

Peripheral versus central extracorporeal membrane oxygenation for postcardiotomy shock: Multicenter registry, systematic review, and meta-analysis



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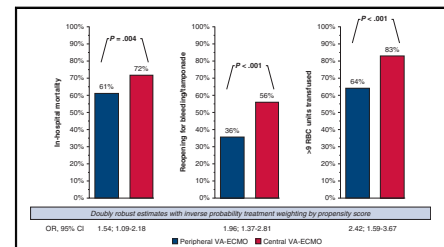
ABSTRACT

Background: We hypothesized that cannulation strategy in venoarterial extracorporeal membrane oxygenation (VA-ECMO) could play a crucial role in the perioperative survival of patients affected by postcardiotomy shock.

Methods: Between January 2010 and March 2018, 781 adult patients receiving VA-ECMO for postcardiotomy shock at 19 cardiac surgical centers were retrieved from the Postcardiotomy Venous-arterial Extracorporeal Membrane Oxygenation study registry. A parallel systematic review and meta-analysis (PubMed/MEDLINE, Embase, and Cochrane Library) through December 2018 was also accomplished.

Results: Central and peripheral VA-ECMO cannulation were performed in 245 (31.4%) and 536 (68.6%) patients, respectively. Main indications for the institution VA-ECMO were failure to wean from cardiopulmonary bypass (38%) and heart failure following cardiopulmonary bypass weaning (48%). The doubly robust analysis after inverse probability treatment weighting by propensity score demonstrated that central VA-ECMO was associated with greater hospital mortality (odds ratio 1.54; 95% confidence interval, 1.09-2.18), reoperation for bleeding/tamponade (odds ratio, 1.96; 95% confidence interval, 1.37-2.81), and transfusion of more than 9 RBC units (odds ratio, 2.42; 95% confidence interval, 1.59-3.67). The systematic review provided a total of 2491 individuals with postcardiotomy shock treated with VA-ECMO. Pooled prevalence of in-hospital/30-day mortality in overall patient population was 66.6% (95% confidence interval, 64.7-68.4%), and pooled unadjusted risk ratio analysis confirmed that patients undergoing peripheral VA-ECMO had a lower in-hospital/30-day mortality than patients undergoing central cannulation (risk ratio, 0.92; 95% confidence interval, 0.87-0.98). Adjustments for important confounders did not alter our results.

Conclusions: In patients with postcardiotomy shock treated with VA-ECMO, central cannulation was associated with greater in-hospital mortality than peripheral cannulation. (J Thorac Cardiovasc Surg 2020;160:1207-16)



Outcomes of central versus peripheral venoarterial extracorporeal membrane oxygenation.

CENTRAL MESSAGE

In postcardiotomy shock, peripheral cannulation for venoarterial extracorporeal membrane oxygenation may be associated with lower hospital mortality and complications than central cannulation.

PERSPECTIVE

The optimal cannulation strategy during venoarterial extracorporeal membrane oxygenation for patients affected by postcardiotomy shock remains controversial. Our study suggests that peripheral cannulation may provide better outcome than central cannulation. These data are corroborated by current literature.

See Commentaries on pages 1217, 1218, and 1220.

Postcardiotomy cardiogenic shock (PCS) is a fatal condition, affecting 0.5% to 1.5% of adult patients undergoing cardiac surgery.^{1,2} Venoarterial (VA) extracorporeal

membrane oxygenation (ECMO) has been proven to be a valid rescue option for patients affected by PCS, providing temporary mechanical circulatory support and favoring

Abbreviations and Acronyms

CI	= confidence interval
CPB	= cardiopulmonary bypass
ECMO	= extracorporeal membrane oxygenation
IQR	= interquartile range
OR	= odds ratio
PC-ECMO	= Postcardiotomy Venous-arterial Extracorporeal Membrane Oxygenation study
PCS	= postcardiotomy cardiogenic shock
RBC	= red blood cell
RR	= risk ratio
VA	= venoarterial

Scanning this QR code will take you to the article title page to access supplementary information.



cardiopulmonary recovery and treatment of the underlying cardiac disease.^{3,4} However, complications following VA-ECMO support are not remote, and unfavorable outcomes are often observed.^{1,2} In this context, the “central” VA-ECMO access, with direct cannulation of the ascending aorta and right atrium, and the “peripheral” access, with cannulation of the femoral artery and vein, seem to contribute significantly to the outcome of patients with PCS managed with this mechanical support.⁵⁻¹⁹ The optimal cannulation strategy remains controversial, especially for its potential impact on myocardial recovery, rate of complications, and postoperative survival.⁵⁻²⁰

We report the results of the large multicenter Postcardiotomy Venous-arterial Extracorporeal Membrane Oxygenation

study (PC-ECMO), analyzing the impact of VA-ECMO cannulation strategy in patients with PCS. A supporting systematic review and meta-analysis of studies, which considered the relationship between central/peripheral VA-ECMO cannulation and early outcomes in patients with PCS, is also presented.

METHODS**PC-ECMO Study Cohort**

The PC-ECMO registry is an observational, multicenter cohort study that enrolled patients undergoing VA-ECMO following adult cardiac surgery at 19 centers from Belgium, Czech Republic, Finland, France, Germany, Italy, Saudi Arabia, Sweden, and the United Kingdom from January 2010 to March 2018. The present study is registered in [Clinicaltrials.gov](https://clinicaltrials.gov) (Identifier: NCT03508505). Data were collected in a dedicated Access database (Microsoft, Inc, Redmond, Wash), and underwent cross-checking validation to ensure high data quality. Transcriptional discrepancies were harmonized; clinical and temporal conflicts and extreme values were corrected or removed.

The present study was approved by the regional or institutional review board of the participating centers, and it was not financially supported. The study complies with the Strengthening the Reporting of Observational Studies in Epidemiology reporting requirements for observational studies (Table E1).²¹

Study Design and Outcome Measures

Patients aged ≥ 18 years who required VA-ECMO for PCS following cardiac surgery were included. Exclusion criteria encompassed patients with preoperative VA-ECMO, or those receiving VA-ECMO after implantation of ventricular assist device or heart transplantation. Patients with an open or hybrid repair of the descending thoracic aorta were also excluded. For each patient, baseline characteristics, demographics, comorbidities, intraoperative factors, postoperative outcomes, and ECMO-related data were collected. Variables were defined according to the European System for Cardiac Operative Risk Evaluation II definition criteria and to the Extracorporeal Life Support Organisation registry.^{22,23} A cut-off of 9 units of red blood cells (RBCs) as per the universal definition of perioperative bleeding in adult cardiac surgery was adopted as marker for massive bleeding.²⁴ The primary end point was in-hospital mortality. Main secondary end-points are defined in Appendix E1 (Outcome Definitions), and included death on VA-ECMO; reoperation for bleeding/tamponade; RBC transfusion; postoperative neurologic, renal, cardiac, and gastrointestinal complications; vascular complications; sternal wound infection; and length of stay in the intensive care unit.

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Systematic Review and Meta-Analysis

The review adhered to the Meta-Analysis of Observational Studies in Epidemiology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Tables E2 and E3, respectively).^{25,26} Complete details, including electronic search strategy, objectives, criteria for study selection, eligibility, and data collection were published online and registered in the International Registry of Systematic Reviews PROSPERO (CRD420160488140).²⁷ To summarize in brief, literature searches were systematically performed with electronic databases (PubMed/MEDLINE, Embase, and Cochrane Library) without date or language restriction from inception to the end of December 2018. References of all eligible studies and review articles were also screened to identify relevant resources that were not previously recognized. Only studies comparing central versus peripheral arterial ECMO cannulation in patients affected by PCS after cardiac surgery were considered for this analysis. The primary outcome of interest was all-cause mortality in-hospital or within 30 days from the index surgical procedure. Inclusion and exclusion criteria for qualitative/quantitative analyses were summarized according to the PICOS (Population, Intervention, Comparator, Outcomes, and Study design) approach (Table E4). Year of publication, study design, country, sample size, recruitment period, number of patients in each treatment group, inclusion and exclusion criteria, measured outcomes, baseline patient demographics, cardiac status, comorbidities, and outcomes were extracted. Reasons for exclusion were also documented (Table E5). Finally, study quality was assessed using the Newcastle–Ottawa Scale and the US Preventive Services Task Force criteria.^{28,29} The Cochrane Risk of Bias tool was also used to evaluate the methodological quality of all included studies.³⁰

Statistical Analysis

Analyses we conducted according to the intention-to-treat-analysis. In the PC-ECMO study, covariates and outcomes were reported as counts and percentages, and as mean and standard deviation or median and interquartile range (IQR). Unpaired *t* test, Mann–Whitney *U* test, Fisher exact test, χ^2 test, and Kruskal–Wallis tests were used for univariable analyses, as appropriate.

A covariate balancing propensity score was developed to minimize the covariate imbalance between the central and the peripheral VA-ECMO cohorts.³¹ In our study, a total of 67 covariates including preoperative baseline, operative characteristics, indications for VA-ECMO and timing of ECMO insertion were used in the model. The full list of these covariates is listed in Table 1, and Tables E6 and E7. Using the estimated propensity scores as weights, we used an inverse probability weighting model to generate a weighted cohort.³² C-statistics were calculated to ascertain the validity of the propensity score. Finally, to adjust for confounding related to the central and peripheral VA-ECMO insertion, a doubly robust method that combines regression model with inverse probability treatment weighting by propensity score was adopted to estimate the causal effect of the exposure on the outcomes of interest.³³ Statistical analyses were performed using the cobalt package of R software (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria).^{34,35}

In the meta-analysis, outcomes of interest were reported as risk ratio (RR) with a 95% confidence interval (CI), using the Mantel–Haenszel method or as pooled prevalence of adverse outcome.³⁶ I^2 statistic was used to estimate the percentage of total variation across studies attributed to heterogeneity rather than chance.³⁷ The Cochran Q test for heterogeneity was applied.³⁰ Publication bias was evaluated using visual inspection of funnel plot asymmetry and by Egger's test.³⁸ The impact of age, sex, pulmonary disease, coronary artery bypass grafting, previous cardiac surgery, intra-aortic balloon pump (VA-ECMO) during VA-ECMO support, and delayed VA-ECMO implantation on in-hospital/30-day mortality was evaluated by meta-regression. Finally, to account for inherent patient selection bias related with the observational design of the included studies, risk-adjusted estimates for odds ratios (ORs) for in-hospital/30-day mortality

were obtained when reported, and pooled adjusted risk estimates were computed by using log transformation and a generic inverse variance weighting method. For the meta-analysis, analyses were conducted using the metafor and meta packages of R software (version 3.5.1; R Foundation for Statistical Computing).^{34,39-41} $P < .05$ was used as the level of significance for all tests.

RESULTS

PC-ECMO Study Cohort

The patient population comprised a total of 781 patients with a mean age of 63.1 ± 12.9 years (range: 18.4–86.7), and 32% were women. Baseline characteristics are detailed in Tables E4 and E6. Central and peripheral ECMO cannulation were performed in 245 (31.4%) and 536 (68.6%) patients, respectively. Among centers, the prevalence of peripheral and central cannulation varied from 25% to 94% and from 5% to 69%, respectively. Data regarding indications, timing, and cannulation, are detailed in Table E7. Main indications for VA-ECMO implantation included failure to wean from cardiopulmonary bypass (CPB, 38%), and heart failure following CPB weaning (48%). A greater proportion of patients received central cannulation in case VA-ECMO was inserted immediately after surgery ($P < .001$), and peripheral cannulation was predominantly initiated later after surgery ($P < .01$). Left ventricular venting and intra-aortic balloon pump were more frequently adopted in the central cannulation group (18% vs 3.5%, $P < .001$ and 46.5% vs 30.6%, $P < .001$, respectively). Twenty-three (9.4%) patients were switched from central to peripheral cannulation to allow definitive chest closure.

Overall, patients receiving peripheral and central VA-ECMO cannulation exhibited different demographic, clinical, and operative characteristics (Tables E6 and E7). To summarize in brief, the central group was younger (61.5 ± 14.0 vs 63.9 ± 12.3 , $P = .019$) and had longer CPB duration (median 220 minutes [IQR, 150–308 minutes] vs median 200 minutes [IQR, 123–280 minutes]; $P = .012$).

Outcome data are summarized in Table 2 and in Table E8, and full details of the overall population after exclusion of patients switched from central to peripheral cannulation are detailed in Tables E9 to E12. As shown in Tables E9 and E13 and in Figures E1 to E3, all the covariates of the weighted cohort were balanced between groups. The C statistics of the propensity score for VA-ECMO cannulation were 0.7499. Under the doubly robust estimation framework, the regression models demonstrated that central VA-ECMO was associated with a significantly greater risk of in-hospital mortality (OR, 1.54; 95% CI, 1.09–2.18; $P = .02$), reoperation for bleeding/tamponade (OR, 1.96; 95% CI, 1.37–2.81; $P < .001$), and transfusion of more than 9 RBC units (OR, 2.42; 95% CI, 1.59–3.67; $P < .001$) (Figure 1). Peripheral VA-ECMO was instead associated with longer hospital stay (linear regression estimate, -5.79 ; standard error, 2.49; $P = .02$), vascular access–

TABLE 1. Baseline characteristics patients receiving peripheral and central cannulation in the overall series*

Variables†	Overall series		P value
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	
Age, y	63.9 ± 12.3	61.5 ± 14.1	.019
Female	172 (32.1)	77 (31.4)	.92
BMI, kg/m ²	26.7 [23.9-30.0]	26.5 [23.3-29.8]	.53
BMI >30 kg/m ²	136 (25.4)	61 (24.9)	.96
Presentation and cardiac status			
Urgent/emergent procedure	288 (53.7)	127 (51.8)	.68
Preoperative IABP	41 (7.6)	21 (8.6)	.76
Previous cardiac surgery	123 (22.9)	63 (25.7)	.45
CCS angina class IV	99 (18.5)	54 (22.0)	.29
NYHA class III-IV	354 (66.0)	152 (62.0)	.31
Previous MI	181 (33.8)	96 (39.2)	.17
Previous PCI	105 (19.6)	41 (16.7)	.39
LVEF 21%-30%	89 (16.6)	47 (19.2)	.44
LVEF <21%	41 (7.6)	26 (10.6)	.22
Comorbidities			
Diabetes	131 (24.4)	69 (28.2)	.31
Hemoglobin, g/L	125.6 ± 21.5	124.6 ± 22.7	.54
eGFR, mL/min/1.73 m ²	66.5 [49.1-85.3]	65.0 [45.1-82.8]	.31
Dialysis	25 (4.7)	7 (2.9)	.32
Stroke	39 (7.3)	21 (8.6)	.63
Extracardiac arteriopathy	77 (14.4)	43 (17.6)	.29
Pulmonary disease	73 (13.6)	37 (15.1)	.66
Atrial fibrillation	143 (26.7)	49 (20.0)	.055
EuroSCORE II, score	9.05 [3.63-9.48]	9.02 [3.37-26.83]	.42

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; BMI, body mass index; IABP, intra-aortic balloon pump; CCS, Canadian Cardiovascular Society (class); NYHA, New York Heart Association (class); MI, myocardial infarction; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II. *Full baseline characteristics and operative data with standardized differences for the overall series are detailed in Table E3. †Continuous data are presented as mean ± standard deviation or median [interquartile range]; categorical variables as number (percent).

site infections (OR, 3.98 95% CI, 1.70-9.34; $P = .002$), liver failure (OR, 1.52 95% CI, 1.09-2.33; $P = .02$), and sepsis (OR, 1.56 95% CI, 1.01-2.841; $P = .05$). No differences were observed between the 2 groups with reference to peripheral vascular complications (OR, 0.80; 95% CI, 0.43-1.48, $P = .47$) or other organ dysfunctions. Outcomes did not change after the exclusion of patients switched from central to peripheral cannulation to allow for definitive chest closure (Table E12), and the year of operation did not impact on mortality (range: 58%-85%, $P = .26$; Figure E4).

Finally, the relationship between hospital volume and VA-ECMO was also analyzed, and centers with greater experience with postcardiotomy VA-ECMO (>50 cases of postcardiotomy VA-ECMO during the study period) less frequently used the central cannulation approach (24.7% vs 42.9%, $P < .0001$), although no differences in outcomes were observed (Table E14).

Sensitivity analyses and variable interactions that considered sex, age, previous cardiac surgery, preoperative left

ventricular ejection fraction, coronary artery bypass grafting, history of stroke, urgent/emergent status, and arterial lactate pre-ECMO insertion ≥ 6 mmol/L showed that central cannulation impacted on in-hospital mortality in the absence of significant interactions with these covariates (Figure 2). The timing of ECMO insertion did not interact with the cannulation strategy in influencing hospital mortality and other secondary outcomes (Table E15 and Figures E2 and E3).

Systematic Review and Meta-Analysis

A literature search yielded a total of 6286 records, and 15 retrospective studies (2 multicenter, 13 single-center) published between 2005 and 2016 were finally included in the systematic review and meta-analysis (Figure E5).⁶⁻¹⁹ Study characteristics and collected outcomes for patients with PCS undergoing VA-ECMO support are summarized in Tables E16-E18, and study quality assessment in Table E19. Including the PC-ECMO study cohort, the final population for the meta-analysis comprised

TABLE 2. Outcomes between patients receiving peripheral/central cannulation, and the doubly robust matching estimators for confounding adjustment*

Variables†	Overall series			Doubly robust adjustment‡		
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	P value	Odds ratio	95% CI	P value
Primary end point						
In-hospital mortality	327 (61.0)	176 (71.8)	.004	1.54	1.09-2.18	.02
Secondary end points						
Reoperation for bleeding/tamponade	191 (35.6)	137 (55.9)	<.001	1.96	1.37-2.81	<.001
Stroke	93 (17.4)	55 (22.4)	.11	1.11	0.72-1.71	.65
Dialysis	286 (53.4)	123 (50.2)	.29	0.84	0.60-1.19	.34
Liver failure	205 (38.2)	60 (24.5)	<.001	0.63	0.43-0.92	.02
Multiorgan failure	279 (52.1)	111 (45.3)	.09	0.85	0.60-1.21	.37
DSWI	19 (3.5)	10 (4.1)	.87	1.00	0.41-2.43	.99
Vascular access–site infection	60 (11.2)	7 (2.9)	<.001	0.25	0.11-0.59	.002
Sepsis	140 (26.1)	39 (15.9)	.002	0.64	0.42-0.99	.05
Peripheral vascular complications	49 (9.1)	20 (8.2)	.76	0.80	0.43-1.48	.47
RBC units transfused, u	15.0 [7.0-28.0]	21.0 [12.0-38.0]	<.001	5.56§	2.07§	.007§
More than 9 RBC units transfused	344 (64.2)	203 (82.9)	<.001	2.42	1.59-3.67	<.001
Chest drains 24 h-output, mL	780 [500-1450]	1389 [750-2500]	<.001	622.52§	132.76§	<.001§
ICU stay, d	12.0 [5.0-24.0]	11.0 [5.0-21.0]	.31	−1.26§	1.57§	.42§
Hospital stay, d	17.0 [5.8-35.0]	13.0 [5.0-27.0]	.04	−5.79§	2.49§	.02§
More than 10 d on VA-ECMO	128 (23.9)	57 (23.3)	.92	0.83	0.55-1.27	.40
Successful weaning from VA-ECMO	271 (50.6)	108 (44.1)	.11	0.74	0.53-1.06	.10
Postoperative VAD or heart transplant	17 (3.2)	12 (4.9)	.33	1.79	0.82-3.93	.14

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; CI, confidence interval; DSWI, deep sternal wound infection; RBC, red blood cell; ICU, intensive care unit; VAD, ventricular assist device. *Full outcomes data in the overall series and the doubly robust matching estimators for confounding adjustment are detailed in Table E5. †Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent). ‡Reference for the events: central VA-ECMO group. §Linear regression has been expressed as standard regression coefficient, standard error, and P value.

2491 patients. Pooled prevalence of in-hospital/30-day mortality in the overall patient population was 66.6% (95% CI, 64.7-68.4%). Pooled unadjusted RRs showed that patients with PCS undergoing peripheral VA-ECMO had a lower in-hospital/30-day mortality when compared with those undergoing central cannulation (RR, 0.92; 95% CI, 0.87-0.98; P = .011; Figure 3). Low heterogeneity among studies (I² = 4%) was observed, and funnel plots revealed no evidence of publication bias (P = .41; Figure E6). To evaluate the robustness of the associated results, we performed a leave-one-out sensitivity analysis by iteratively removing one study at a time and recalculating the summary RRs. A beneficial effect of the peripheral VA-ECMO in terms of reduced in-hospital/30-day mortality was observed by removing the study of Rastan and colleagues,⁶ an outlier in term of in-hospital mortality (Figure E7). Again, peripheral VA-ECMO was associated with lower in-hospital/30-day mortality than central VA-ECMO (RR, 0.88; 95% CI, 0.82-0.95; P = .0005), but no heterogeneity was observed (I² = 0%, Figure E8). Overall, 2 studies with the present one reported on adjusted effect size of VA-ECMO cannulation site on mortality (Table E18).^{6,11} Adjusted risk estimates of in-hospital/30-day mortality revealed no differences in

in-hospital/30-day mortality between the 2 cohorts of patients (RR, 1.27; 95% CI, 0.88-1.83; P = .21, Figure E9).

Pooled estimates also demonstrated that peripheral VA-ECMO cannulation was also associated with a lower rate of reoperation for bleeding/tamponade (RR, 0.63; 95% CI, 0.54-0.73; I² = 0%). No differences were observed for neurologic events (RR, 0.79; 95% CI, 0.59-1.05; I² = 0%) and lower-limb complications (RR, 1.60; 95% CI, 0.99-2.89; I² = 32.7%) between peripheral and central cannulation (Figures E9-E11). Meta-regression analysis confirmed that covariates did not represent a source of heterogeneity (Figure E12).

DISCUSSION

In the present cohort study, patients with PCS treated with peripheral VA-ECMO had better in-hospital survival than those with central cannulation. This observation was supported by a large systematic review of 15 studies that included nearly 2500 patients from 15 countries and by a sensitivity analyses that have also substantiated these observations in older patients, in those with severe coronary artery disease, reduced left ventricular function, pre-ECMO organ failure, and in patients requiring complex and urgent/emergent cardiac operations.

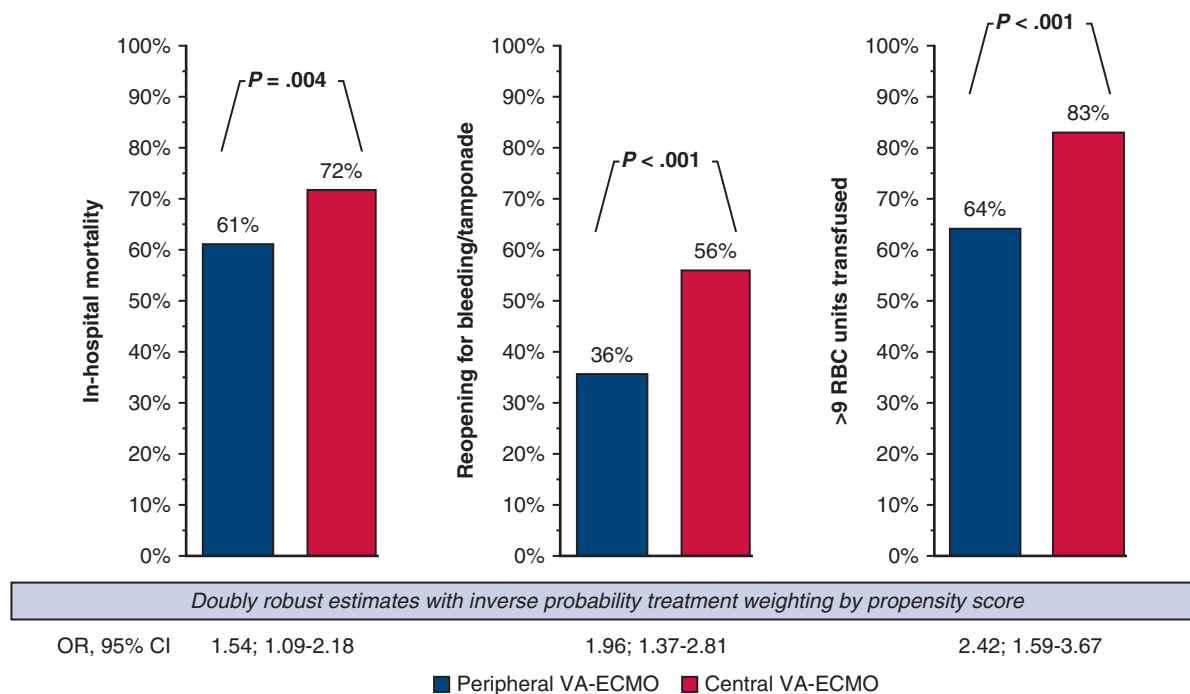


FIGURE 1. Central VA-ECMO is associated with greater in-hospital mortality, reopening for bleeding, and blood transfusion than peripheral cannulation in patients affected by postcardiotomy shock following cardiac surgery. The obtained doubly robust estimates (OR and 95% confidence intervals) with inverse probability treatment weighting by propensity score are shown for the main outcomes (group of reference: central cannulation). VA-ECMO, Venoarterial extracorporeal membrane oxygenation; RBC, red blood cells; OR, odds ratio; CI, confidence intervals.

The aforementioned results are important in light of the increasing use of ECMO for refractory PCS, providing temporary circulatory support, allowing myocardial recovery as well as bridging of patients for further diagnostic and therapeutic options.¹⁻⁴ However, despite refinements in ECMO components and improvements in intensive care unit management, mortality remains high, ranging from 43% to 85%, even in patients who were successfully weaned from VA-ECMO.⁶⁻¹⁹ The rate of complications is also not negligible, including multiorgan failure, bleeding, vascular complications, and infections.⁶⁻¹⁹ As a consequence, several efforts have been made to identify risk factors that are most likely associated with poor outcomes following ECMO initiation. In this context, the optimal cannulation strategy for VA-ECMO in terms of in-hospital mortality and complications remains unsettled.⁶⁻²⁰ Central configuration favors better cardiac unloading with an antegrade flow and multiple options for left ventricular venting, although greater risks of bleeding, cerebral emboli, systemic infections, and cardiac compression are often encountered.⁶⁻²⁰ Peripheral cannulation is faster and less invasive, allowing for sternal closure and early extubation, which are beneficial in terms of bleeding and infections, whereas suboptimal venous drainage and left ventricular unloading, Harlequin

syndrome, compromised ECMO flow, and vascular complications are the typical drawbacks.^{6,20} Ko and colleagues⁵ first investigated the impact of ECMO delivered by different cannulation routes in the outcomes of 76 patients affected by PCS, concluding that the underlying cardiac disease rather than the cannulation site influenced patient outcomes. Similarly, Rastan and colleagues⁶ reported the lack of clinical benefits exerted by the cannulation strategy in a cohort of 517 adult patients with PCS treated with VA-ECMO. Consonant data have been recently observed by Raffa and colleagues²⁰ in a meta-analysis of peripheral versus central ECMO. However, patients affected by postcardiotomy and non-postcardiotomy shock were indistinctly included, hindering the generalizability of their results in the specific setting of refractory PCS following cardiac surgery.²⁰

In our cohort study and the accompanying systematic review with meta-analysis, we included only patients who were affected by PCS following cardiac surgery and treated with VA-ECMO support. The greater rate of major bleeding, chest reopening for bleeding/tamponade, and the need for a large amount of blood product transfusions encountered in the central cannulation group seemed to play a harmful role in patient survival. Administration of large volumes of blood products is unavoidably related to

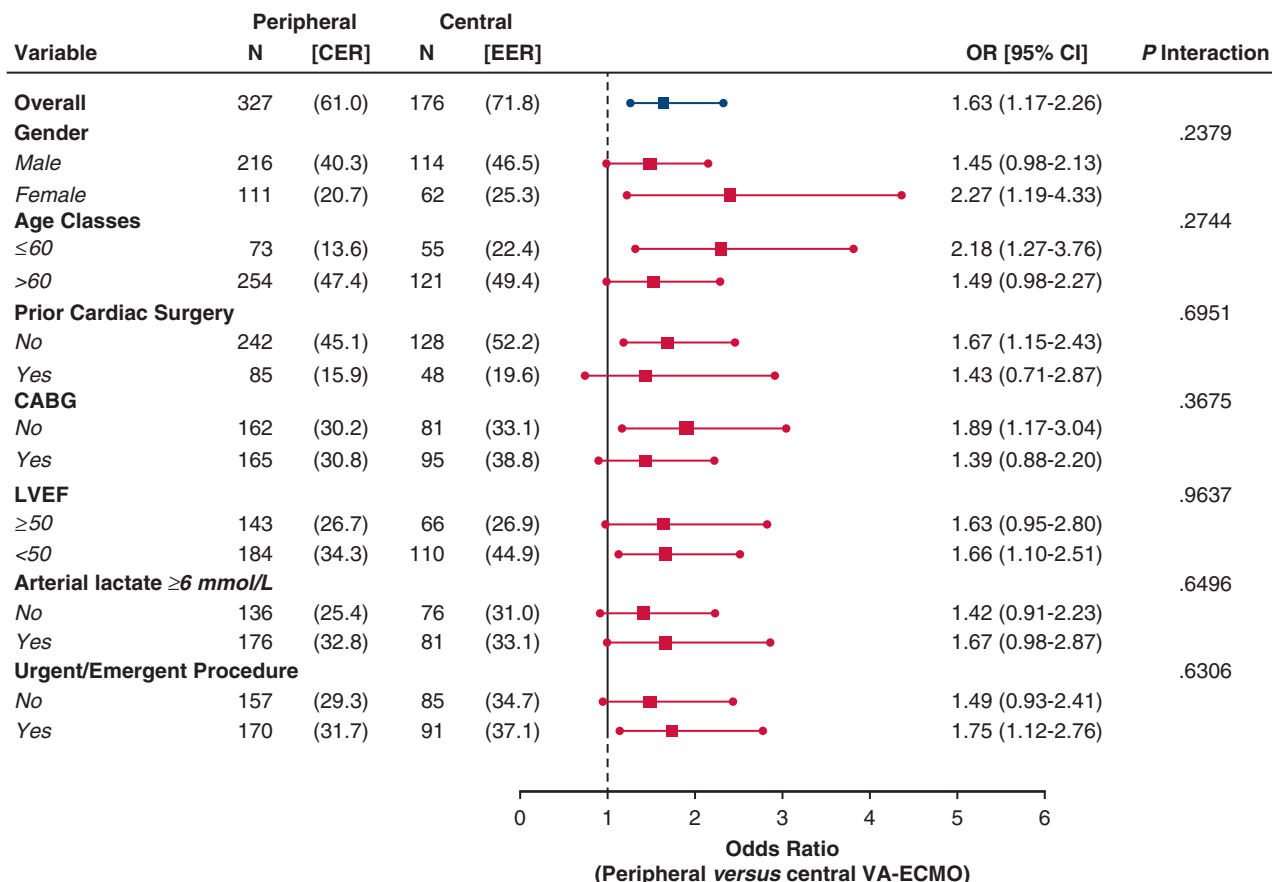


FIGURE 2. Subgroup analysis with reference to in-hospital mortality. Comparison is made between peripheral (reference group) and central VA-ECMO cannulation. CER, Control event rate; EER, experimental event rate; OR, odds ratio; CI, confidence interval; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; VA-ECMO, venoarterial extracorporeal membrane oxygenation.

the risks of transfusion-associated circulatory overload, and transfusion-related acute lung injury, both potentially fatal conditions especially in patients with an already-impaired cardiac function.^{42,43} In our series, 80% of the patients with central cannulation required transfusion of more than 9 RBC units, and an indirect negative impact on patient outcomes has been reported even after transfusion of as little as 1 or 2 RBC units.⁴⁴ Therefore, the correlation between central cannulation and greater in-hospital mortality observed in both our cohort study and in the systematic review is not surprising. As a matter of fact, bleeding, transfusion, and reopening for bleeding/tamponade have been already recognized as common complications of the central VA-ECMO strategy.^{5,9} Mikus and colleagues⁹ reported a 95% rate of reopening for bleeding/tamponade in the central group, with a median number of 39 and 18 units of RBC and fresh-frozen plasma units transfused, respectively. Decreased blood component use in this patient population has also been proven to decrease complications and improve survival, although a conservative transfusion

policy is difficult in this very critically ill patient population.⁴⁵ Therefore, the potential beneficial aspects of the central ECMO cannulation with antegrade flow, improved cardiac drainage, reduced cardiac compression (in case of open-chest), seem to be not justified by the present data, in that, these aspects have been largely overcome by the associated detrimental effects of major bleeding and blood transfusions.

Interestingly, although peripheral cannulation was associated with a greater risk of vascular-site infections, this did not translate into reduced in-hospital survival. This observation is consistent with other published studies,^{5,10,13} where the routine use of small cannula size, distal perfusion cannulas, and insertion of vascular grafts played a beneficial role. Another interesting finding from our study is the lack of differences in terms of hemodynamics and end-organ dysfunction between the 2 ECMO cannulation strategies. Saeed and colleagues⁴⁶ investigated the influence of femoro-femoral versus atrio-aortic ECMO on metabolic and hemodynamic data

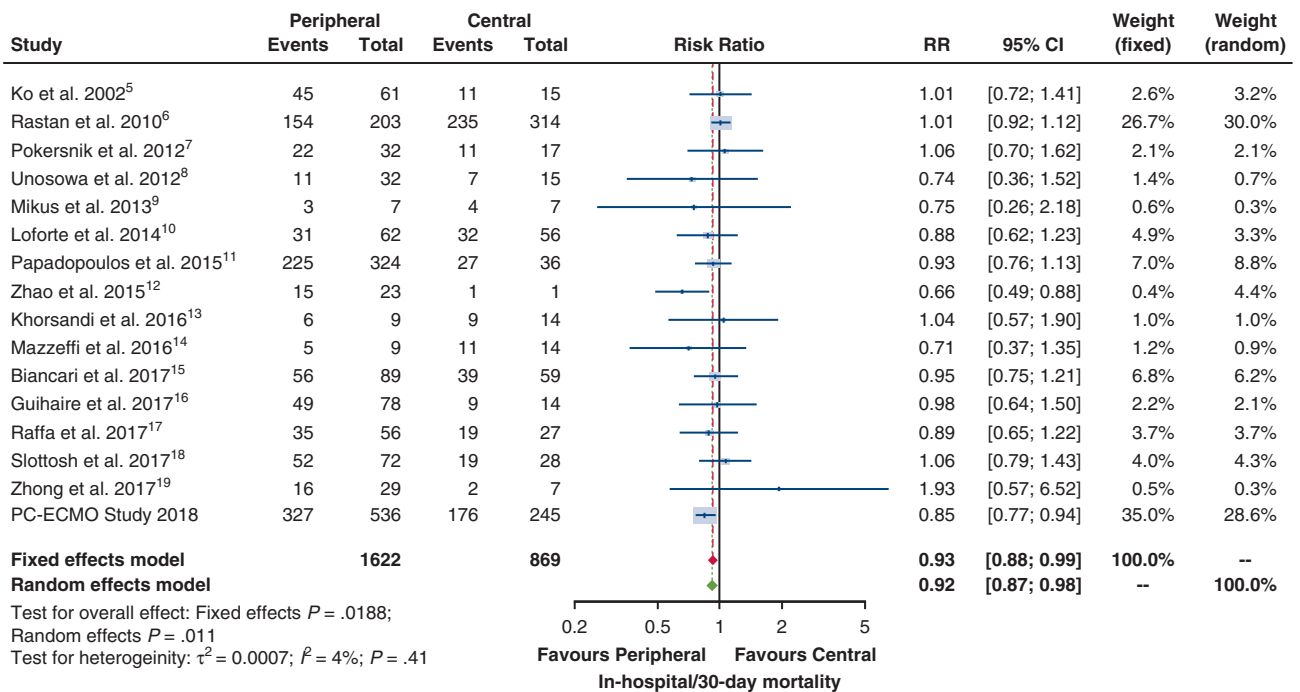


FIGURE 3. Forest plot with risk estimates for in-hospital/30-day mortality. RR, Risk ratio; CI, confidence interval.

in a series of 52 patients affected by cardiogenic shock, respiratory distress syndrome, and pulmonary embolism. No differences in terms of hemodynamics, arterial blood gas values, and end-organ function were observed between groups.⁴⁶ Kanji and colleagues⁴⁷ confirmed similar mean peak lactate levels in both the peripheral and central cannulation populations. Finally, although we did not document any significant difference in terms of neurologic, renal, and lung complications between the 2 cannulation strategies, an increased risk of liver failure was observed in the peripheral ECMO cannulation cohort, possibly due to the associated suboptimal venous drainage and compromised ECMO flow as opposed to central venous drainage.⁶ Similarly, a greater rate of sepsis, probably driven by vascular access-site infections, was also observed in the peripheral patient cohort.

Our cohort study is not exempted from several limitations, although it is the largest registry evaluating the impact of ECMO cannulation strategy in the PCS setting. First, because of the observational nature of our registry, the present analysis is subjected to all limitations inherent to a nonrandomized study. Nevertheless, the PC-ECMO registry included a large number of baseline and ECMO-related parameters as well as a consecutive series of patients treated in teaching and regional tertiary hospitals from different countries. This allowed the capture of a more-inclusive patient population in centers with different

referral pathways, preoperative selection criteria, and treatment strategies, rendering these results generalizable in different health care systems. Second, the limited number of patients in each subgroup prevented an adequate analysis of interinstitutional differences in terms of ECMO management and weaning protocols. Similarly, the impact of variables such as the axillary cannulation, the conversion from central to peripheral cannulation to allow primary chest closure on outcomes, and the left ventricular unloading impact were not addressed in the present analysis; a limitation shared with all previously published experiences.⁵⁻¹⁹ Third, we do not have data on whether the decision to leave the chest open and maintain central cannulation was dictated by poorer patient conditions or excessive edema of the intrathoracic organs. Similarly, the meta-analysis has its own limitations. Principally, we were able to include a limited number of studies focusing on the impact of ECMO cannulation strategies among those effectively screened. The heterogeneity of the populations included, and the unclear inclusion/exclusion criteria prevented us from conducting a large study analysis.⁵⁻¹⁹ Finally, owing to the emergent nature of PCS, no randomized trials of peripheral versus central ECMO cannulation were retrieved, therefore limiting our qualitative and quantitative analysis to observational studies only, often with limited sample size. The meta-analysis also had limitations. Principally, only a limited

number of studies focusing on the outcome differences between central and peripheral VA-ECMO was included. Despite the fact that risk-adjusted estimates were obtained, we cannot exclude the presence of residual confounding factors between the peripheral and central VA-ECMO cohorts.

In summary, in the context of refractory PCS following cardiac surgery, peripheral VA-ECMO cannulation was associated with reduced in-hospital mortality, lower risk of reoperation for bleeding/tamponade, perioperative bleeding, and blood transfusion requirements. Peripheral and central accesses in VA-ECMO revealed comparable results in terms of neurologic, renal, pulmonary, and other complications.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: extracorporeal membrane oxygenation, ECMO, postcardiotomy, cardiac surgery

APPENDIX E1. SUPPLEMENTAL METHODS

Literature Search Strategy

Our key words and MeSH terms pertinent to the exposure of interest were used in relevant combinations and they are shown to follow.

PubMed

Web site: <https://www.ncbi.nlm.nih.gov/pubmed>

Accessed December 31, 2018

Filters none

Fields: Title, Abstract

Search terms: “extracorporeal membrane oxygenation”
“extracorporeal life support”

“ECLS”

“ECMO”

“cardiac surgery”

“postcardiotomy”

“cardiogenic shock”

“outcomes”

“mortality”

Number of articles: 4107 (3347 + 760)

Search: 3347

(“extracorporeal membrane oxygenation” or “extracorporeal life support” or “ECMO” or “ECLS”) AND (“cardiac surgery” or “postcardiotomy” or “cardiogenic shock” or “postoperative”)

Search; 760

(“extracorporeal membrane oxygenation” or “extracorporeal life support” or “ECMO” or “ECLS”) AND (“outcomes” or “all-cause mortality”) AND (“cardiac surgery” or “postcardiotomy” or “cardiogenic shock” or “postoperative”)

EMBASE

Web site: <https://hdas.nice.org.uk/>

Accessed December, 31 2018

Filters: none

Fields: Title, Abstract

Search terms: “extracorporeal membrane oxygenation”
“extracorporeal life support”

“ECLS”

“ECMO”

“cardiac surgery”

“postcardiotomy”

“cardiogenic shock”

“outcomes”

“mortality”

Search: 1117

(((“extracorporeal membrane oxygenation” OR “extracorporeal life support” OR “ECMO” OR “ECLS”) AND (“outcomes” OR “all-cause mortality”)) AND (“cardiac surgery” OR “postcardiotomy” OR “cardiogenic shock” OR “postoperative”)).ti,ab”

Cochrane Library

Web site: <https://www.cochranelibrary.com/search>

Accessed December, 31 2018

Search option: Search Manager - Trials

Field: Title, Abstract

Search terms: “extracorporeal membrane oxygenation”
“extracorporeal life support”

“ECLS”

“ECMO”

“cardiac surgery”

“postcardiotomy”

“cardiogenic shock”

“outcomes”

“mortality”

Number of articles: 720 (557 + 123 + 40)

Search: 557

(“extracorporeal membrane oxygenation” or “extracorporeal life support” or “ECMO” or “ECLS”)

Search: 123

(“extracorporeal membrane oxygenation” or “extracorporeal life support” or “ECMO” or “ECLS”) AND (“cardiac surgery” or “postcardiotomy” or “cardiogenic shock” or “postoperative”)

Search: 40

(“extracorporeal membrane oxygenation” or “extracorporeal life support” or “ECMO” or “ECLS”) AND (“outcomes” or “all-cause mortality”) AND (“cardiac surgery” or “postcardiotomy” or “cardiogenic shock” or “postoperative”)

Citations identified through “first-generation” reference list.

Study (author/year)	Reference no.
Ko et al, 2002 ^{E1}	18
Rastan et al, 2010 ^{E2}	19
Pokersnik et al, 2012 ^{E3}	25
Unosowa et al, 2012 ^{E4}	18
Mikus et al, 2013 ^{E5}	25
Loforte et al, 2014 ^{E6}	25
Papadopoulos et al, 2015 ^{E7}	24
Zhao et al, 2015 ^{E8}	31
Khorsandi et al, 2016 ^{E9}	23
Mazzeffi et al, 2016 ^{E10}	21
Biancari et al, 2017 ^{E11}	21
Guihaire et al, 2017 ^{E12}	21
Raffa et al, 2017 ^{E13}	24
Slottosch et al, 2017 ^{E14}	24
Zhong et al, 2017 ^{E15}	21
Total	340

Outcome Definitions

Neurologic complications were defined according to the Valve Academic Research Consortium 2 (VARC-2)

criteria^{E16}: “as acute episodes of a focal or global neurological deficit with at least 1 of the following: change in the level of consciousness, hemiplegia, hemiparesis, numbness, or sensory loss affecting 1 side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke. Stroke: duration of a focal or global neurological deficit ≥ 24 hours; OR < 24 hours if available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death. TIA: duration of a focal or global neurological deficit < 24 hours, any variable neuroimaging does not demonstrate a new hemorrhage or infarct.”

Gastrointestinal complications were defined as any intestinal complication that required surgical intervention.

Peripheral vascular injury was defined as any of the following conditions: aortic rupture, type A aortic dissection, type B aortic dissection, peripheral artery dissection, vascular perforation, arterial thrombosis, and major lower limb amputation.

Renal failure was defined as any use of renal-replacement therapy after surgery. In the present study, we did not consider less severe grades of acute kidney injury because most of patients were expected to experience any significant increase in creatinine level postoperatively.

E-References

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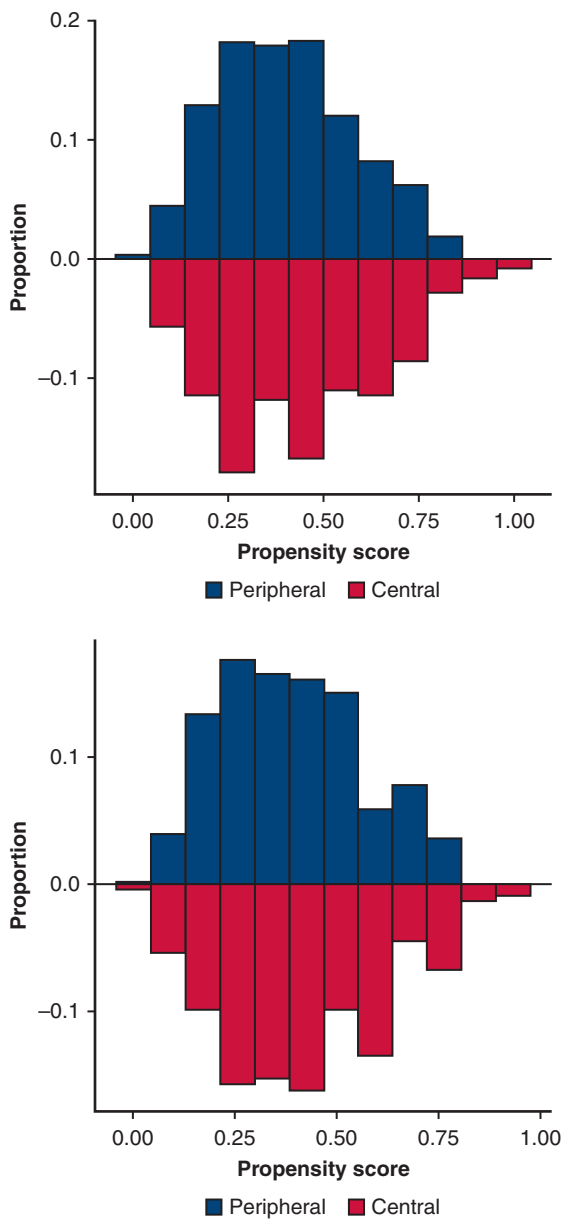


FIGURE E1. Mirror histogram of the propensity score with distribution balance for the entire cohort of patients in the *upper panel*, and mirror histogram of the propensity score with distribution balance without patient crossed from peripheral to central venoarterial extracorporeal membrane oxygenation group during the study period.

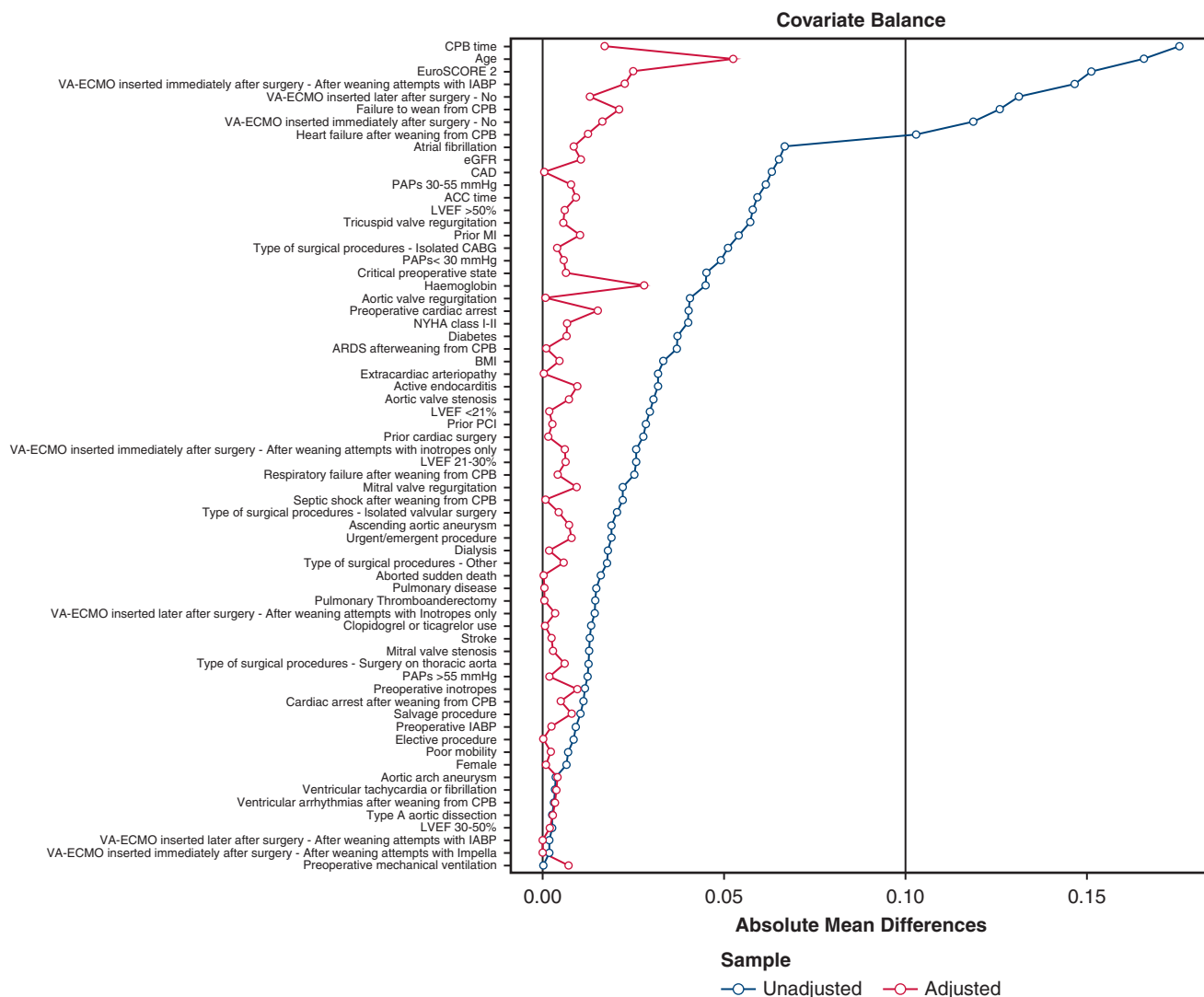


FIGURE E2. Love plot summarizing covariate balance before and after conditioning for the entire patient cohort. *CPB*, Cardiopulmonary bypass; *EuroSCORE II*, European System for Cardiac Operative Risk Evaluation II; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *eGFR*, estimated glomerular filtration rate; *CAD*, coronary artery disease; *PAP*, pulmonary artery pressure; *ACC*, aortic crossclamp; *LVEF*, left ventricular ejection fraction; *MI*, myocardial infarction; *CABG*, coronary artery bypass grafting; *NYHA*, New York Heart Association; *ARDS*, acute respiratory distress syndrome; *BMI*, body mass index; *PCI*, percutaneous coronary intervention.

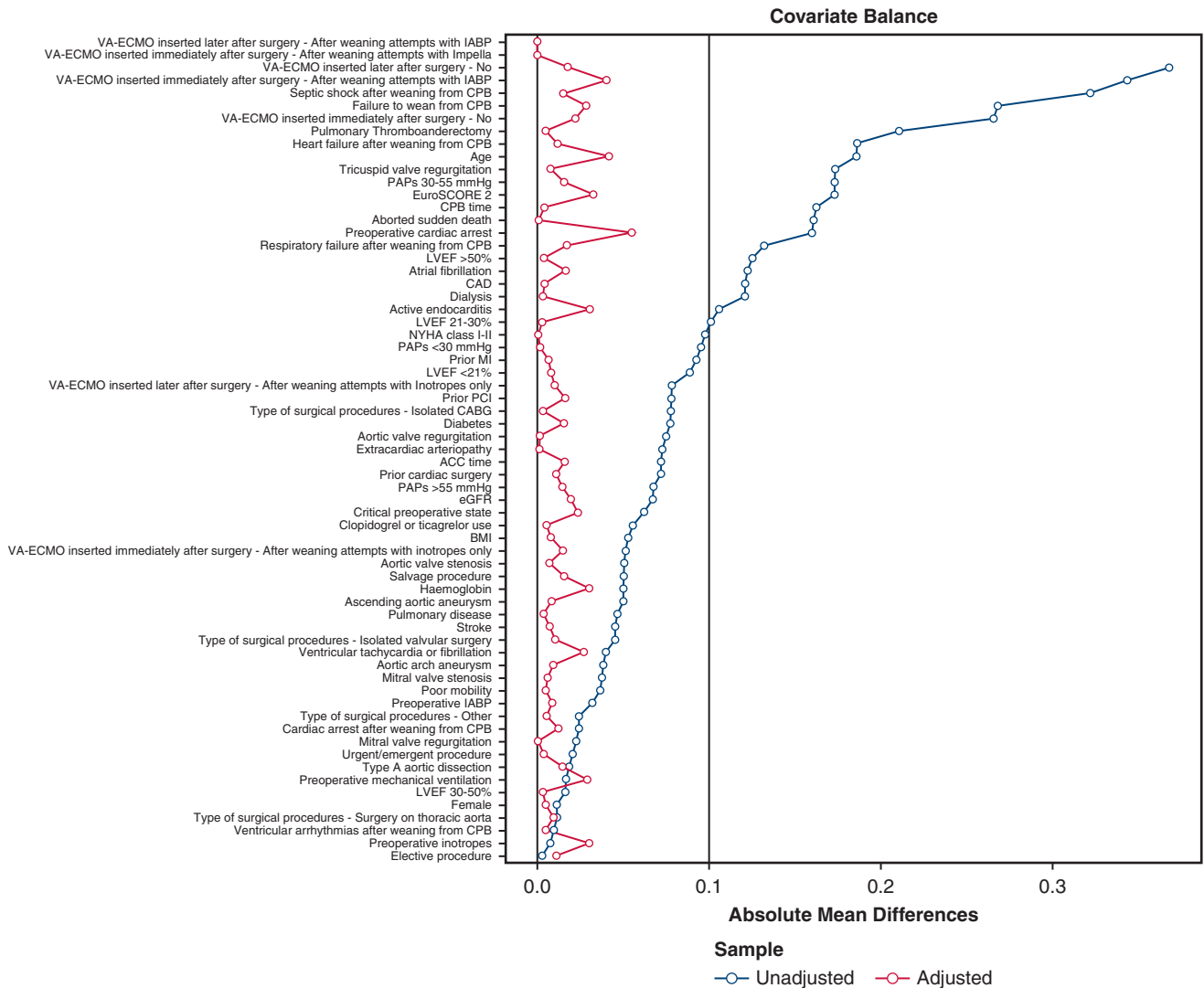


FIGURE E3. Love plot summarizing covariate balance before and after conditioning without patient crossed from peripheral to central VA-ECMO group during the study period. *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *CPB*, cardiopulmonary bypass; *PAP*, pulmonary artery pressure; *EuroSCORE II*, European System for Cardiac Operative Risk Evaluation II; *LVEF*, left ventricular ejection fraction; *CAD*, coronary artery disease; *NYHA*, New York Heart Association; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *ACC*, aortic crossclamp; *eGFR*, estimated glomerular filtration rate; *BMI*, body mass index.

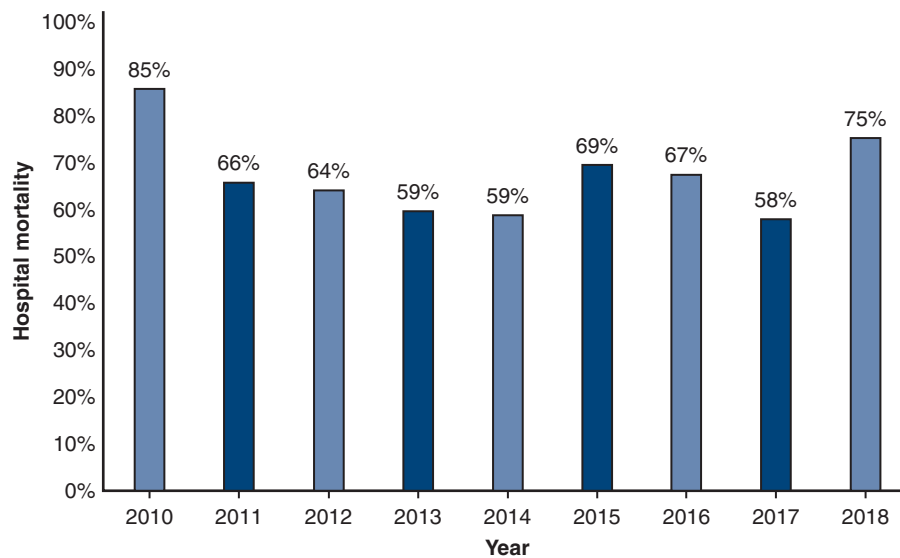


FIGURE E4. Hospital mortality during the entire study period (χ^2 test for independence: $P = .26$).

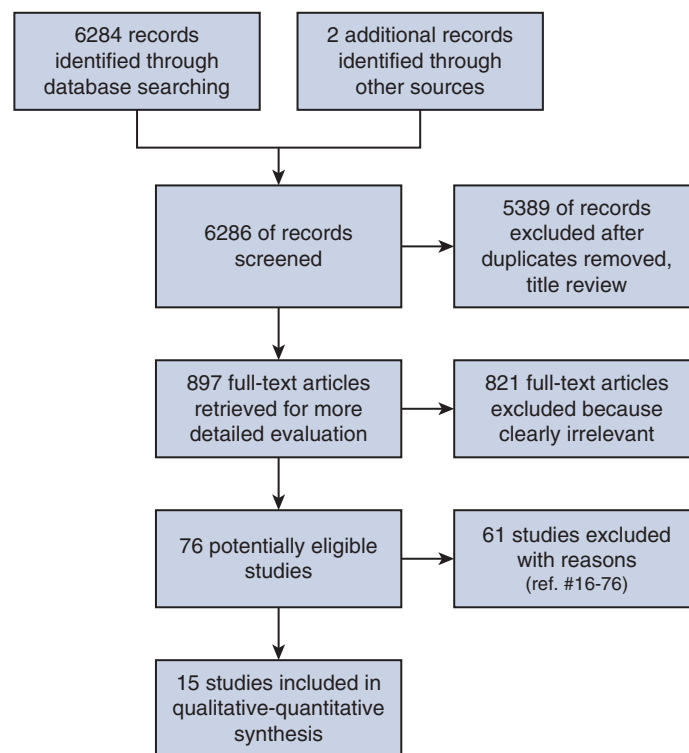


FIGURE E5. PRISMA flow chart of search strategy.^{E81} PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

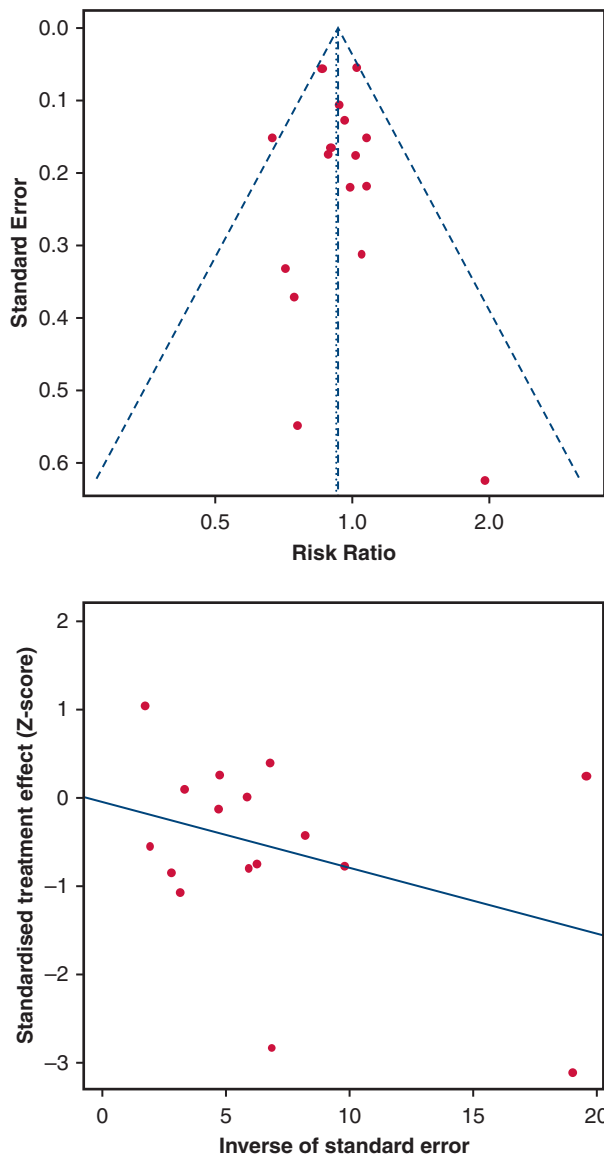


FIGURE E6. Funnel plot (*upper panel*) and radial plot (*lower panel*) for in-hospital/30-day mortality showing no heterogeneity among studies and evidence of publication bias (Egger’s test, $df = 14$, $P = .916$), respectively.

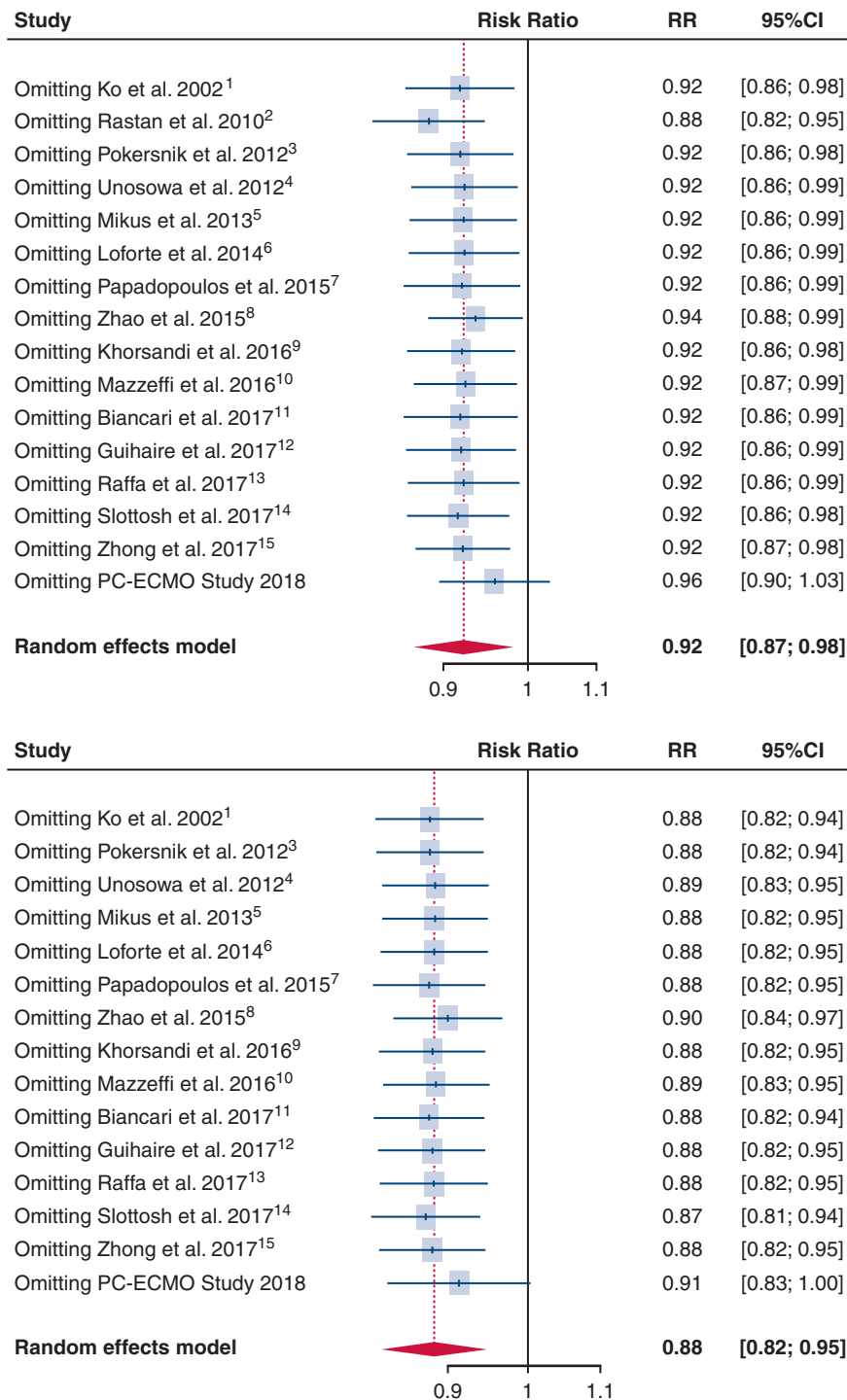


FIGURE E7. Leave-one-out meta-analysis (influence analysis) on in-hospital/30-day mortality (*upper panel*), and leave-one-out meta-analysis for sensitivity analysis on in-hospital/30-day mortality after exclusion of the study of Rastan et al.^{E2} (*lower panel*). Pooled estimates are calculated omitting one study at a time.

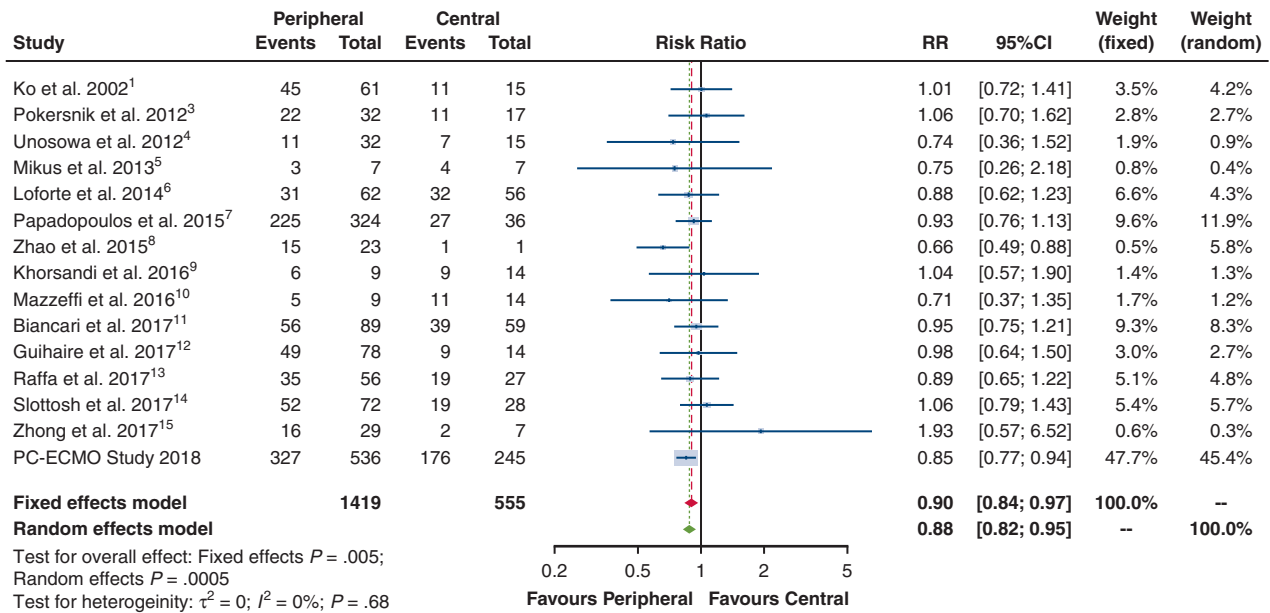


FIGURE E8. Forest plots with unadjusted risk estimates for in-hospital/30-day mortality in patients who underwent peripheral versus central extracorporeal membrane oxygenation. *RR*, Risk ratio; *CI*, confidence interval.

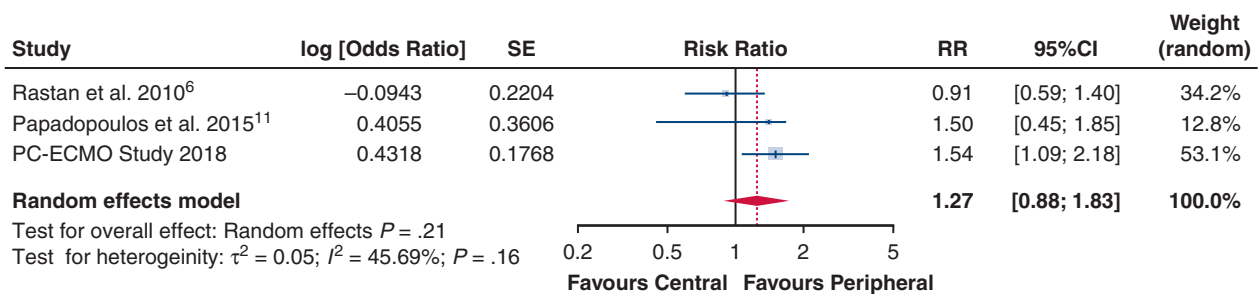


FIGURE E9. Forest plot with adjusted risk estimates for in-hospital/30-day mortality in patients who underwent peripheral versus central extracorporeal membrane oxygenation. *SE*, Standard error. *RR*, risk ratio; *CI*, confidence interval.

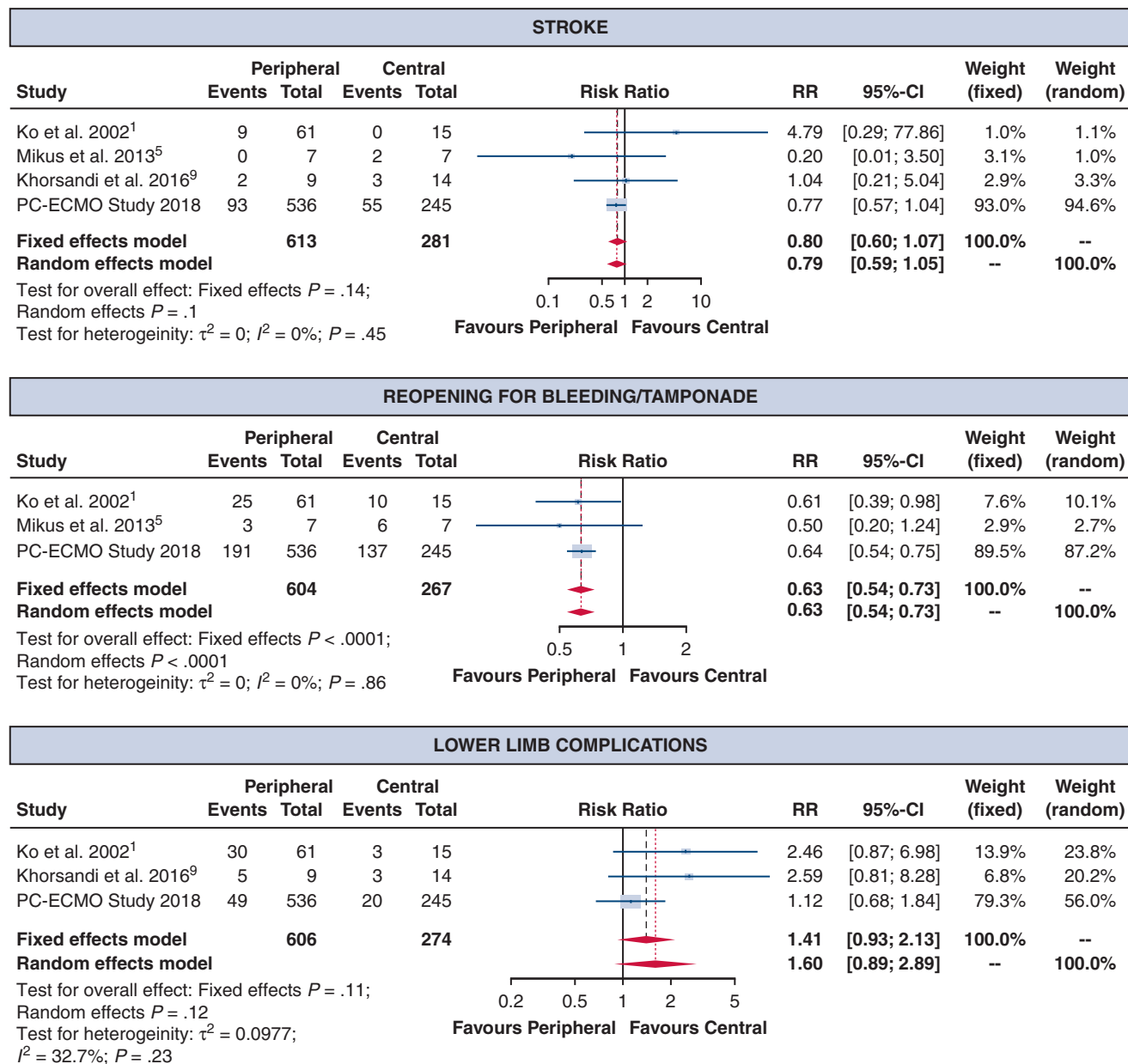


FIGURE E10. Forest plots with unadjusted risk estimates for stroke (*top*), reopening for bleeding/tamponade (*central*), and lower-limb complications (*bottom*) in patients who underwent peripheral versus central arterial extracorporeal membrane oxygenation cannulation. RR, Risk ratio; CI, confidence interval.

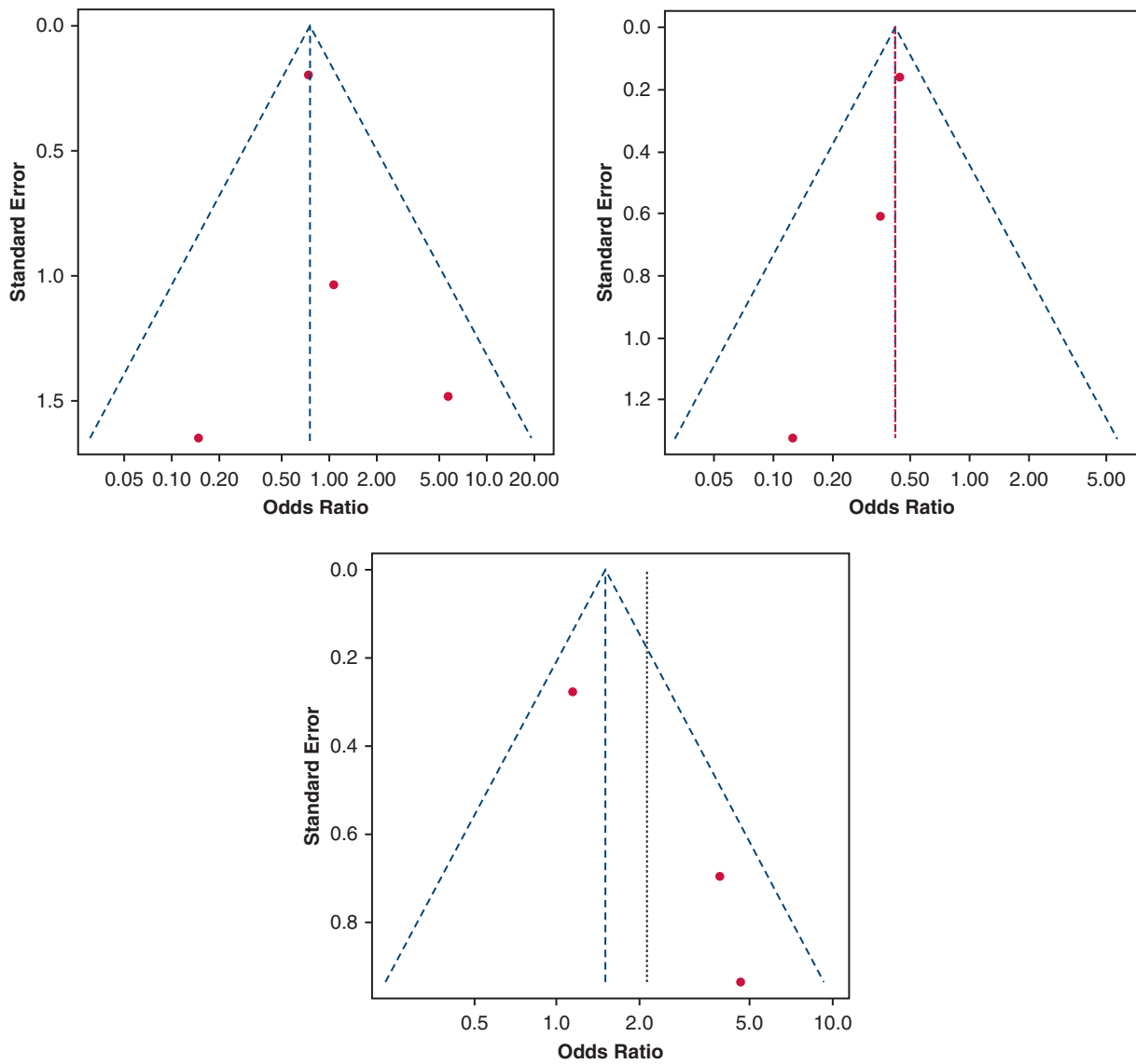


FIGURE E11. Funnel plots showing the absence of publication bias in secondary outcomes, stroke (*top left*), reopening for bleeding/tamponade (*top right*), and leg complications (*bottom*).

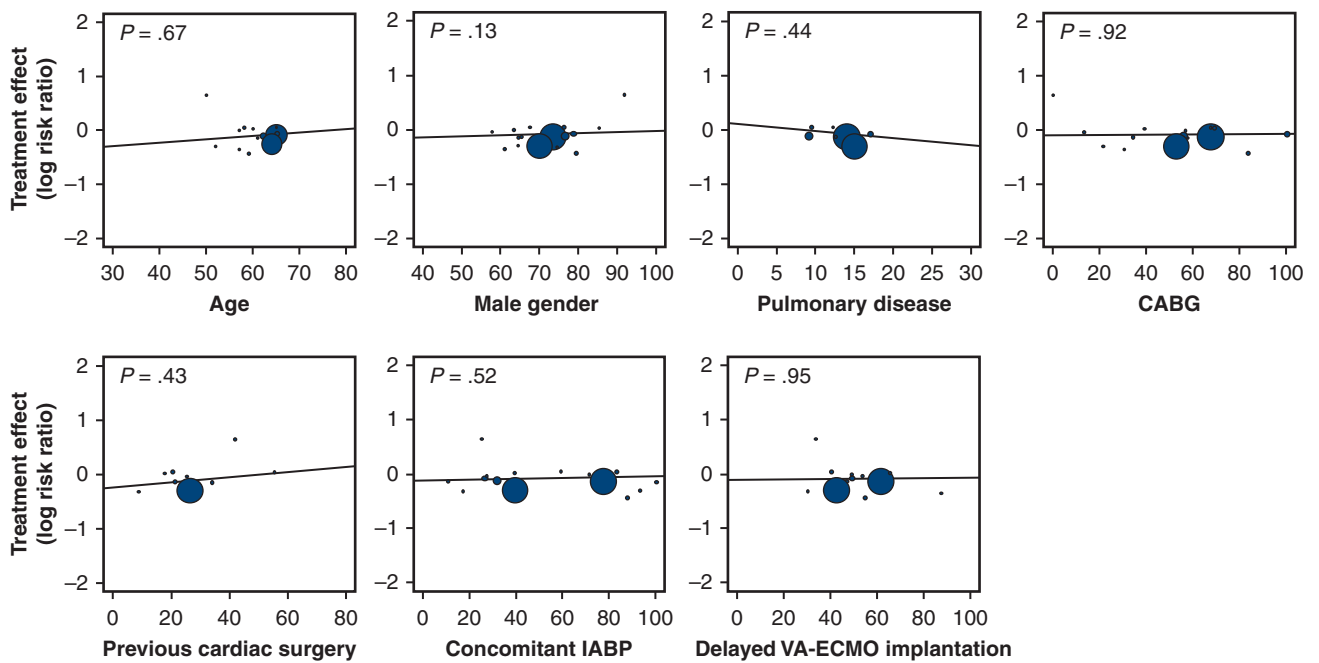


FIGURE E12. Meta-regression bubble plots showing the effect of age, sex (proportion of male patients), pulmonary disease, previous cardiac surgery, proportion of patients undergoing CABG, IABP, and delayed VA-ECMO implantation on cannulation site (peripheral versus central VA-ECMO), and in-hospital/30-day mortality. *CABG*, Coronary artery bypass grafting; *IABP*, intra-aortic balloon pump; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation.

TABLE E1. STROBE Statement for observational studies^{E82}

	Item no.	Recommendation	Reported on page no.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1 1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1,2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	2
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	2
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3
Bias	9	Describe any efforts to address potential sources of bias	3
Study size	10	Explain how the study size was arrived at	2,3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	3 3 3 – 3
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed (b) Give reasons for nonparticipation at each stage (c) Consider use of a flow diagram	3 6 –
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest	3 7
Outcome data	15*	Report numbers of outcome events or summary measures	3,4
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	3,4 – –
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	4,5, Appendix E1
Discussion			
Key results	18	Summarize key results with reference to study objectives	5,6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6,7,8
Generalizability	21	Discuss the generalizability (external validity) of the study results	8,9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9

TABLE E2. MOOSE Checklist for Meta-analyses of Observational Studies^{E83}

Item N.	Recommendation	Reported on page no.
Reporting of background should include		
1	Problem definition	2
2	Hypothesis statement	2
3	Description of study outcome(s)	2,3, Appendix E1
4	Type of exposure or intervention used	2,3, Appendix E1
5	Type of study designs used	2,3
6	Study population	2,3
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	3
8	Search strategy, including time period included in the synthesis and key words	3, Appendix E1
9	Effort to include all available studies, including contact with authors	3, Appendix E1, Tables E5 and E16
10	Databases and registries searched	3, Appendix E1
11	Search software used, name and version, including special features used (eg, explosion)	3
12	Use of hand searching (eg, reference lists of obtained articles)	Appendix E1
13	List of citations located and those excluded, including justification	Appendix E1, Tables E5 and E16
14	Method of addressing articles published in languages other than English	3
15	Method of handling abstracts and unpublished studies	Appendix E1
16	Description of any contact with authors	3
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	3
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	3
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	3
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	3
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	3, Table E19
22	Assessment of heterogeneity	3
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose–response models, or cumulative meta-analysis) in sufficient detail to be replicated	3
24	Provision of appropriate tables and graphics	3, Figures 3, E7–E12, Tables E16–E19
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figures E7–E12
26	Table giving descriptive information for each study included	Tables E16–E19
27	Results of sensitivity testing (eg, subgroup analysis)	4,5
28	Indication of statistical uncertainty of findings	4,5
Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	4,5, Figures E6 and E11
30	Justification for exclusion (eg, exclusion of non–English-language citations)	Table E5
31	Assessment of quality of included studies	Table E19
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	9
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	8,9
34	Guidelines for future research	8,9
35	Disclosure of funding source	9

MOOSE, Meta-Analysis of Observational Studies in Epidemiology.

TABLE E3. PRISMA checklist of items to include when reporting a systematic review or meta-analysis^{E81}

Section/topic	No.	Checklist item	Reported on page no.
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1,2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Table E4
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (eg, Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (eg, PICOS, length of follow-up) and report characteristics (eg, y considered, language, publication status) used as criteria for eligibility, giving rationale.	2,3, Table E4
Information sources	7	Describe all information sources (eg, databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3, Appendix E1
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix E1
Study selection	9	State the process for selecting studies (ie, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4,5, Appendix E1
Data collection process	10	Describe method of data extraction from reports (eg, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3,4,5
Data items	11	List and define all variables for which data were sought (eg, PICOS, funding sources) and any assumptions and simplifications made.	Appendix E1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	3
Summary measures	13	State the principal summary measures (eg, risk ratio, difference in means).	3
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (eg, I^2) for each meta-analysis.	3
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (eg, publication bias, selective reporting within studies).	3
Additional analyses	16	Describe methods of additional analyses (eg, sensitivity or subgroup analyses, meta-regression), if done, indicating which were prespecified.	3

(Continued)

TABLE E3. Continued

Section/topic	No.	Checklist item	Reported on page no.
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4
Study characteristics	18	For each study, present characteristics for which data were extracted and provide the citations.	Tables E16–E18
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table E19
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	4,5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 3, E7–E12, Tables E16–E18
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15).	4,5
Additional analysis	23	Give results of additional analyses, if done (eg, sensitivity or subgroup analyses, meta-regression [see item 16]).	4,5
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (eg, health care providers, users, and policy makers).	9
Limitations	25	Discuss limitations at study and outcome level (eg, risk of bias), and at review-level (eg, incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8,9
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (eg, supply of data); role of funders for the systematic review.	9

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

TABLE E4. PICOS criteria for inclusion and exclusion of studies into meta-analysis

Parameter	Inclusion criteria	Exclusion criteria
Patients	Adult patients (≥ 18 y)	–
Intervention	VA-ECMO for postcardiotomy syndrome	VA-ECMO before index cardiac surgery VA-ECMO after HTx/VAD VV-ECMO
Comparator	VA-ECMO cannulation site	No comparison between peripheral versus central VA-ECMO
Outcomes	Primary: in-hospital/30-d mortality Secondary (postoperative): re-exploration for bleeding/ tamponade; CVA; RRT/dialysis; GI complications; limb ischemia; sepsis; successful ECMO weaning	–
Study design	Clinical randomized trials Controlled before-and-after studies Prospective and retrospective cohort studies Cross-sectional studies Case–control studies	Repeat publications of the same analysis or dataset Conference abstracts Editorials and opinion pieces Books or gray literature

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; HTx, heart transplant; VAD, ventricular assist device; VV-ECMO, venovenous extracorporeal membrane oxygenation; CVA, cerebrovascular accident; RRT, renal-replacement therapy; GI, gastrointestinal.

TABLE E5. List of studies excluded with reasons from the final systematic review and meta-analysis

Study (author, y)	Design	Country	Study period	Number of patients	Reason for exclusion			
					Etiology for ECMO	No data on cannulation	Review/editorial	Other
Acheampong et al, 2016 ^{E17}	Retr. Monoc.	US	2001-2013	24		X		
Ariyaratnam et al, 2014 ^{E18}	Retr. Monoc.	UK	–	14		X	X	
Aso et al, 2016 ^{E19}	Retr. Monoc.	Japan	2010-2013	1650	Cardiogenic shock	X		
Bakhtiary et al, 2007 ^{E20}	Retr. Monoc.	Germany	2003-2006	20	Cardiogenic shock			
Bartko et al, 2017 ^{E21}	Retr. Monoc.	Austria	2003-2014	240		X		
Bata et al, 2018 ^{E22}	Retr. Monoc.	France	2005-2014	46		X		
Becher et al, 2018 ^{E23}	Retr. Multic.	Germany	2007-2015	8351	Mixed (PCS = 0%)	X		No PCS data
Beiras-Fernandez et al, 2011 ^{E24}	Retr. Monoc.	Germany	1996-2006	108		X		Pediatric Pts
Charlesworth et al, 2017 ^{E25}	(Review)	UK	–	–			X	
Chen et al, 2018 ^{E26}	Retr. Monoc.	China	2006-2017	60		X		
Chen et al, 2018 ^{E27}	(Editorial)	US	–	–			X	
Distelmaier et al, 2013 ^{E28}	Retr. Monoc.	Austria	2002-2009	191		X		
Distelmaier et al, 2018 ^{E29}	Retr. Monoc.	Austria	2003-2014	354		X		
Doll et al, 2003 ^{E30}	Retr. Monoc.	Germany	1997-2000	95		X		
Doll et al, 2004 ^{E31}	Retr. Monoc.	Germany	1997-2002	219		X		
Du et al, 2018 ^{E32}	Prosp. Monoc.	China	–	17		X		
Ellouze et al, 2018 ^{E33}	Retr. Monoc.	France	2014-2016	57	Mixed (PCS = 33%)	X		
Elsharkawy et al, 2010 ^{E34}	Prosp. Monoc.	US	1995-2005	233		X		
Formica et al, 2008 ^{E35}	Retr. Monoc.	Italy	2000-2007	25	Mixed (PCS = 50%)	X		
Fukuhara et al, 2016 ^{E36}	(Review)	US	–	–			X	
Fux et al, 2018 ^{E37}	Retr. Monoc.	Sweden	2006-2015	105				90d-mortality
Golding et al, 1992 ^{E38}	Retr. Monoc.	US	1979-1991	79		X		VAD
Hsu et al, 2010 ^{E39}	Retr. Monoc.	Taiwan	2002-2006	51		X		
Kanji et al, 2010 ^{E40}	Retr. Monoc.	Canada	2002-2006	50	Mixed (PCS = 74%)			
Khorsandi et al, 2016 ^{E41}	Retr. Monoc.	UK	1995-2015	16				Duplicatio
Klotz et al, 2007 ^{E42}	Retr. Monoc.	Germany	1995-2006	183		X		VAD

(Continued)

TABLE E5. Continued

Study (author, y)	Design	Country	Study period	Number of patients	Reason for exclusion		
					Etiology for ECMO	No data on cannulation	Review/ editorial
Lamarche et al, 2010 ^{E43}	Retr. Monoc.	Canada	2000-2008	20	Mixed (PCS = 75%)	X	
Liden et al, 2009 ^{E44}	Retr. Monoc.	Sweden	2000-2007	52	Mixed (PCS = 63%)	X	
Li et al, 2015 ^{E45}	Retr. Monoc.	China	2011-2012	123		X	
Lin et al, 2017 ^{E46}	Retr. Monoc.	Taiwan	2008-2015	162		X	
Lorusso et al, 2016 ^{E47}	Prosp. Multic.	ELSO Registry	1992-2013	4522	Mixed (PCS = 19%)	X	
Lorusso et al, 2017 ^{E48}	Prosp. Multic.	ELSO Registry	1992-2015	5408	Mixed (PCS = 1.4%)	X	
Magovern et al, 1994 ^{E49}	Retr. Monoc.	US	1991-1993	21		X	
Maybauer et al, 2017 ^{E50}	Retr. Monoc.	UK	2011-2016	4			Case series/VAD
Mazzeffi et al, 2016 ^{E51}	Retr. Monoc.	US	2010-2013	132	Mixed (PCS = 29%)	X	
Mohite et al, 2018 ^{E52}	Retr. Monoc.	UK	2005-2014	56		X	VAD
Muehrcke et al, 1996 ^{E53}	Retr. Monoc.	US	1992-1994	23		X	No data on mortality
Musial et al, 2017 ^{E54}	Retr. Monoc.	Poland	2009-2016	27		X	
Norkiene et al, 2018 ^{E55}	Retr. Monoc.	Lithuania	2009-2014	15		X	
Oshima et al, 2007 ^{E56}	Retr. Monoc.	Japan	1991-2006	13		X	
Park et al, 2014 ^{E57}	Retr. Monoc.	Korea	2005-2011	93		X	
Ranney et al, 2017 ^{E58}	Retr. Monoc.	US	2009-2015	131	Mixed (PCS = 67%)	X	
Rousse et al, 2015 ^{E59}	Retr. Monoc.	France	2006-2011	98	Mixed (PCS = 30%)	X	
Russo et al, 2010 ^{E60}	Retr. Monoc.	Italy	2005-2009	15	Mixed (PCS = 20%)		VAD
Ruzevich et al, 1987 ^{E61}	Retr. Monoc.	US	1980-1987	22		X	VAD/Pediatric Pts
Ruzevich et al, 1988 ^{E62}	Retr. Monoc.	US	1980-1987	22		X	VAD/Pediatric Pts
Saeed et al, 2014 ^{E63}	Retr. Monoc.	Germany	2009-2011	37	Mixed (PCS = 87%)		
Santarpino et al, 2015 ^{E64}	Retr. Multic.	Europe	2005-2015	85		X	Preop ECMO
Saxena et al, 2015 ^{E65}	Retr. Monoc.	Italy	2013-2017	92		X	
Silveti et al, 2018 ^{E66}	Retr. Monoc.	Australia	2003-2013	45		X	
Slottosch et al, 2013 ^{E67}	Retr. Monoc.	Germany	2006-2010	77		X	

(Continued)

TABLE E5. Continued

Study (author, y)	Design	Country	Study period	Number of patients	Reason for exclusion			
					Etiology for ECMO	No data on cannulation	Review/editorial	Other
Temam et al, 2014 ^{E68}	Retr. Monoc.	US	2004-2012	104		X		VAD
Wang et al, 1996 ^{E69}	Retr. Monoc.	Taiwan	1994-1995	18		X		
Wang et al, 2009 ^{E70}	Retr. Monoc.	China	2004-2008	62		X		
Wang et al, 2013 ^{E71}	Retr. Monoc.	China	2004-2011	87		X		
Wong et al, 2017 ^{E72}	Retr. Monoc.	US	2010-2015	103		X		VV-ECMO/VAD-ECMO
Wu et al, 2010 ^{E73}	Retr. Monoc.	Taiwan	2003-2009	110		X		
Xie et al, 2017 ^{E74}	Retr. Monoc.	China	2011-2015	177		X		
Yang et al, 2018 ^{E75}	Retr. Monoc.	China	2004-2015	432		X		
Zalawadiya et al, 2016 ^{E76}	Prosp. Multic.	UNOS registry	2000-2015	157	Postheart transplant	X		
Zhang et al, 2006 ^{E77}	Retr. Monoc.	Germany	1996-2004	32		X		

ECMO, Extracorporeal membrane oxygenation; Retr., retrospective; Monoc., mono-center; Multic., multicenter; PCS, postcardiomy shock; Prosp., prospective; ELSO, Extracorporeal Life Support Organization; VAD, ventricular assist device; VV-ECMO, venovenous extracorporeal membrane oxygenation; UNOS, United Network for Organ Sharing.

TABLE E6. Baseline characteristics and operative data in the overall series

Variables*	Overall series		
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	P value
Demographics			
Age, y	63.9 (12.3)	61.5 (14.1)	.02
Female	172 (32.1)	77 (31.4)	.92
BMI, kg/m ²	26.7 [23.9-30.0]	26.5 [23.3-29.8]	.53
BMI >30 kg/m ²	136 (25.4)	61 (24.9)	.96
Cardiac status			
Elective procedure	223 (41.6)	104 (42.4)	.89
Urgent/emergent procedure	288 (53.7)	127 (51.8)	.69
Salvage procedure	25 (4.7)	14 (5.7)	.65
Critical preoperative state	197 (36.8)	79 (32.2)	.25
Preoperative IABP	41 (7.6)	21 (8.6)	.76
Previous cardiac surgery	123 (22.9)	63 (25.7)	.45
CCS angina class IV	99 (18.5)	54 (22.0)	.29
NYHA class I-II	182 (34.0)	93 (38.0)	.31
NYHA class III-IV	354 (66.0)	152 (62.0)	.31
Previous MI	181 (33.8)	96 (39.2)	.17
Previous PCI	105 (19.6)	41 (16.7)	.39
Recent myocardial infarction	128 (23.9)	71 (29.0)	.15
LVEF >50%	228 (42.5)	90 (36.7)	.15
LVEF 30%-50%	178 (33.2)	82 (33.5)	1.00
LVEF 21%-30%	89 (16.6)	47 (19.2)	.44
LVEF <21%	41 (7.6)	26 (10.6)	.22
Active endocarditis	53 (9.9)	32 (13.1)	.23
PAPs >55 mm Hg	94 (17.5)	46 (18.8)	.75
Comorbidities			
Diabetes	131 (24.4)	69 (28.2)	.31
Diabetes type			.49
No diabetes	405 (75.6)	176 (71.8)	
IDDM	68 (12.7)	38 (15.5)	
NIDDM	63 (11.8)	31 (12.7)	
Hemoglobin, g/L	125.6 (21.5)	124.6 (22.7)	.54
eGFR, mL/min/1.73 m ²	66.5 [49.1-85.3]	65.0 [45.1-82.8]	.31
Dialysis	25 (4.7)	7 (2.9)	.32
Stroke	39 (7.3)	21 (8.6)	.63
Extracardiac arteriopathy	77 (14.4)	43 (17.6)	.29
Pulmonary disease	73 (13.6)	37 (15.1)	.66
Atrial fibrillation	143 (26.7)	49 (20.0)	.06
Poor mobility	29 (5.4)	15 (6.1)	.82
EuroSCORE II, score	0.09 [0.04-0.19]	0.09 [0.03-0.27]	.42
Indications for cardiac surgery			
CAD	233 (43.5)	122 (49.8)	.12
Aortic valve stenosis	93 (17.4)	50 (20.4)	.36
Aortic valve regurgitation	94 (17.5)	33 (13.5)	.19
Mitral valve stenosis	31 (5.8)	11 (4.5)	.57
Mitral valve regurgitation	165 (30.8)	70 (28.6)	.59
Tricuspid valve regurgitation	81 (15.1)	23 (9.4)	.05
Ascending aortic aneurysm	43 (8.0)	15 (6.1)	.43
Aortic arch aneurysm	9 (1.7)	5 (2.0)	.95
Type A aortic dissection	43 (8.0)	19 (7.8)	1.00
Pulmonary thromboembolism	10 (1.9)	1 (0.4)	.20

(Continued)

TABLE E6. Continued

Variables*	Overall series		
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	P value
Cardiac procedures			
CABG	257 (47.9)	133 (54.3)	.12
Off-pump CABG	8 (1.5)	3 (1.2)	1.00
On-pump CABG	242 (45.1)	125 (51.0)	.15
Beating-heart CABG on CPB	7 (1.3)	6 (2.4)	.39
SIMA	162 (30.2)	78 (31.8)	.71
BIMA	62 (11.6)	15 (6.1)	.025
Incomplete revascularization	59 (11.0)	33 (13.5)	.38
AVR	144 (26.9)	69 (28.2)	.77
Aortic valve repair	6 (1.1)	1 (0.4)	.57
MVR	129 (24.1)	48 (19.6)	.19
Mitral valve repair	66 (12.3)	30 (12.2)	1.00
TVR	15 (2.8)	7 (2.9)	1.00
Tricuspid valve repair	60 (11.2)	18 (7.3)	.13
Bentall-De Bono procedure	53 (9.9)	22 (9.0)	.79
Aortic valve sparing	4 (0.7)	6 (2.4)	.11
Ascending aortic replacement	35 (6.5)	19 (7.8)	.64
Aortic arch replacement	28 (5.2)	11 (4.5)	.79
PTE	10 (1.9)	0 (0.0)	.07
Other major cardiac surgery	8 (1.5)	10 (4.1)	.05
Intraoperative data			
ACC time, min	113.0 [75.0-158.0]	109.0 [68.0-161.0]	.58
CPB time, min	200.0 [123.0-280.50]	220.0 [150.0-308.0]	.01

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; BMI, body mass index; IABP, intra-aortic balloon pump; CCS, Canadian Cardiovascular Society (class); NYHA, New York Heart Association (class); MI, myocardial infarction; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; PAP, pulmonary artery pressure; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; eGFR, estimated glomerular filtration rate; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; CAD, coronary artery disease; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; SIMA, single internal mammary artery (use); BIMA, bilateral internal mammary artery (use); AVR, aortic valve replacement; MVR, mitral valve replacement; TVR, tricuspid valve replacement; PTE, pulmonary thromboendarterectomy; ACC, aortic crossclamp. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent).

TABLE E7. VA-ECMO-related characteristics and indications for insertion

Variables*	Overall series		P value
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	
Indications for VA-ECMO			
Failure to wean from CPB	184 (34.3)	115 (46.9)	.001
Heart failure after weaning from CPB	274 (51.1)	100 (40.8)	.009
Ventricular arrhythmias after CPB weaning	42 (7.8)	20 (8.2)	.99
Cardiac arrest after weaning from CPB	42 (7.8)	22 (9.0)	.69
Respiratory failure after weaning from CPB	42 (7.8)	13 (5.3)	.26
ARDS after weaning from CPB	22 (4.1)	1 (0.4)	.009
Septic shock after weaning from CPB	14 (2.6)	1 (0.4)	.07
Pulmonary embolism	1 (0.2)	4 (1.6)	.06
Timing of ECMO insertion			
VA-ECMO inserted immediately after surgery			<.001
No	230 (42.9)	76 (31.0)	
After weaning attempts with inotropes only	248 (46.3)	107 (43.7)	
After weaning attempts with IABP	57 (10.6)	62 (25.3)	
After weaning attempts with Impella	1 (0.2)	0 (0.0)	
VA-ECMO inserted later after surgery			.002
No	306 (57.1)	169 (69.0)	
After weaning attempts with inotropes only	182 (34.0)	51 (20.8)	
After weaning attempts with IABP	47 (8.8)	25 (10.2)	
After weaning attempts with Impella	1 (0.2)	0	
Timing between heart failure after CPB and ECMO†	1 (0.79-1.01)	0.78 (0.46-1.10)	<.001
Cannulation ECMO data			
Primary arterial cannulation for VA-ECMO			<.001
Ascending aorta	–	245 (100)	
Femoral artery	467 (87.1)	0 (0.0)	
Another artery	69 (12.9)	0 (0.0)	
Primary venous cannulation for VA-ECMO	523 (97.6)	84 (34.3)	<.001
Conversion from mini- to full sternotomy	8 (1.5)	2 (0.8)	.66
Switch from central to peripheral cannulation	0	23 (9.4)	<.001
IABP			<.001
No	372 (69.4)	131 (53.5)	
IABP immediately after surgery with ECMO	41 (7.6)	37 (15.1)	
IABP immediately after surgery without ECMO	46 (8.6)	27 (11.0)	
IABP inserted later after surgery with ECMO	21 (3.9)	18 (7.3)	
IABP inserted later after surgery without ECMO	15 (2.8)	11 (4.5)	
IABP preoperatively inserted	41 (7.6)	21 (8.6)	
Impella, n (%)			.32
No	531 (99.1)	245 (100)	
Impella immediately after surgery with ECMO	3 (0.6)	0 (0.0)	
Impella inserted later after surgery with ECMO	2 (0.4)	0 (0.0)	
Left ventricular venting, n (%)			<.001
No	517 (96.5)	201 (82.0)	
Right superior pulmonary vein	13 (2.4)	37 (15.1)	
Left ventricular apex	5 (0.9)	3 (1.2)	
Another site	1 (0.2)	4 (1.6)	
Lower-leg perfusion during peripheral VA-ECMO from the arterial cannula site‡	396 (73.9)	12 (4.9)	<.001
Other data			
Duration of ECMO support, d	6.0 [4.0-11.0]	6.0 [3.0-9.0]	.39
Arterial pH before VA-ECMO	7.30 (0.14)	7.30 (0.13)	.73
Arterial lactate before VA-ECMO	6.0 [3.4-9.9]	5.6 [3.1-8.9]	.34
Target ACT during VA-ECMO, s	200 [180-220]	180 [150-200]	<.001

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; CPB, cardiopulmonary bypass; ARDS, acute respiratory distress syndrome; IABP, intra-aortic balloon pump; ACT, activated clotting time. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent). †Data expressed in days (mean and interquartile range). ‡In the central group, this refers to patients switched to peripheral cannulation.

TABLE E8. Primary and secondary outcomes after VA-ECMO implantation and the doubly robust matching estimators for confounding adjustment

Variables*	Overall series			Doubly robust adjustment†,‡		
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	P value	Odds ratio	95% CI	P value
Primary end point						
In-hospital mortality	327 (61.0)	176 (71.8)	.004	1.54	1.09-2.18	.02
Secondary end points						
Reoperation for bleeding/tamponade	191 (35.6)	137 (55.9)	<.001	1.96	1.37-2.81	<.001
Reoperation for bleeding at cannulation site	43 (8.0)	23 (9.4)	.62	0.81	0.42-1.57	.53
Tracheostomy	132 (24.6)	48 (19.6)	.15	0.76	0.49-1.17	.21
Stroke	93 (17.4)	55 (22.4)	.11	1.11	0.72-1.71	.65
Dialysis			.29	0.84	0.60-1.19	.34
No	250 (46.6)	122 (49.8)				
Transient	231 (43.1)	92 (37.6)				
Permanent	55 (10.3)	31 (12.7)				
Pancreatitis	8 (1.5)	4 (1.6)	1.00	1.45	0.36-5.85	.60
Liver failure	205 (38.2)	60 (24.5)	<.001	0.63	0.43-0.92	.02
Gastrointestinal complications requiring surgical treatment	32 (6.0)	15 (6.1)	1.00	0.93	0.45-1.92	.84
Multiorgan failure	279 (52.1)	111 (45.3)	.09	0.85	0.60-1.21	.37
DSWI	19 (3.5)	10 (4.1)	.87	1.00	0.41-2.43	.99
Vascular access–site infection	60 (11.2)	7 (2.9)	<.001	0.25	0.11-0.59	.002
Pneumonia	208 (38.8)	77 (31.4)	.06	0.88	0.61-1.28	.50
Sepsis	140 (26.1)	39 (15.9)	.002	0.64	0.42-0.99	.05
Other severe infections	55 (10.3)	13 (5.3)	.03	0.57	0.35-1.34	.27
Peripheral vascular complications	49 (9.1)	20 (8.2)	.76	0.80	0.43-1.48	.47
Aortic rupture	0 (0.0)	2 (0.8)				
Type A aortic dissection	6 (1.1)	2 (0.8)				
Type B aortic dissection	1 (0.2)	2 (0.8)				
Peripheral artery dissection	8 (1.5)	1 (0.4)				
Vascular perforation	3 (0.6)	4 (1.6)				
Thrombosis	32 (6.0)	11 (4.5)				
Stenosis	2 (0.4)	1 (0.4)				
Pseudoaneurysm	1 (0.2)	1 (0.4)				
Major lower-limb amputation			.37		NA	
No	530 (98.9)	239 (97.6)				
Femoral cannulation side	5 (0.9)	5 (2.0)				
Other side	1 (0.2)	1 (0.4)				
Atrial fibrillation			.13	1.26	0.89-1.78	.20
No	294 (54.9)	128 (52.2)				
Paroxysmal	174 (32.5)	95 (38.8)				
Permanent	68 (12.7)	22 (9.0)				
RBC units transfused, U	15.0 [7.0-28.0]	21.0 [12.0-38.0]	<.001	5.56§	2.07§	.007§
More than 9 RBC units transfused	344 (64.2)	203 (82.9)	<.001	2.42	1.59-3.67	<.001
Chest drains output 24 h after surgery, mL	780 [500-1450]	1389 [750-2500]	<.001	622.52§	132.76§	<.001§
ICU stay, d	12.0 [5.0-24.0]	11.0 [5.0-21.0]	.31	-1.26§	1.57§	.42§
Hospital stay, d	17.0 [5.8-35.0]	13.0 [5.0-27.0]	.04	-5.79§	2.49§	.02§
More than 10 d on VA-ECMO	128 (23.9)	57 (23.3)	.92	0.83	0.55-1.27	.40
Successful weaning from VA-ECMO	271 (50.6)	108 (44.1)	.11	0.74	0.53-1.06	.10
Postoperative VAD or heart transplant	17 (3.2)	12 (4.9)	.33	1.79	0.82-3.93	.14
VAD from VA-ECMO	12 (2.2)	10 (4.1)	.23	2.23	0.92-5.42	.08

(Continued)

TABLE E8. Continued

Variables*	Overall series			Doubly robust adjustment ^{†,‡}		
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 245 patients	P value	Odds ratio	95% CI	P value
Heart transplant			.80		NA	
No	527 (98.3)	240 (98.0)				
From VA-ECMO	5 (0.9)	2 (0.8)				
From LVAD	4 (0.7)	3 (1.2)				
Any new cardiac procedure [‡]	46 (8.6)	26 (0.6)	.44	1.21	0.67-2.19	.52
New cardiac surgery procedure during ECMO [‡]	44 (8.2)	23 (9.4)	.63	1.16	0.64-2.13	.62
Oxygenator failure for clots	58 (10.8)	11 (4.5)	.006	0.48	0.24-0.96	.04
Nadir arterial pH during VA-ECMO	7.22 (0.13)	7.24 (0.15)	.07	0.01§	0.01§	.39§
Peak arterial lactate during VA-ECMO, mmol/L	7.5 [4.6-12.0]	7.6 [4.1-13.0]	.99	0.14§	0.55§	.80§
Nadir postoperative hemoglobin, g/L	74.30 (10.91)	75.35 (12.64)	.24	0.26§	1.03§	.80§

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; CI, confidence interval; DSWI, deep sternal wound infection; NA, not applicable; RBC, red blood cell; CPB, cardiopulmonary bypass; ICU, intensive cardiac unit; VAD, ventricular assist device; LVAD, left ventricular assist device. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent). †Reference for the events: central VA-ECMO group. ‡This include percutaneous balloon angioplasty (cardiac procedure) and bypass surgery, aortic valve replacement or aortic repair (new cardiac surgery). §Linear regression expressed as standard regression coefficient, standard error and P value.

TABLE E9. Covariate balance analyses in unweighted and weighted samples for patients receiving VA-ECMO

Variable	Unadjusted sample							Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 245 patients		Balance measures			Peripheral VA-ECMO, n = 263,224 patients		Central VA-ECMO, n = 245 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
Age	63.846	12.323	61.514	14.059	-0.166	1.302	0.114	62.253	14.042	61.514	14.059	-0.053	<0.1	1.003	0.105
Female	0.321	0.467	0.314	0.465	-0.014			0.313	0.465	0.314	0.465	0.002	<0.1		
BMI	27.263	5.025	27.085	5.337	-0.033	1.128	0.066	27.060	4.864	27.085	5.337	0.005	<0.1	1.204	0.068
Hemoglobin	125.591	21.485	124.567	22.739	-0.045	1.120	0.033	125.202	21.257	124.567	22.739	-0.028	<0.1	1.144	0.050
eGFR	68.561	30.992	66.694	28.651	-0.065	0.855	0.061	66.995	30.709	66.694	28.651	-0.011	<0.1	0.870	0.069
Dialysis	0.047	0.211	0.029	0.167	-0.108			0.030	0.172	0.029	0.167	-0.010	<0.1		
Diabetes	0.244	0.430	0.282	0.451	0.083			0.275	0.447	0.282	0.451	0.015	<0.1		
Poor mobility	0.054	0.226	0.061	0.240	0.030			0.064	0.245	0.061	0.240	-0.010	<0.1		
Stroke	0.073	0.260	0.086	0.281	0.046			0.088	0.284	0.086	0.281	-0.009	<0.1		
Atrial fibrillation	0.267	0.443	0.200	0.401	-0.167			0.209	0.407	0.200	0.401	-0.022	<0.1		
ARDS after weaning from CPB	0.041	0.199	0.004	0.064	-0.579			0.005	0.071	0.004	0.064	-0.016	<0.1		
Extracardiac arteriopathy	0.144	0.351	0.176	0.381	0.084			0.175	0.381	0.176	0.381	0.001	<0.1		
Pulmonary disease	0.136	0.343	0.151	0.359	0.041			0.152	0.359	0.151	0.359	-0.002	<0.1		
Previous cardiac surgery	0.230	0.421	0.257	0.438	0.063			0.256	0.437	0.257	0.438	0.004	<0.1		
Previous MI	0.338	0.473	0.392	0.489	0.111			0.381	0.487	0.392	0.489	0.021	<0.1		
NYHA class I-II	0.340	0.474	0.380	0.486	0.082			0.373	0.485	0.380	0.486	0.014	<0.1		
LVEF >50%	0.425	0.495	0.367	0.483	-0.120			0.374	0.485	0.367	0.483	-0.013	<0.1		
LVEF 30%-50%	0.332	0.471	0.335	0.473	0.006			0.337	0.474	0.335	0.473	-0.004	<0.1		
LVEF 21%-30%	0.166	0.373	0.192	0.395	0.065			0.186	0.389	0.192	0.395	0.016	<0.1		
LVEF <21%	0.077	0.266	0.106	0.309	0.096			0.104	0.306	0.106	0.309	0.006	<0.1		
Elective procedure	0.416	0.493	0.425	0.495	0.017			0.425	0.495	0.425	0.495	0.000	<0.1		
Urgent/emergent procedure	0.537	0.499	0.518	0.501	-0.038			0.526	0.500	0.518	0.501	-0.016	<0.1		
Salvage procedure	0.047	0.211	0.057	0.233	0.045			0.049	0.216	0.057	0.233	0.035	<0.1		
Previous PCI	0.196	0.397	0.167	0.374	-0.076			0.170	0.376	0.167	0.374	-0.007	<0.1		

(Continued)

TABLE E9. Continued

Variable	Unadjusted sample							Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 245 patients		Balance measures			Peripheral VA-ECMO, n = 263,224 patients		Central VA-ECMO, n = 245 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
Critical preoperative state	0.368	0.483	0.322	0.468	-0.096			0.316	0.466	0.322	0.468	0.014	<0.1		
Preoperative cardiac arrest	0.037	0.190	0.078	0.268	0.150			0.062	0.242	0.078	0.268	0.057	<0.1		
Ventricular tachycardia or fibrillation	0.049	0.215	0.045	0.208	-0.017			0.041	0.199	0.045	0.208	0.019	<0.1		
Aborted sudden death	0.024	0.154	0.008	0.090	-0.179			0.009	0.092	0.008	0.090	-0.004	<0.1		
Preoperative IABP	0.077	0.266	0.086	0.281	0.033			0.083	0.277	0.086	0.281	0.009	<0.1		
Preoperative inotropes	0.289	0.454	0.278	0.449	-0.026			0.268	0.444	0.278	0.449	0.021	<0.1		
Preoperative mechanical ventilation	0.090	0.286	0.090	0.287	0.001			0.083	0.276	0.090	0.287	0.025	<0.1		
EuroSCORE II	0.147	0.160	0.176	0.193	0.151	1.461	0.112	0.171	0.204	0.176	0.193	0.026	<0.1	0.894	0.085
Clopidogrel or ticagrelor use	0.140	0.347	0.127	0.333	-0.040			0.126	0.333	0.127	0.333	0.002	<0.1		
PAPs <30 mm Hg	0.502	0.501	0.551	0.498	0.099			0.545	0.499	0.551	0.498	0.012	<0.1		
PAPs 30-55 mm Hg	0.323	0.468	0.261	0.440	-0.140			0.269	0.444	0.261	0.440	-0.018	<0.1		
PAPs >55 mm Hg	0.175	0.381	0.188	0.391	0.032			0.186	0.390	0.188	0.391	0.005	<0.1		
CAD	0.435	0.496	0.498	0.501	0.126			0.498	0.501	0.498	0.501	-0.001	<0.1		
Aortic valve stenosis	0.174	0.379	0.204	0.404	0.076			0.197	0.398	0.204	0.404	0.018	<0.1		
Aortic valve regurgitation	0.175	0.381	0.135	0.342	-0.119			0.134	0.341	0.135	0.342	0.002	<0.1		
Mitral valve stenosis	0.058	0.234	0.045	0.208	-0.062			0.048	0.214	0.045	0.208	-0.014	<0.1		
Mitral valve regurgitation	0.308	0.462	0.286	0.453	-0.049			0.295	0.457	0.286	0.453	-0.021	<0.1		
Tricuspid valve regurgitation	0.151	0.359	0.094	0.292	-0.196			0.100	0.300	0.094	0.292	-0.020	<0.1		
Ascending aortic aneurysm	0.080	0.272	0.061	0.240	-0.079			0.054	0.226	0.061	0.240	0.031	<0.1		

(Continued)

TABLE E9. Continued

Variable	Unadjusted sample							Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 245 patients		Balance measures			Peripheral VA-ECMO, n = 263,224 patients		Central VA-ECMO, n = 245 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
Aortic arch aneurysm	0.017	0.129	0.020	0.142	0.026			0.016	0.127	0.020	0.142	0.030	<0.1		
Type A aortic dissection	0.080	0.272	0.078	0.268	-0.010			0.081	0.273	0.078	0.268	-0.011	<0.1		
Pulmonary thromboembolism	0.019	0.135	0.004	0.064	-0.228			0.005	0.068	0.004	0.064	-0.008	<0.1		
Active endocarditis	0.099	0.299	0.131	0.338	0.094			0.121	0.327	0.131	0.338	0.029	<0.1		
Type of surgical procedures - isolated CABG	0.218	0.414	0.269	0.445	0.115			0.265	0.442	0.269	0.445	0.009	<0.1		
Type of surgical procedures - isolated valvular surgery	0.216	0.412	0.196	0.398	-0.052			0.200	0.401	0.196	0.398	-0.011	<0.1		
Type of surgical procedures - surgery on thoracic aorta	0.1026	0.304	0.090	0.287	-0.045			0.084	0.277	0.090	0.287	0.022	<0.1		
Type of surgical procedures - other*	0.463	0.499	0.445	0.498	-0.036			0.451	0.499	0.445	0.498	-0.012	<0.1		
ACC time	125.754	77.586	121.241	76.270	-0.059	0.966	0.054	120.534	74.936	121.241	76.266	0.009	<0.1	1.036	0.034
CPB time	219.787	116.352	241.310	122.550	0.176	1.109	0.118	239.215	122.026	241.310	122.547	0.017	<0.1	1.009	0.089
Failure to wean from CPB	0.343	0.475	0.469	0.500	0.252			0.448	0.498	0.469	0.500	0.042	<0.1		
Heart failure after weaning from CPB	0.511	0.500	0.408	0.493	-0.209			0.421	0.495	0.408	0.493	-0.025	<0.1		
Ventricular arrhythmias after weaning from CPB	0.078	0.269	0.082	0.274	0.012			0.085	0.280	0.082	0.274	-0.013	<0.1		
Cardiac arrest after weaning from CPB	0.078	0.269	0.090	0.287	0.040			0.095	0.294	0.090	0.287	-0.018	<0.1		

(Continued)

TABLE E9. Continued

Variable	Unadjusted sample								Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 245 patients		Balance measures			Peripheral VA-ECMO, n = 263,224 patients		Central VA-ECMO, n = 245 patients		Balance measures				
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS	
Respiratory failure after weaning from CPB	0.078	0.269	0.053	0.225	-0.113			0.057	0.233	0.053	0.225	-0.018	<0.1			
Septic shock after weaning from CPB	0.026	0.160	0.004	0.064	-0.345			0.005	0.071	0.004	0.064	-0.015	<0.1			
VA-ECMO inserted immediately after surgery - no	0.429	0.495	0.310	0.464	-0.257			0.327	0.470	0.310	0.464	-0.036	<0.1			
VA-ECMO inserted immediately after surgery - after weaning attempts with inotropes only	0.463	0.499	0.437	0.497	-0.052			0.443	0.498	0.437	0.497	-0.012	<0.1			
VA-ECMO inserted immediately after surgery - after weaning attempts with IABP	0.106	0.309	0.253	0.436	0.337			0.230	0.422	0.253	0.436	0.052	<0.1			
VA-ECMO inserted immediately after surgery - after weaning attempts with Impella	0.002	0.043	0.000	0.000				0.000	0.000	0.000	0.000	0.000	<0.1			
VA-ECMO inserted later after surgery - no	0.340	0.474	0.208	0.407	-0.323			0.221	0.416	0.208	0.407	-0.032	<0.1			
VA-ECMO inserted later after surgery - after weaning attempts with Inotropes only	0.088	0.283	0.102	0.303	0.047			0.106	0.308	0.102	0.303	-0.012	<0.1			

(Continued)

TABLE E9. Continued

Variable	Unadjusted sample						Adjusted sample								
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 245 patients		Balance measures			Peripheral VA-ECMO, n = 263,224 patients		Central VA-ECMO, n = 245 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
VA-ECMO inserted later after surgery - after weaning attempts with IABP	0.002	0.043	0.000	0.000				0.000	0.000	0.000	0.000	0.000	<0.1		

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; SD, standard deviation; KS, Kolmogorov–Smirnov statistics; BMI, body mass index; eGFR, estimated glomerular filtration rate; ARDS, acute respiratory distress syndrome; MI, myocardial infarction; NYHA, New York Heart Association (class); LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; IABP, intra-aortic balloon pump; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; PAP, pulmonary artery pressure; CAD, coronary artery disease; CABG, coronary artery bypass grafting; ACC, aortic crossclamp; CPB, cardiopulmonary bypass. *Other includes combined procedures and other major cardiac surgical procedures

TABLE E10. Baseline characteristics and operative data in the overall series after the removal of patients switched from central to peripheral cannulation

Variables*	Overall series		P value
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 222 patients	
Demographics			
Age, y	63.9 (12.3)	61.3 (13.9)	<.001
Female	172 (32.1)	30 (31.5)	.95
BMI, kg/m ²	26.7 [23.9-30.0]	26.3 [23.0-29.8]	.31
BMI >30 kg/m ²	136 (25.4)	54 (24.3)	.83
Cardiac status			
Elective procedure	223 (41.6)	92 (41.4)	1.000
Urgent/emergent procedure	288 (53.7)	117 (52.7)	.86
Salvage procedure	25 (4.7)	13 (5.9)	.62
Critical preoperative state	197 (36.8)	75 (33.8)	.49
Preoperative IABP	41 (7.6)	19 (8.6)	.78
Previous cardiac surgery	123 (22.9)	58 (26.1)	.40
CCS angina class IV	99 (18.5)	49 (22.1)	.29
NYHA class I-II	182 (34.0)	86 (38.7)	.24
NYHA class III-IV	354 (66.0)	136 (61.3)	.24
Previous MI	181 (33.8)	85 (38.3)	.27
Previous PCI	105 (19.6)	38 (16.7)	.40
Recent myocardial infarction	128 (23.9)	63 (28.4)	.23
LVEF >50%	228 (42.5)	81 (36.5)	.14
LVEF 30%-50%	178 (33.2)	72 (32.4)	.91
LVEF 21%-30%	89 (16.6)	46 (20.7)	.21
LVEF <21%	41 (7.6)	23 (10.4)	.28
Active endocarditis	53 (9.9)	30 (13.5)	.19
PAPs >55 mm Hg	94 (17.5)	45 (20.3)	.43
Comorbidities			
Diabetes	131 (24.4)	62 (27.9)	.36
Diabetes type			.56
No diabetes	405 (75.6)	160 (72.1)	
IDDM	68 (12.7)	34 (15.3)	
NIDDM	63 (11.8)	28 (12.6)	
Hemoglobin, g/L	125.6 (21.5)	124.4 (22.8)	.51
eGFR, mL/min/1.73 m ²	66.5 [49.1-85.3]	65.0 [45.2-82.6]	.39
Dialysis	25 (4.7)	6 (2.7)	.29
Stroke	39 (7.3)	19 (8.6)	.65
Extracardiac arteriopathy	77 (14.4)	38 (17.1)	.39
Pulmonary disease	73 (13.6)	34 (15.3)	.62
Atrial fibrillation	143 (26.7)	48 (21.6)	.17
Poor mobility	29 (5.4)	14 (6.3)	.75
EuroSCORE II, score	0.09 [0.04-0.19]	0.10 [0.03-0.27]	.26
Indications for cardiac surgery			
CAD	233 (43.5)	110 (49.5)	.15
Aortic valve stenosis	93 (17.4)	43 (19.4)	.58
Aortic valve regurgitation	94 (17.5)	33 (14.9)	.43
Mitral valve stenosis	31 (5.8)	11 (5.0)	.78
Mitral valve regurgitation	165 (30.8)	66 (29.7)	.84
Tricuspid valve regurgitation	81 (15.1)	22 (9.9)	.07
Ascending aortic aneurysm	43 (8.0)	15 (6.8)	.66
Aortic arch aneurysm	9 (1.7)	5 (2.3)	.81
Type A aortic dissection	43 (8.0)	19 (8.6)	.92
Pulmonary thromboembolism	10 (1.9)	1 (0.5)	.25

(Continued)

TABLE E10. Continued

Variables*	Overall series		P value
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 222 patients	
Cardiac procedures			
CABG	257 (47.9)	116 (52.3)	.32
Off-pump CABG	8 (1.5)	3 (1.4)	1.00
On-pump CABG	242 (45.1)	110 (49.5)	.31
Beating-heart CABG on CPB	7 (1.3)	4 (1.8)	.85
SIMA	162 (30.2)	66 (29.7)	.96
BIMA	62 (11.6)	9 (4.1)	.002
Incomplete revascularization	59 (11.0)	29 (13.1)	.49
AVR	144 (26.9)	61 (27.5)	.93
Aortic valve repair	6 (1.1)	1 (0.5)	.65
MVR	129 (24.1)	46 (20.7)	.37
Mitral valve repair	66 (12.3)	28 (12.6)	1.00
TVR	15 (2.8)	7 (3.2)	.98
Tricuspid valve repair	60 (11.2)	17 (7.7)	.18
Bentall-De Bono procedure	53 (9.9)	21 (9.5)	.96
Aortic valve sparing	4 (0.7)	6 (2.7)	.07
Ascending aortic replacement	35 (6.5)	19 (8.6)	.41
Aortic arch replacement	28 (5.2)	11 (5.0)	1.000
PTE	10 (1.9)	0 (0.0)	.09
Other major cardiac surgery	8 (1.5)	8 (3.6)	.12
Intraoperative data			
ACC time, min	113.0 [75.0-158.0]	108.5 [68.0-161.0]	.58
CPB time, min	200.0 [123.0-280.50]	220.0 [154.3-302.0]	.02

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; BMI, body mass index; IABP, intra-aortic balloon pump; CCS, Canadian Cardiovascular Society (class); NYHA, New York Heart Association (class); MI, myocardial infarction; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; PAP, pulmonary artery pressure; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; eGFR, estimated glomerular filtration rate; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; CAD, coronary artery disease; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; SIMA, single internal mammary artery (use); BIMA, bilateral internal mammary artery (use); AVR, aortic valve replacement; MVR, mitral valve replacement; TVR, tricuspid valve replacement; PTE, pulmonary thromboendarterectomy; ACC, aortic crossclamp. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent).

TABLE E11. VA-ECMO–related characteristics and indications after the removal of patients switched from central to peripheral cannulation

Variables*	Overall series		P value
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 222 patients	
Indications for VA-ECMO			
Failure to wean from CPB	184 (34.3)	106 (47.7)	.001
Heart failure after weaning from CPB	274 (51.1)	93 (41.9)	.03
Ventricular arrhythmias after CPB weaning	42 (7.8)	18 (8.1)	1.00
Cardiac arrest after weaning from CPB	42 (7.8)	16 (7.2)	.88
Respiratory failure after weaning from CPB	42 (7.8)	11 (5.0)	.21
ARDS after weaning from CPB	22 (4.1)	0 (0)	.005
Septic shock after weaning from CPB	14 (2.6)	1 (0.5)	.10
Pulmonary embolism	1 (0.2)	4 (1.8)	.05
Timing of ECMO insertion			
VA-ECMO inserted immediately after surgery			<.001
No	230 (42.9)	68 (30.6)	
After weaning attempts with inotropes only	248 (46.3)	97 (43.7)	
After weaning attempts with IABP	57 (10.6)	57 (25.7)	
After weaning attempts with Impella	1 (0.2)	0 (0.0)	
VA-ECMO inserted later after surgery			.001
No	306 (57.1)	154 (69.4)	
After weaning attempts with inotropes only	182 (34.0)	43 (19.4)	
After weaning attempts with IABP	47 (8.8)	25 (11.3)	
After weaning attempts with Impella	1 (0.2)	0	
Cannulation ECMO data			
Primary arterial cannulation for VA-ECMO			<.001
Ascending aorta	–	222 (100)	
Femoral artery	467 (87.1)	0 (0.0)	
Another artery	69 (12.9)	0 (0.0)	
Primary venous cannulation for VA-ECMO	523 (97.6)	80 (36.0)	<.001
Conversion from mini- to full sternotomy	8 (1.5)	1 (0.5)	.40
IABP			.002
No	372 (69.4)	121 (54.5)	
IABP immediately after surgery with ECMO	41 (7.6)	32 (14.4)	
IABP immediately after surgery without ECMO	46 (8.6)	24 (10.8)	
IABP inserted later after surgery with ECMO	21 (3.9)	17 (7.7)	
IABP inserted later after surgery without ECMO	15 (2.8)	9 (4.1)	
IABP preoperatively inserted	41 (7.6)	19 (8.6)	
Impella, n (%)			.35
No	531 (99.1)	222 (100)	
Impella immediately after surgery with ECMO	3 (0.6)	0 (0.0)	
Impella inserted later after surgery with ECMO	2 (0.4)	0 (0.0)	
Left ventricular venting, n (%)			<.001
No	517 (96.5)	180 (81.1)	
Right superior pulmonary vein	13 (2.4)	36 (16.2)	
Left ventricular apex	5 (0.9)	2 (0.9)	
Another site	1 (0.2)	4 (1.8)	
Other data			
Duration of ECMO support, d	6.0 [4.0-11.0]	6.0 [3.0-9.0]	.16
Arterial pH before VA-ECMO	7.30 (0.14)	7.30 (0.13)	.94
Arterial lactate before VA-ECMO, s	6.0 [3.4-9.9]	5.6 [3.1-8.9]	.31
Target ACT during VA-ECMO, s	200 [180-220]	180 [150-200]	<.001

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; CPB, cardiopulmonary bypass; ARDS, acute respiratory distress syndrome; IABP, intra-aortic balloon pump; ACT, activated clotting time. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent).

TABLE E12. Principal primary and secondary outcomes after VA-ECMO implantation after the removal of patients switched from central to peripheral cannulation

Variables*	Overall series			Doubly robust adjustment†		
	Peripheral VA-ECMO, n = 536 patients	Central VA-ECMO, n = 222 patients	P value	Odds ratio	95% CI	P value
Primary end point						
In-hospital mortality	327 (61.0)	158 (71.2)	.01	1.55	1.05-2.27	.03
Secondary end points						
Reoperation for bleeding/tamponade	191 (35.6)	122 (55.0)	<.001	1.95	1.35-2.82	<.001
Stroke	93 (17.4)	50 (22.5)	.12	1.11	0.71-1.74	.64
Dialysis	286 (53.4)	109 (49.1)	.34	0.82	0.57-1.18	.29
Liver failure	205 (38.2)	53 (23.9)	<.001	0.61	0.41-0.791	.01
Multiorgan failure	279 (52.1)	98 (44.1)	.06	0.84	0.59-1.21	.36
DSWI	19 (3.5)	10 (4.5)	.68	1.05	0.42-2.61	.91
Vascular access–site infection	60 (11.2)	5 (2.3)	<.001	0.18	0.07-0.48	<.001
Sepsis	140 (26.1)	35 (15.8)	.003	0.61	0.38-0.96	.03
Peripheral vascular complications	49 (9.1)	13 (5.9)	.18	0.51	0.25-1.02	.06
RBC units transfused, U	15.0 [7.0-28.0]	20.5 [12.0-38.0]	<.001	6.02‡	2.15‡	.01‡
More than 9 RBC units transfused	344 (64.2)	184 (82.9)	<.001	2.49	1.61-3.84	<.001
Chest drains output 24 h after surgery, mL	780 [500-1450]	1760 [850-2210]	<.001	681‡	139.74‡	<.001‡
ICU stay, d	12.0 [5.0-24.0]	11.0 [4.0-20.0]	.17	-0.97‡	1.63‡	.55‡
Hospital stay, d	17.0 [5.8-35.0]	13.0 [5.0-25.0]	.02	-4.64‡	2.29‡	.04‡
More than 10 d on VA-ECMO	128 (23.9)	49 (22.1)	.66	0.81	0.52-1.26	.34
Successful weaning from VA-ECMO	271 (50.6)	96 (43.2)	.08	0.75	0.52-1.08	.12
Postoperative VAD or heart transplant	17 (3.2)	12 (5.4)	.21	2.07	0.94-4.53	.07

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; CI, confidence interval; DSWI, deep sternal wound infection; RBC, red blood cell; ICU, intensive cardiac unit; VAD, left ventricular assist device. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent). †Reference for the events: central VA-ECMO group. ‡Linear regression expressed as standard regression coefficient, standard error, and P value.

TABLE E13. Covariate balance analyses in unweighted and weighted samples for patients receiving VA-ECMO after the removal of patients switched from central to peripheral cannulation

Variable	Unadjusted sample							Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 222 patients		Balance measures			Peripheral VA-ECMO, n = 254.78 patients		Central VA-ECMO, n = 222 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
Age	63.846	12.323	61.262	13.888	-0.186	1.270	0.136	61.844	14.358	61.262	13.888	-0.042	<0.1	0.936	0.111
Female	0.321	0.467	0.315	0.466	-0.012			0.313	0.465	0.315	0.466	0.005	<0.1		
BMI	27.263	5.025	26.974	5.421	-0.053	1.164	0.087	27.017	4.963	26.974	5.421	-0.008	<0.1	1.193	0.081
Hemoglobin	125.591	21.485	124.437	22.821	-0.051	1.128	0.034	125.135	21.128	124.437	22.821	-0.031	<0.1	1.167	0.057
eGFR	68.561	30.992	66.685	27.822	-0.067	0.806	0.059	67.236	31.594	66.685	27.822	-0.020	<0.1	0.776	0.072
Dialysis	0.047	0.211	0.027	0.163	-0.121			0.028	0.164	0.027	0.163	-0.004	<0.1		
Diabetes	0.244	0.430	0.279	0.450	0.078			0.272	0.446	0.279	0.450	0.016	<0.1		
Poor mobility	0.054	0.226	0.063	0.244	0.037			0.064	0.246	0.063	0.244	-0.005	<0.1		
Stroke	0.073	0.260	0.086	0.280	0.046			0.088	0.283	0.086	0.280	-0.007	<0.1		
Atrial fibrillation	0.267	0.443	0.216	0.413	-0.123			0.223	0.417	0.216	0.413	-0.017	<0.1		
ARDS after weaning from CPB	0.041	0.199	0.000	0.000				0.000	0.000	0.000	0.000		<0.1		
Extracardiac arteriopathy	0.144	0.351	0.171	0.378	0.073			0.171	0.377	0.171	0.378	0.002	<0.1		
Pulmonary disease	0.136	0.343	0.153	0.361	0.047			0.152	0.360	0.153	0.361	0.004	<0.1		
Previous cardiac surgery	0.230	0.421	0.261	0.440	0.072			0.256	0.437	0.261	0.440	0.011	<0.1		
Previous MI	0.338	0.473	0.383	0.487	0.093			0.380	0.486	0.383	0.487	0.007	<0.1		
NYHA class I-II	0.340	0.474	0.387	0.488	0.098			0.387	0.488	0.387	0.488	0.001	<0.1		
LVEF >50%	0.425	0.495	0.365	0.483	-0.125			0.367	0.483	0.365	0.483	-0.004	<0.1		
LVEF 30%-50%	0.332	0.471	0.324	0.469	-0.017			0.326	0.470	0.324	0.469	-0.004	<0.1		
LVEF 21%-30%	0.166	0.373	0.207	0.406	0.101			0.206	0.405	0.207	0.406	0.003	<0.1		
LVEF <21%	0.077	0.266	0.104	0.305	0.089			0.101	0.302	0.104	0.305	0.008	<0.1		
Elective procedure	0.416	0.493	0.414	0.494	-0.003			0.420	0.495	0.414	0.494	-0.011	<0.1		
Urgent/emergent procedure	0.537	0.499	0.527	0.500	-0.021			0.525	0.500	0.527	0.500	0.004	<0.1		
Salvage procedure	0.047	0.211	0.059	0.235	0.051			0.055	0.228	0.059	0.235	0.016	<0.1		
Previous PCI	0.196	0.397	0.167	0.374	-0.078			0.173	0.379	0.167	0.374	-0.017	<0.1		
Critical preoperative state	0.368	0.483	0.338	0.474	-0.063			0.327	0.470	0.338	0.474	0.024	<0.1		
Preoperative cardiac arrest	0.037	0.190	0.081	0.274	0.160			0.066	0.249	0.081	0.274	0.055	<0.1		

(Continued)

TABLE E13. Continued

Variable	Unadjusted sample							Adjusted sample									
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 222 patients		Balance measures			Peripheral VA-ECMO, n = 254.78 patients		Central VA-ECMO, n = 222 patients		Balance measures					
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold		Variance ratio	KS	
													<0.1	<0.1			
Ventricular tachycardia or fibrillation	0.049	0.215	0.041	0.198	-0.040					0.035	0.185	0.041	0.198	0.027	<0.1		
Aborted sudden death	0.024	0.154	0.009	0.095	-0.161					0.009	0.095	0.009	0.095	-0.001	<0.1		
Preoperative IABP	0.077	0.266	0.086	0.280	0.032					0.083	0.277	0.086	0.280	0.009	<0.1		
Preoperative inotropes	0.289	0.454	0.293	0.456	0.008					0.279	0.449	0.293	0.456	0.030	<0.1		
Preoperative mechanical ventilation	0.090	0.286	0.095	0.293	0.017					0.086	0.281	0.095	0.293	0.029	<0.1		
EuroSCORE II	0.147	0.160	0.181	0.198	0.173	1.530	0.117			0.175	0.207	0.181	0.198	0.033	<0.1	0.915	0.081
Clopidogrel or ticagrelor use	0.140	0.347	0.122	0.328	-0.056					0.124	0.330	0.122	0.328	-0.006	<0.1		
PAPs <30 mm Hg	0.502	0.501	0.550	0.499	0.096					0.549	0.499	0.550	0.499	0.002	<0.1		
PAPs 30-55 mm Hg	0.323	0.468	0.248	0.433	-0.173					0.255	0.437	0.248	0.433	-0.016	<0.1		
PAPs >55 mm Hg	0.175	0.381	0.203	0.403	0.068					0.197	0.398	0.203	0.403	0.015	<0.1		
CAD	0.435	0.496	0.496	0.501	0.121					0.493	0.501	0.496	0.501	0.004	<0.1		
Aortic valve stenosis	0.174	0.379	0.194	0.396	0.051					0.191	0.394	0.194	0.396	0.007	<0.1		
Aortic valve regurgitation	0.175	0.381	0.149	0.357	-0.075					0.148	0.356	0.149	0.357	0.002	<0.1		
Mitral valve stenosis	0.058	0.234	0.050	0.218	-0.038					0.051	0.220	0.050	0.218	-0.006	<0.1		
Mitral valve regurgitation	0.308	0.462	0.297	0.458	-0.023					0.298	0.458	0.297	0.458	-0.001	<0.1		
Tricuspid valve regurgitation	0.151	0.359	0.099	0.300	-0.174					0.102	0.303	0.099	0.300	-0.008	<0.1		
Ascending aortic aneurysm	0.080	0.272	0.068	0.252	-0.050					0.066	0.248	0.068	0.252	0.008	<0.1		
Aortic arch aneurysm	0.017	0.129	0.023	0.149	0.039					0.024	0.153	0.023	0.149	-0.009	<0.1		
Type A aortic dissection	0.080	0.272	0.086	0.280	0.019					0.090	0.286	0.086	0.280	-0.015	<0.1		
Pulmonary thromboembolism	0.019	0.135	0.005	0.067	-0.211					0.005	0.070	0.005	0.067	-0.005	<0.1		
Active endocarditis	0.099	0.299	0.135	0.343	0.106					0.125	0.331	0.135	0.343	0.031	<0.1		
Type of surgical procedures - isolated CABG	0.218	0.414	0.252	0.435	0.078					0.251	0.434	0.252	0.435	0.003	<0.1		
Type of surgical procedures - isolated valvular surgery	0.216	0.412	0.198	0.400	-0.046					0.194	0.396	0.198	0.400	0.011	<0.1		

(Continued)

TABLE E13. Continued

Variable	Unadjusted sample							Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 222 patients		Balance measures			Peripheral VA-ECMO, n = 254.78 patients		Central VA-ECMO, n = 222 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
Type of surgical procedures - surgery on thoracic aorta	0.103	0.304	0.099	0.300	-0.012			0.102	0.303	0.099	0.300	-0.010	<0.1		
Type of surgical procedures - other*	0.463	0.499	0.451	0.499	-0.025			0.453	0.499	0.451	0.499	-0.006	<0.1		
ACC time	125.754	77.586	120.487	72.683	-0.073	0.878	0.050	121.671	74.627	120.487	72.683	-0.016	<0.1	0.949	0.048
CPB time	219.787	116.352	238.784	116.750	0.163	1.007	0.125	238.264	120.932	238.784	116.75	0.005	<0.1	0.932	0.090
Failure to wean from CPB	0.343	0.475	0.478	0.501	0.268			0.463	0.500	0.478	0.501	0.029	<0.1		
Heart failure after weaning from CPB	0.511	0.500	0.419	0.495	-0.187			0.425	0.495	0.419	0.495	-0.012	<0.1		
Ventricular arrhythmias after weaning from CPB	0.078	0.269	0.081	0.274	0.010			0.082	0.276	0.081	0.274	-0.005	<0.1		
Cardiac arrest after weaning from CPB	0.078	0.269	0.072	0.259	-0.024			0.075	0.264	0.072	0.259	-0.013	<0.1		
Respiratory failure after weaning from CPB	0.078	0.269	0.050	0.218	-0.133			0.053	0.225	0.050	0.218	-0.018	<0.1		
Septic shock after weaning from CPB	0.026	0.160	0.005	0.067	-0.322			0.006	0.074	0.005	0.067	-0.015	<0.1		
VA-ECMO inserted immediately after surgery - no	0.429	0.495	0.306	0.462	-0.266			0.317	0.466	0.306	0.462	-0.022	<0.1		
VA-ECMO inserted immediately after surgery - after weaning attempts with inotropes only	0.463	0.499	0.437	0.497	-0.052			0.444	0.498	0.437	0.497	-0.015	<0.1		
VA-ECMO inserted immediately after surgery - after weaning attempts with IABP	0.106	0.309	0.257	0.438	0.344			0.239	0.427	0.257	0.438	0.041	<0.1		
VA-ECMO inserted immediately after surgery - after weaning attempts with Impella	0.002	0.043	0.000	0.000				0.000	0.000	0.000	0.000	0.000	<0.1		

(Continued)

TABLE E13. Continued

Variable	Unadjusted sample							Adjusted sample							
	Peripheral VA-ECMO, n = 536 patients		Central VA-ECMO, n = 222 patients		Balance measures			Peripheral VA-ECMO, n = 254.78 patients		Central VA-ECMO, n = 222 patients		Balance measures			
	Mean	SD	Mean	SD	Mean difference	Variance ratio	KS	Mean	SD	Mean	SD	Mean difference	Mean difference threshold	Variance ratio	KS
VA-ECMO inserted later after surgery - no	0.340	0.474	0.194	0.396	-0.368			0.201	0.401	0.194	0.396	-0.018	<0.1		
VA-ECMO inserted later after surgery - after weaning attempts with Inotropes only	0.088	0.283	0.113	0.317	0.079			0.116	0.321	0.113	0.317	-0.011	<0.1		
VA-ECMO inserted later after surgery - after weaning attempts with IABP	0.002	0.043	0.000	0.000				0.000	0.000	0.000	0.000	0.000	<0.1		

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; SD, standard deviation; KS, Kolmogorov–Smirnov statistics; BMI, body mass index; eGFR, estimated glomerular filtration rate; ARDS, acute respiratory distress syndrome; CPB, cardiopulmonary bypass; MI, myocardial infarction; NYHA, New York Heart Association (class); LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; IABP, intra-aortic balloon pump; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; PAP, pulmonary artery pressure; CAD, coronary artery disease; CABG, coronary artery bypass grafting; ACC, aortic crossclamp. *Other includes combined procedures and other major cardiac surgical procedures.

TABLE E14. Primary and secondary end points after peripheral and central VA-ECMO implantation stratified by institutional volume

Variables*	Peripheral VA-ECMO			Central VA-ECMO		
	Low-volume, n = 164 patients	High-volume,† n = 372 patients	P value	Low-volume, n = 123 patients	High-volume,† n = 122 patients	P value
Primary end point						
In-hospital mortality	110 (67.1)	217 (58.3)	.07	93 (75.6)	83 (68.0)	.24
Secondary end points						
Reoperation for bleeding/ tamponade	60 (36.6)	131 (35.2)	.84	75 (61.0)	62 (50.8)	.14
Stroke	27 (16.5)	66 (17.7)	.81	31 (25.2)	24 (19.7)	.38
Dialysis	65 (39.6)	221 (59.4)	<.001	52 (42.3)	71 (58.2)	.01
Liver failure	49 (29.9)	156 (41.9)	.01	25 (20.3)	35 (28.7)	.17
Multiorgan failure	87 (53.0)	192 (51.6)	.83	64 (52.0)	47 (38.5)	.05
DSWI	6 (3.7)	13 (3.5)	1.00	2 (1.6)	8 (6.6)	.10
Vascular access-site infection	10 (6.1)	50 (13.4)	.02	1 (0.8)	6 (4.9)	.12
Sepsis	23 (14.0)	117 (31.5)	<.001	17 (13.8)	22 (18.0)	.47
Peripheral vascular complications	9 (5.5)	40 (10.8)	.07	9 (7.3)	11 (9.0)	.80
RBC units transfused, U	15 [8-28]	15 [7-27]	.47	19 [13-39]	22 [10-38]	.65
More than 9 RBC units transfused	105 (64.0)	239 (64.2)	1.00	109 (88.6)	94 (77.0)	.03
Chest drains output 24h after surgery, mL	1116 [610-1280]	800 [500-1341]	.03	1790 [863-1960]	1580 [766-2385]	.68
ICU stay, d	9.5 [4.0-22.25]	13.0 [5.0-24.25]	.06	11.0 [5.5-19.0]	13.0 [3.0-23.0]	.69
Hospital stay, d	13.0 [5.0-30.25]	18.0 [6.0-38.25]	.09	13.0 [6.00-25.0]	14.0 [4.0-27.75]	.95
More than 10 d on VA-ECMO	27 (16.5)	101 (27.2)	.01	24 (19.5)	33 (27.0)	.21
Successful weaning from VA-ECMO	82 (50.0)	189 (50.8)	.94	57 (46.3)	51 (41.8)	.56
Postoperative VAD or Heart transplant	9 (5.5)	8 (2.2)	.08	7 (5.7)	5 (4.1)	.78

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; DSWI, deep sternal wound infection; RBC, red blood cell; ICU, intensive cardiac unit; VAD, ventricular assist device. *Continuous data are presented as median [interquartile range]; categorical variables as number (percent). †High-volume centers are defined as per >50 cases of postcardiotomy VA-ECMO implanted during the study period.

TABLE E15. Subgroup analysis for mortality and bleeding according to peripheral and central VA-ECMO with reference to timing of ECMO insertion

Outcomes*	Peripheral VA-ECMO, n = 184 patients	Central VA-ECMO, n = 115 patients	P value	Odds ratio†	95% CI	P value	P _{interaction} ‡
Failure to wean from CPB in the operating room							
In-hospital mortality	127 (69)	90 (78.3)	.11	2.02	1.12-3.63	.02	.58
Reoperation for bleeding/tamponade	77 (41.8)	62 (53.9)	.06	1.59	0.99-2.56	.06	.75
More than 9 RBC units transfused	130 (70.7)	96 (83.5)	.02	2.20	1.21-3.99	.01	.07
Successful weaning from VA-ECMO	80 (43.5)	44 (38.3)	.44	0.68	0.41-1.13	.13	.80
Outcomes*	Peripheral VA-ECMO, n = 274 patients	Central VA-ECMO, n = 100 patients	P value	Odds Ratio†	95% CI	P value	P _{interaction} ‡
Heart failure after weaning from CPB							
In-hospital mortality	155 (56.6)	68 (68.0)	.06	2.04	1.21-3.42	.007	.80
Reoperation for bleeding/tamponade	88 (32.1)	55 (55.0)	<.001	2.67	1.64-4.34	<.001	.88
More than 9 RBC units transfused	164 (59.9)	85 (85.0)	<.001	3.92	2.11-7.29	<.001	.41
Successful weaning from VA-ECMO	154 (56.2)	50 (50.0)	.34	0.66	0.41-1.07	.09	.87

VA-ECMO, Venoarterial extracorporeal membrane oxygenation; CI, confidence interval; CPB, cardiopulmonary bypass; RBC, red blood cell. *Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent). †Reference for the events: central VA-ECMO group. Model adjusted for sex, age, previous cardiac surgery, preoperative left ventricular ejection fraction, coronary artery bypass grafting, history of stroke, urgent/emergent status, and arterial lactate pre-ECMO insertion ≥ 6 mmol/L. ‡P_{interaction}: P value for main interaction effect using likelihood ratio test fitting the models with and without interaction terms.

TABLE E16. Demographic and preoperative characteristics of the studies included in the systematic review*

Study (author, y)	Design	Country	Study period	Number of patients	Age, y	Male	BMI	COPD	Redo	EuroSCORE II	Emergency	CABG†
Ko et al, 2002 ^{E1}	Retr. Monoc.	Taiwan	1994-2000	76	57 ± 16	63.2	–	–	–	–	–	56.6
Rastan et al, 2010 ^{E2}	Retr. Monoc.	Germany	1996-2008	517	64 ± 11	71.5	–	13.0	–	21.6 ± 20.7‡	39.7	64.5
Pokersnik et al, 2012 ^{E3}	Retr. Monoc.	USA	2005-2010	49	65 ± 13	67.3	–	12.2	55.1	–	–	67.4
Unosowa et al, 2012 ^{E4}	Retr. Monoc.	Japan	1992-2007	47	64 ± 13	74.5	23.2 ± 3.3	–	8.5	–	46.8	51.1
Mikus et al, 2013 ^{E5}	Retr. Monoc.	Italy	2007-2011	14	52 ± 19	64.3	27.9 ± 5.0	14.3	28.6	–	42.9	21.4
Loforte et al, 2014 ^{E6}	Retr. Multic.	Italy	2006-2012	118	61§	64.4	–	–	33.8	25.7‡,§	–	57.6
Papadopoulos et al, 2015 ^{E7}	Retr. Monoc.	Germany	2001-2013	360	62 ± 17	76.1	–	8.9	–	–	–	55.3
Zhao et al, 2015 ^{E8}	Retr. Monoc.	China	2004-2012	24	59 ± 12	79.2	–	–	–	–	–	83.3
Khorsandi et al, 2016 ^{E9}	Retr. Multic.	UK	1995-2015	23	60 ± 15	85.2	–	–	17.4	–	–	39.1
Mazzeffi et al, 2016 ^{E10}	Retr. Monoc.	USA	2010-2015	23	57 ± 15	60.9	–	–	–	–	–	30.4
Biancari et al, 2017 ^{E11}	Retr. Multic.	Europe/Arabia	2005-2016	148	65 ± 9	78.4	–	16.9	–	19.2 ± 17.7	54.1	100.0
Guihaire et al, 2017 ^{E12}	Retr. Monoc.	France	2005-2014	92	–	57.6	–	–	25.0	–	35.9	13.0
Raffa et al, 2017 ^{E13}	Retr. Monoc.	The Netherlands	2007-2017	83	65§	65.1	26.6 ± 5.35	12.5	20.9	6.6 ± 9.9	38.4	34.2
Slottosh et al, 2017 ^{E14}	Retr. Monoc.	Germany	2008-2016	100	58 ± 15	76.0	26.9 ± 4.9	9.4	20.0	–	37.0	69.0
Zhong et al, 2017 ^{E15}	Retr. Monoc.	China	2009-2016	36	50 ± 12	91.7	25.4 ± 4.3	–	41.7	–	25.0	0.0

BMI, Body mass index; COPD, chronic obstructive pulmonary disease; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; CABG, coronary artery bypass grafting; Retr., retrospective; Monoc., mono-center; Multic., multicenter. *Data are expressed as mean and standard deviation for continuous variables, and as percentage for categorical variables. †Isolated CABG or CABG with concomitant cardiac procedures are all included. ‡Expressed as Logistic EuroSCORE II. §Expressed as mean only, no standard deviation provided. ||Patients with for postcardiotomy ECMO n = 100 among a total 139 ECMO patients; other variables refer to the entire patient cohort.

TABLE E17. Detailed ECMO characteristics of the studies included in the systematic review*

Study (author, y)	Number of patients	ECMO cannulation		ECMO at surgery	ECMO duration, d	Weaning success	IABP
		Central (aorta)	Axillary artery				
Ko et al, 2002 ^{E1}	76	19.7	0.0	51.3	4.1 ± 1.3	48.7	76.0
Rastan et al, 2010 ^{E2}	517	60.8	11.9	41.9	3.3 ± 2.9	63.5	74.1
Pokersnik et al, 2012 ^{E3}	49	34.7	0.0	–	–	55.1	59.2
Unosowa et al, 2012 ^{E4}	47	31.9	0.0	70.2	2.7 ± 2.6	61.7	17.0
Mikus et al, 2013 ^{E5}	14	50.0	0.0	–	9 ± 13.8	50.0	92.9
Loforte et al, 2014 ^{E6}	118	47.5	–	–	10.8*	55.1	100.0
Papadopoulos et al, 2015 ^{E6}	360	36.0	63.1	–	7 ± 1	58.1	31.1
Zhao et al, 2015 ^{E7}	24	4.2	0.0	45.8	4.8 ± 2.9	66.7	87.5
Khorsandi et al, 2016 ^{E9}	23	60.9	0.0	34.8	5.4†	–	39.1
Mazzeffi et al, 2016 ^{E10}	23	60.9	–	13.0	3‡	60.8	–
Biancari et al, 2017 ^{E11}	148	39.9	59.1	51.4	6.4 ± 5.6	–	32.0
Guihaire et al, 2017 ^{E12}	92	15.2	–	46.7	–	–	27.2
Raffa et al, 2017 ^{E13}	83	32.8	–	53.5	5.0‡	49.4	10.5
Slottosh et al, 2017 ^{E14}	100	28.0	0.0	60.0	4.9 ± 3.3	–	83.0
Zhong et al, 2017 ^{E15}	36	19.4	25.0	66.7	3.2 ± 1.4	–	25.0

ECMO, Extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump. *Data are expressed as mean and standard deviation for continuous variables, and as percentage for those categorical. †Expressed as mean only, no standard deviation provided. ‡Expressed as median only, no mean or standard deviation provided.

TABLE E18. Postoperative complications following ECMO implantation in the included studies*

Study (author, y)	Mortality	Bleeding tamponade	CVA	GI complications	RRT	Limb ischemia†	Sepsis
Ko et al, 2002 ^{E1}	43.4	46.1	11.8	–	–	43.4	–
Rastan et al, 2010 ^{E2}	75.2‡	58.0	17.4	18.8	65.0	19.9	–
Pokersnik et al, 2012 ^{E3}	67.3	71.4	6.1	–	32.7	–	–
Unosowa et al, 2012 ^{E4}	70.2	70.2	21.3	–	31.9	25.5	–
Mikus et al, 2013 ^{E5}	50.0	64.3	14.3	–	57.1	–	42.9
Loforte et al, 2014 ^{E6}	53.4	58.4	16.9	–	55.1	5.9	22.0
Papadopoulos et al, 2015 ^{E7}	70.0§	41.1	11.9	16.1	61.1	13.1	–
Zhao et al, 2015 ^{E8}	66.7	16.7	8.3	20.8	29.2	8.3	45.8
Khorsandi et al, 2016 ^{E10}	65.2	8.7	21.7	–	26.0	21.7	–
Mazzeffi et al, 2016 ^{E11}	69.6	8.7	17.4	–	47.8	–	18.8
Biancari et al, 2017 ^{E11}	64.2	41.9	23.6	10.8	45.3	10.8	24.3
Guihaire et al, 2017 ^{E12}	63.0	19.6	3.3	–	–	9.8	–
Raffa et al, 2017 ^{E13}	62.8	46.4	20.2	15.5	29.8	10.7	21.4
Slottosh et al, 2017 ^{E14}	71.0	63.0	–	–	–	–	–
Zhong et al, 2017 ^{E15}	50.0	25.0	11.1	–	25.0	13.9	13.9

CVA, Cerebrovascular accident; GI, gastrointestinal; RRT, renal-replacement therapy. *Data are expressed in percentages. †Lower-limb ischemia defined as an acute impaired circulation to the lower extremities, necessitating endovascular or surgical revascularization, and/or major surgery (ie, amputation). ‡Adjusted mortality for central VA-ECMO cannulation: OR, 0.91 (95% CI, 0.59-1.40, $P = .666$). §Adjusted mortality for central VA-ECMO cannulation: OR, 1.5 (95% CI, 0.45-1.85, $P = .37$).

TABLE E19. Quality assessment of the included studies

Study (author/year)	Newcastle-Ottawa Scale ^{E78}			Cochrane risk of bias analysis ^{E79}					USPSTF design-specific quality criteria ^{E80}
	Selection	Comparability	Outcome	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	
Ko et al, 2002 ^{E1}	**	**	***	Low	High	High	High	High	Poor
Rastan et al, 2010 ^{E2}	**	**	***	High	Low	Low	High	High	Fair
Pokersnik et al, 2012 ^{E3}	**	**	**	High	Low	Low	Low	Low	Fair
Unosowa et al, 2012 ^{E4}	**	**	**	High	High	Unclear	High	Unclear	Poor
Mikus et al, 2013 ^{E5}	**	**	***	Low	Low	Low	Low	Low	Fair
Loforte et al, 2014 ^{E6}	**	*	**	Low	Low	Low	Low	Low	Poor
Papadopoulos et al, 2015 ^{E7}	**	**	**	High	High	Low	High	High	Poor
Zhao et al, 2015 ^{E8}	**	**	**	High	High	Low	High	High	Fair
Khorsandi et al, 2016 ^{E9}	*	*	**	High	High	Low	Low	Low	Poor
Mazzeffi et al, 2016 ^{E10}	***	***	***	High	Low	Low	Low	Low	Fair
Biancari et al, 2017 ^{E11}	***	**	***	Low	High	Low	Low	Low	Fair
Guihaire et al, 2017 ^{E12}	***	*	***	Low	High	Low	Low	Low	Fair
Raffa et al, 2017 ^{E13}	**	*	**	Low	High	High	Low	Low	Fair
Slottosh et al, 2017 ^{E14}	***	***	**	High	High	Low	High	High	Fair
Zhong et al, 2017 ^{E15}	**	**	**	High	High	Low	High	High	Poor

USPSTF, US Preventive Services Task Force; *, 1; **, 2; ***, 3.