	(65.4%)	81	(63.3%)	0.730
Smoking	16	(14.7%)	31	(28.4%)	0.013
Diabetes mellitus	32	(23.9%)	31	(23.1%)	0.885
Previous myocardial infarction	14	(10.4%)	25	(18.7%)	0.057
Myocardial infarction (last 30 days)	4	(3.1%)	4	(3.1%)	1.000
Previous percutaneous coronary intervention	15	(11.3%)	26	(19.5%)	0.062
Previous stroke	16	(11.9%)	22	(16.4%)	0.293
Peripheral artery disease	10	(7.5%)	16	(11.9%)	0.216
Atrial fibrillation	74	(55.2%)	70	(52.2%)	0.624
Chronic obstructive pulmonary disease	16	(12.5%)	18	(13.8%)	0.749
Pulmonary hypertension (>50 mmHg)	48	(36.4%)	57	(42.5%)	0.303
Previous cardiac surgery	42	(31.3%)	47	(35.1%)	0.517
Preoperative creatinine (umol/L)	107.42	(85.6-141)	109.18	(85.7-152.1)	0.476
Dialysis	9	(7.1%)	15	(11.5%)	0.220
Left ventricular ejection fraction (%)	55.00	(40-60)	50.00	(40-60)	0.159
Euroscore II*	9.01	(4.4-20.7)	9.80	(3.7-21.1)	0.698
Preoperative condition					
New York Heart Association class					0.071
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%)	0.726
Preoperative cardiac arrest	6	(4.5%)	6	(4.5%)	1.000
Preoperative intubation	13	(9.7%)	8	(6%)	0.256
Preoperative septic shock	2	(1.6%)	4	(3.1%)	0.684
Preoperative vasopressors	15	(11.2%)	17	(12.8%)	0.690
Preoperative right ventricular failure	22	(19.5%)	23	(18.9%)	0.904
Emergency surgery	11	(8.5%)	23	(17.3%)	0.033

Urgent surgery	35	(26.5%)	22	(16.5%)	0.048
Diagnosis					
Coronary artery disease	46	(34.3%)	53	(39.6%)	0.376
Aortic vessel disease	12	(9%)	12	(9%)	1.000
Aortic valve disease	50	(37.3%)	53	(39.6%)	0.706
Mitral valve disease	100	(74.6%)	104	(77.6%)	0.567
Tricuspid valve disease	117	(87.3%)	120	(89.6%)	0.567
Pulmonary valve disease	2	(1.5%)	0	(0%)	0.498
Post-AMI ventricular septal rupture	2	(1.5%)	1	(0.7%)	1.000
Free wall/Papillary mucle rupture	0	(0%)	0	(0%)	n.a.
Active endocarditis	7	(5.2%)	9	(6.7%)	0.606
Atrial septal defect	5	(3.7%)	4	(3%)	1.000
Other diagnosis	6	(4.5%)	16	(11.9%)	0.026

Data are reported as n (% as valid percentage excluding missing values) or median (1^{st} and 3^{rd} quartile). AMI. Acute Myocardial Infarction.

Supplemental Table 22 - Procedural characteristics of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		p-value
Coronary Artery Bypass Graft	45	(33.6%)	36	(26.9%)	0.231
Aortic valve surgery	52	(38.8%)	47	(35.1%)	0.527
Mitral valve surgery	101	(75.4%)	102	(76.1%)	0.887
Aortic surgery	15	(11.2%)	15	(11.2%)	1.000
Pulmonary valve surgery	2	(1.5%)	0	(0%)	0.498
Atrial septal defect repair	5	(3.7%)	6	(4.5%)	0.758
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%)	0.051
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)	0.801
Crossclamp time (min)	121.00	(88-160)	118.00	(84-161)	0.669

Data are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile).

Supplemental Table 23 - Details on Extracorporeal Life Support of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		P-value
ECLS implantation timing					0,543
Intraoperative	82	(61.2%)	77	(57.5%)	
Postoperative	52	(38.8%)	57	(42.5%)	
Cannulation approach					0.235
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%)	0.387
IABP during any time of hospitalization	25	(19.7%)	36	(27.1%)	0.16
IABP implantation timing					0.727
Pre-operative	5	(20%)	5	(13.9%)	
Intra-operative	20	(80%)	31	(86.1%)	
ECLS duration (hours)	123.00	(56.2-195.8)	131.27	(72-192)	0.822

DData are reported as n (% as valid percentage excluding missing values) or median (1st and 3rd quartile). ECLS. Extracorporeal Life Support. IABP. Intra-Aortic Balloon Pump.

Supplemental Table 24 - Postoperative outcomes of patients who underwent tricuspid valve surgery.

	Females (n=127)		Males (n=128)		P-value
Intensive care unit stay (days)	14.00	(6-31)	12.00	(6-20.5)	0.188
Hospital stay (days)	21.00	(7-39)	18.00	(9-33)	0.613
Postoperative bleeding	69	(52.3%)	84	(63.2%)	0.073
Requiring re-thoracotomy	56	(44.8%)	50	(38.5%)	0.305
Cannulation site bleeding	16	(12.1%)	18	(13.5%)	0.731
Diffuse no-surgical related bleeding	26	(23%)	43	(36.4%)	0.026
Neurological complications					
Cerebral hemorrhage	1	(0.8%)	3	(2.4%)	0.37
Stroke	5	(3.7%)	6	(4.5%)	0.739
Arrhythmia	37	(31.4%)	41	(33.1%)	0.776
Leg ischemia	10	(7.9%)	8	(6.4%)	0.65
Cardiac arrest	19	(16.2%)	13	(10.5%)	0.188
Pacemaker implantation	5	(4.2%)	6	(4.8%)	0.822
Bowel ischemia	3	(2.5%)	9	(7.3%)	0.091
Right ventricular failure	32	(28.1%)	35	(28.7%)	0.916
Acute kidney injury	79	(64.2%)	69	(57%)	0.25
Pneumonia	33	(28.7%)	34	(28.3%)	0.951
Septic shock	18	(15.8%)	32	(26.9%)	0.039
Distributive shock syndrome	10	(8.8%)	14	(11.7%)	0.466
Acute respiratory distress syndrome	9	(7.6%)	3	(2.4%)	0.062
Embolism	6	(5.3%)	8	(6.6%)	0.674
Postoperative procedures					
Percutaneous coronary intervention	3	(2.7%)	1	(0.9%)	0.361
Cardiac surgery	21	(17.8%)	31	(25.2%)	0.162
Abdominal surgery	3	(2.7%)	3	(2.6%)	1
Vascular surgery	5	(4.5%)	7	(5.9%)	0.617
In-hospital mortality	95	(70.9%)	92	(68.7%)	0.690
In-hospital mortality timing					0.720
Deceased on support	55	(42%)	60	(44.8%)	
Deceased after weaning	37	(28.2%)	32	(23.9%)	
Main cause of death					0.285
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 (1st and 3rd quartile).