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



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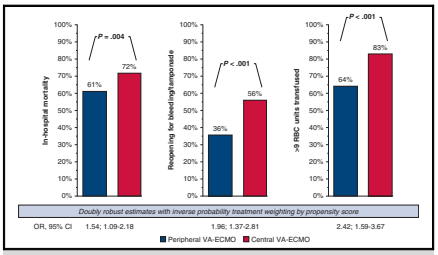
## ABSTRACT

**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 Veno-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 Veno-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 Veno-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 (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, $\chi^2$ 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 | | |
|---|---|---|---|
| | Peripheral VA-ECMO, n = 536 patients | Central VA-ECMO, n = 245 patients | *P* value |
| 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 ($I^2 = 4\%$) 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 ($I^2 = 0\%$, 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; $I^2 = 0\%$). No differences were observed for neurologic events (RR, 0.79; 95% CI, 0.59-1.05; $I^2 = 0\%$) and lower-limb complications (RR, 1.60; 95% CI, 0.99-2.89; $I^2 = 32.7\%$) 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.

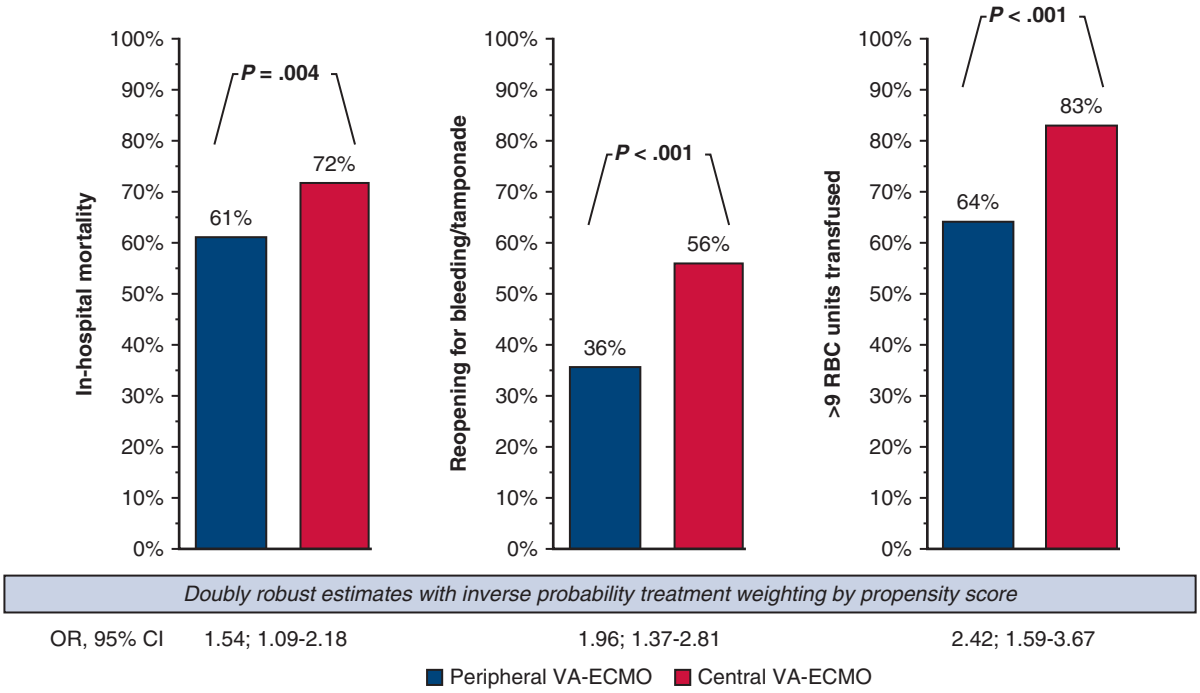


**FIGURE 1.** Central VA-ECMO is associated with greater in-hospital mortality, reopening for bleeding, and blood transfusion than peripheral cannulation in patients affected by postcardiotomy shock following cardiac surgery. The obtained doubly robust estimates (OR and 95% confidence intervals) with 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 colleagues[5] 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 colleagues[6] 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 colleagues[20] 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

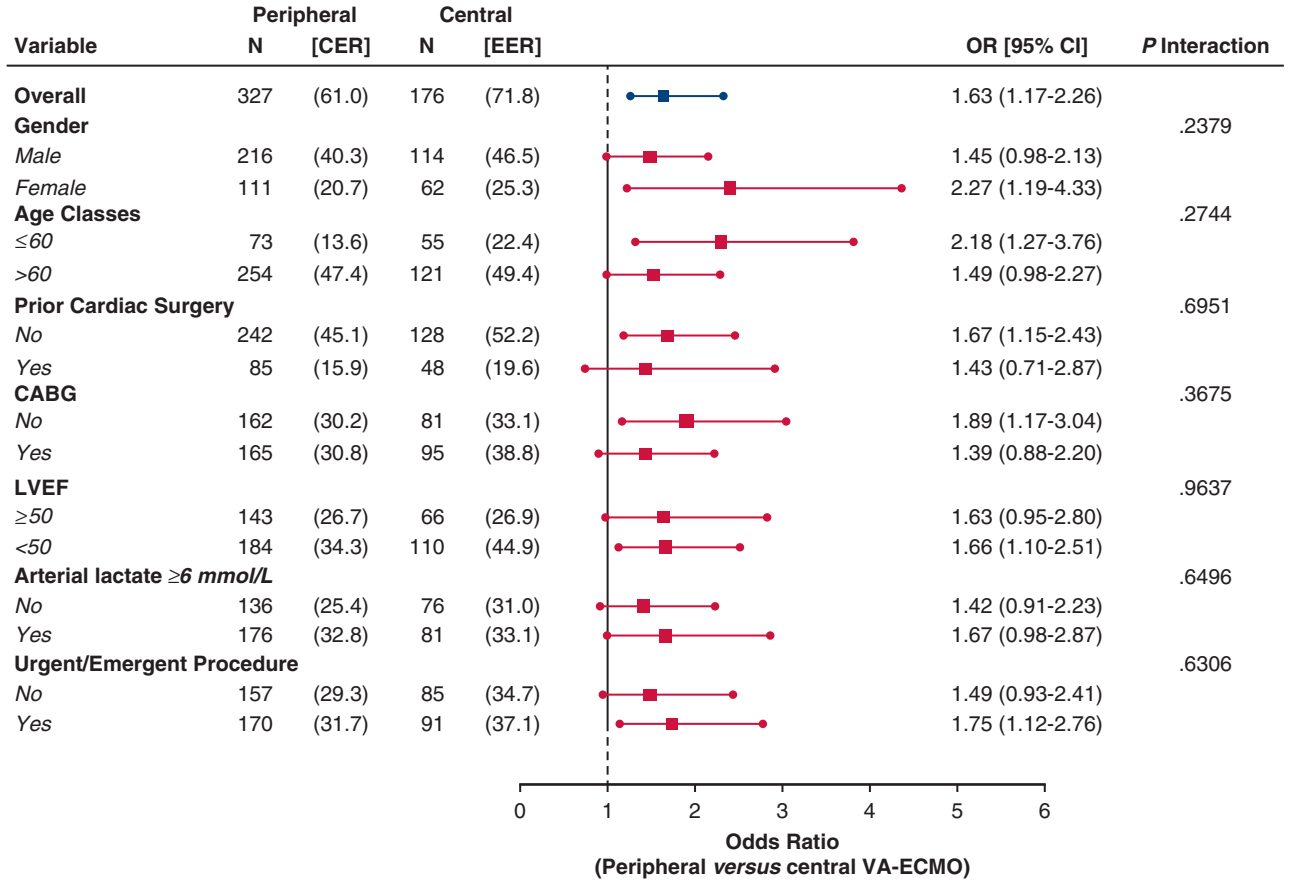


**FIGURE 2.** Subgroup analysis with reference to in-hospital mortality. Comparison is made between peripheral (reference group) and central VA-ECMO cannulation. *CER*, Control event rate; *EER*, experimental event rate; *OR*, odds ratio; *CI*, confidence interval; *CABG*, coronary artery bypass grafting; *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 colleagues[9] 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 colleagues[46] investigated the influence of femoro-femoral versus atrio-aortic ECMO on metabolic and hemodynamic data

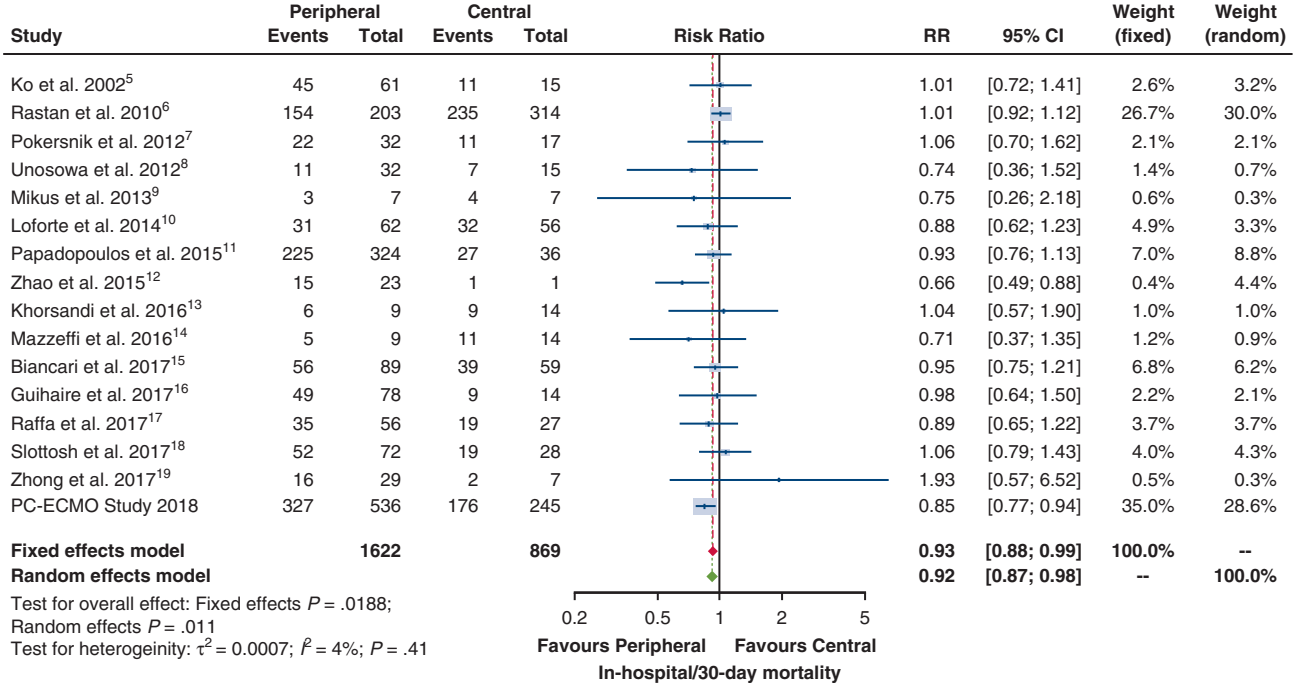


**FIGURE 3.** Forest plot with risk estimates for in-hospital/30-day mortality. *RR*, Risk ratio; *CI*, confidence interval.

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 colleagues[47] 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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E2. Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T, et al. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg*. 2010;139:302-11.

E3. Pokersnik JA, Buda T, Bashour CA, Gonzalez-Stawinski GV. Have changes in ECMO technology impacted outcomes in adult patients developing postcardiotomy cardiogenic shock? *J Card Surg*. 2012;27:246-52.

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E12. Guihaire J, Dang Van S, Rouze S, Rosier S, Roisne A, Langanay T, et al. Clinical outcomes in patients after extracorporeal membrane oxygenation support for post-cardiotomy cardiogenic shock: a single-centre experience of 92 cases. *Interact Cardiovasc Thorac Surg*. 2017;25:363-9.

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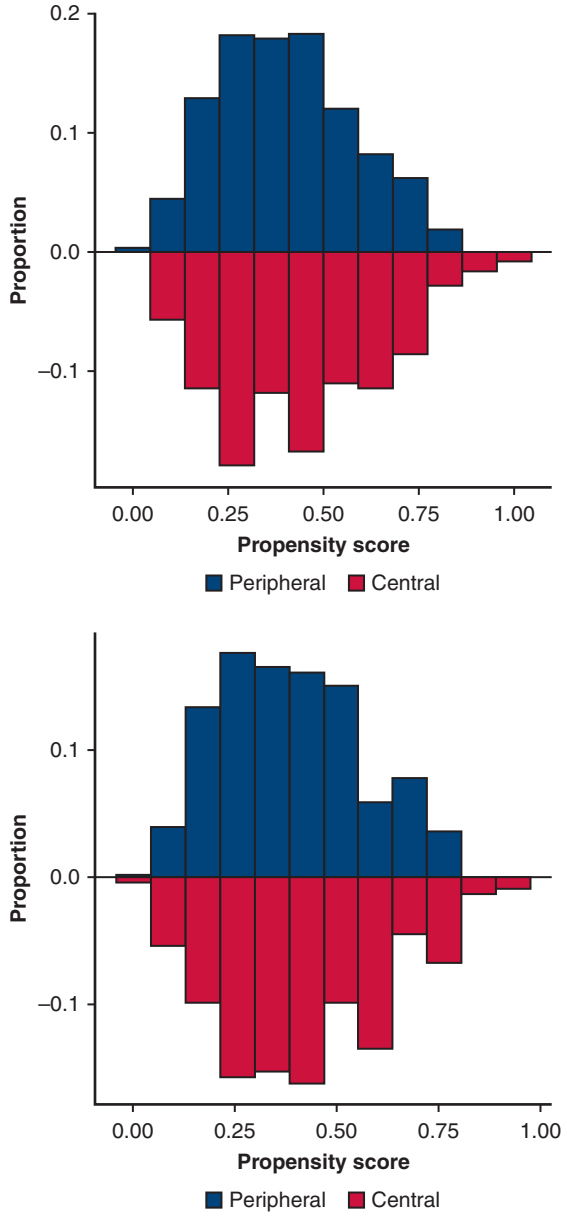



**FIGURE E1.** Mirror histogram of the propensity score with distribution balance for the entire cohort of patients in the *upper panel*, and mirror histogram of the propensity score with distribution balance without patient crossed from peripheral to central venoarterial extracorporeal membrane oxygenation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

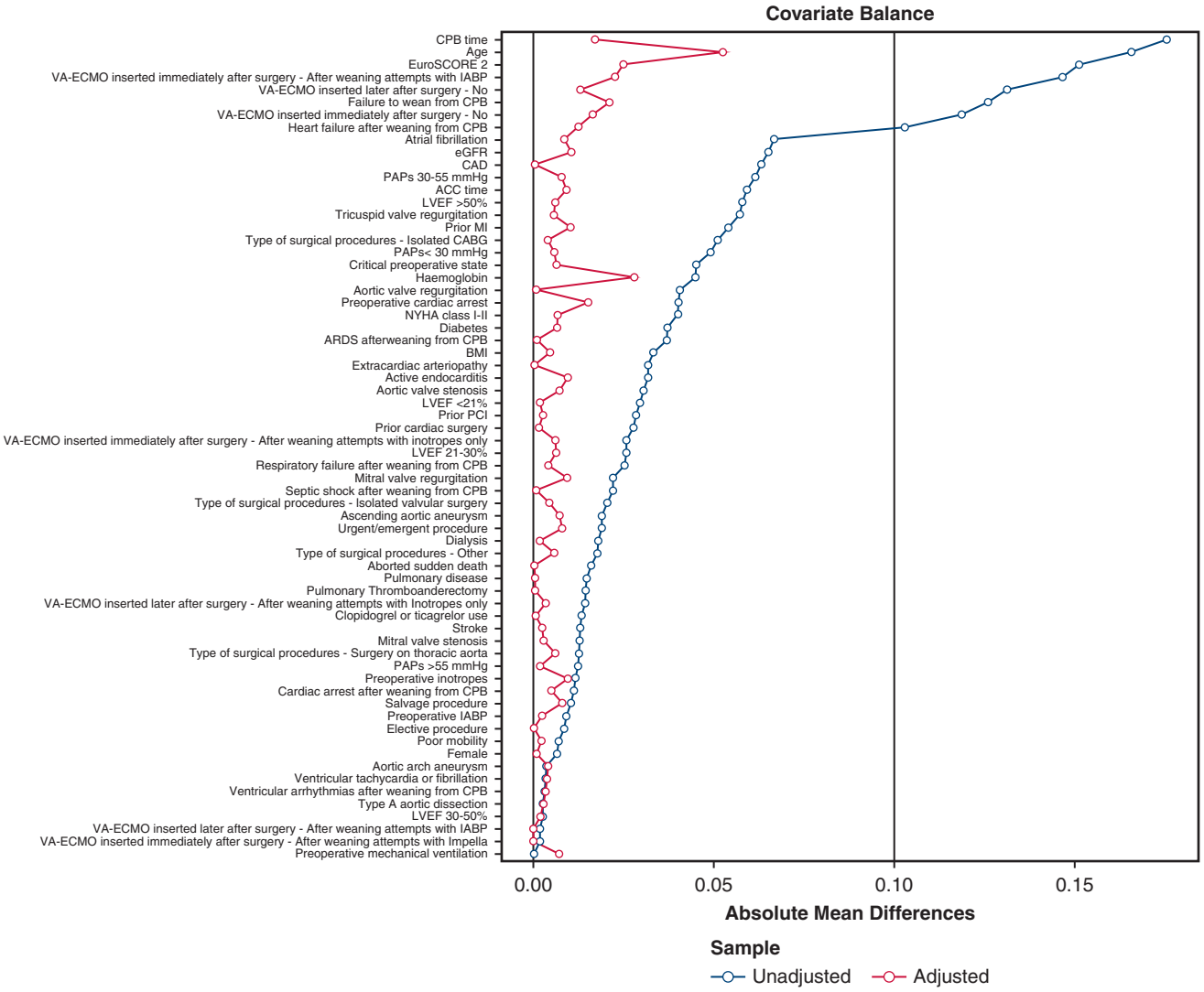



**FIGURE E2.** Love plot summarizing covariate balance before and after conditioning for the entire patient cohort. *CPB*, Cardiopulmonary bypass; *EuroSCORE II*, European System for Cardiac Operative Risk Evaluation II; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *IABP*, intra-aortic 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.

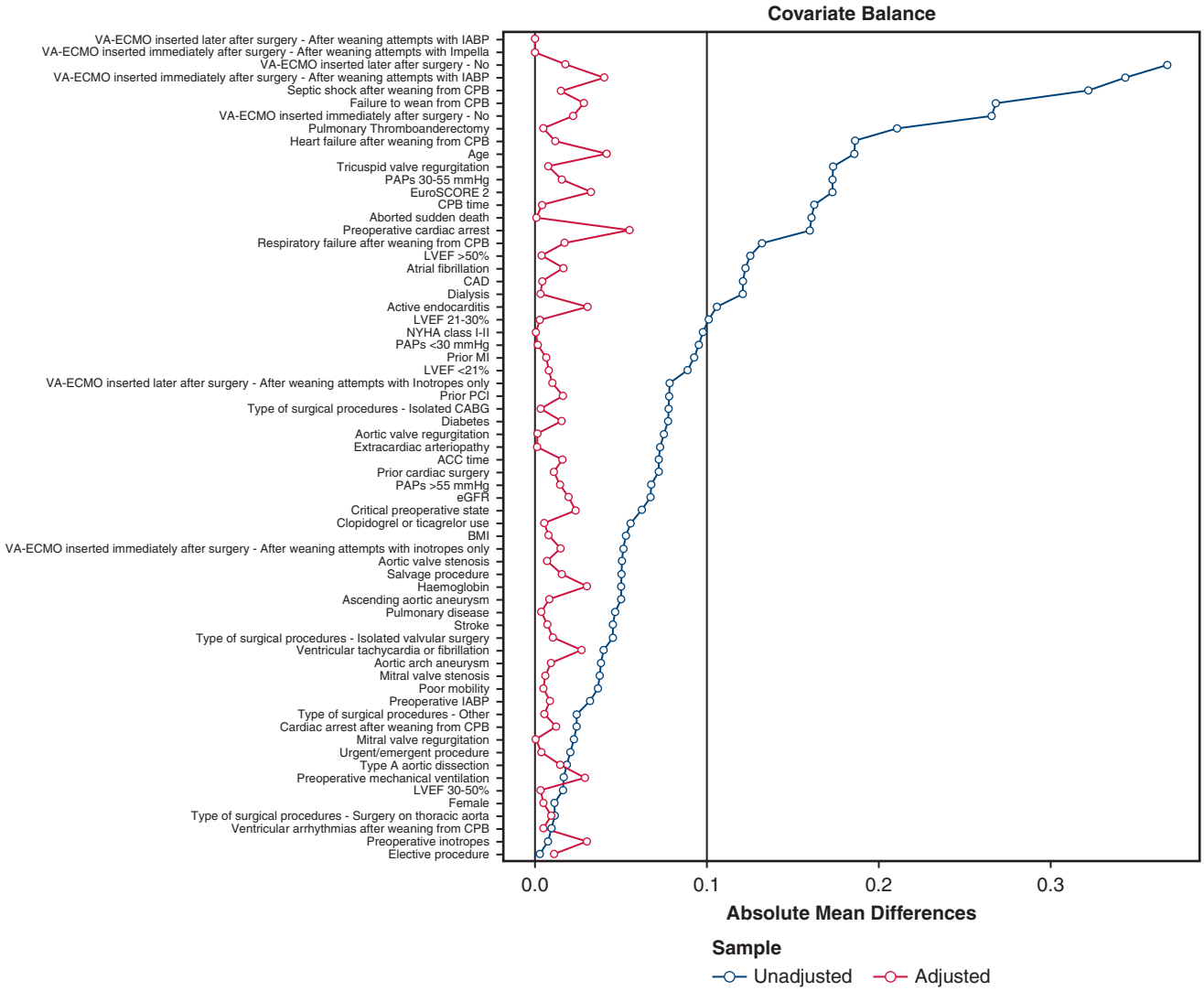



**FIGURE E3.** Love plot summarizing covariate balance before and after conditioning without patient crossed from peripheral to central VA-ECMO group during the study period. *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *CPB*, cardiopulmonary bypass; *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.

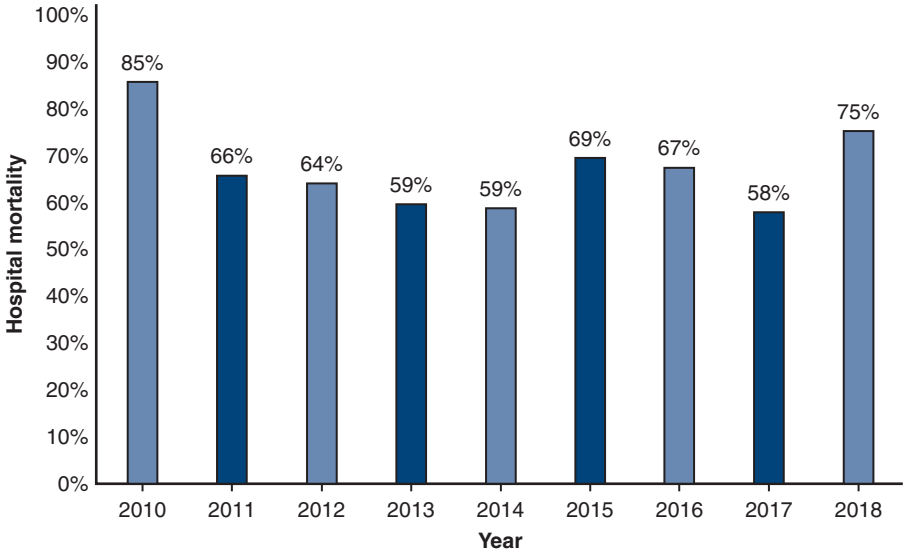



**FIGURE E4.** Hospital mortality during the entire study period ($\chi^2$ test for independence: $P = .26$).

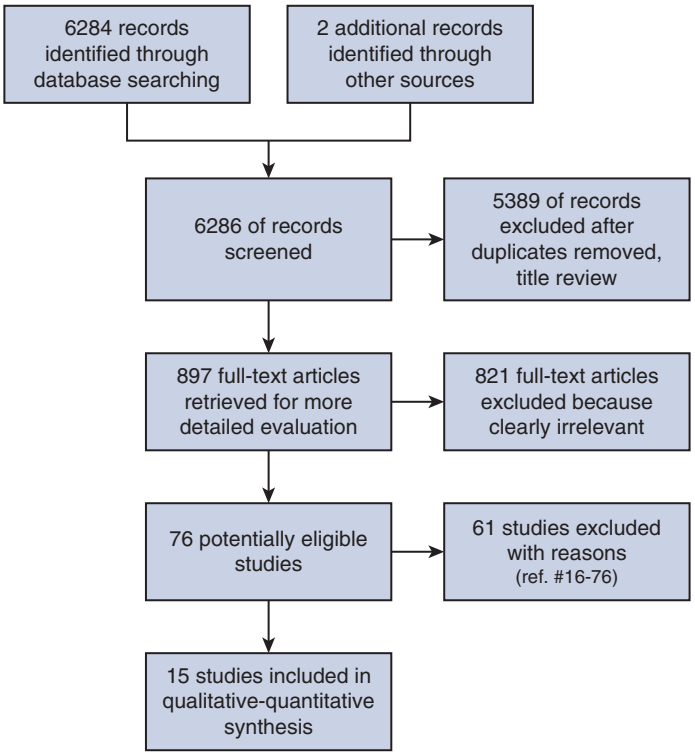



**FIGURE E5.** PRISMA flow chart of search strategy.[E81] *PRISMA*, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

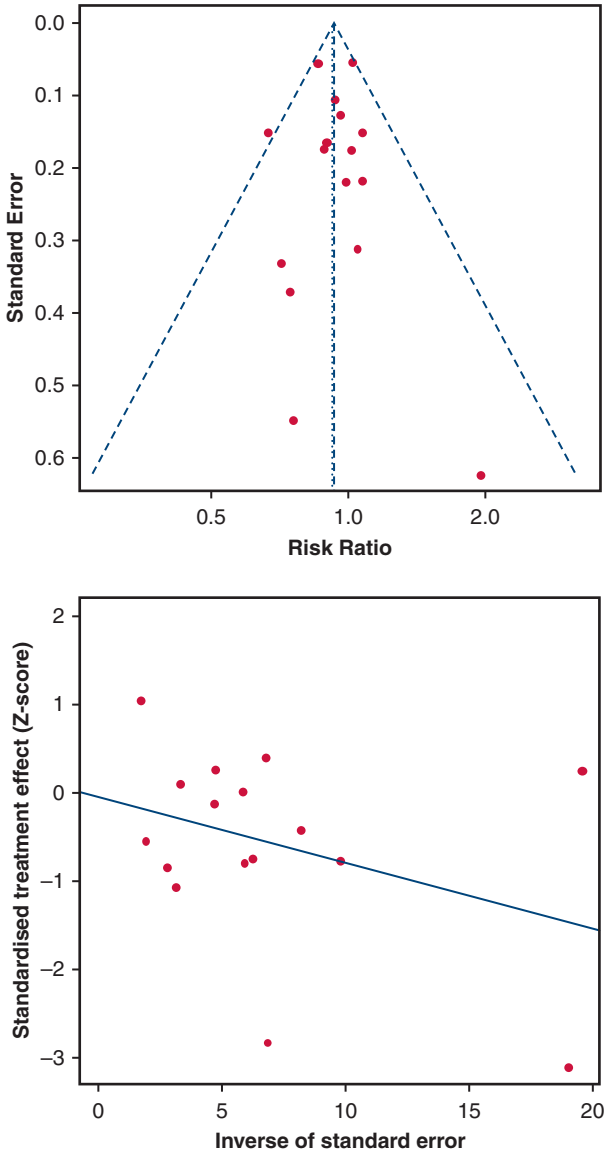



**FIGURE E6.** Funnel plot (*upper panel*) and radial plot (*lower panel*) for in-hospital/30-day mortality showing no heterogeneity among studies and evidence of publication bias (Egger's test, df = 14, $P = .916$), respectively.

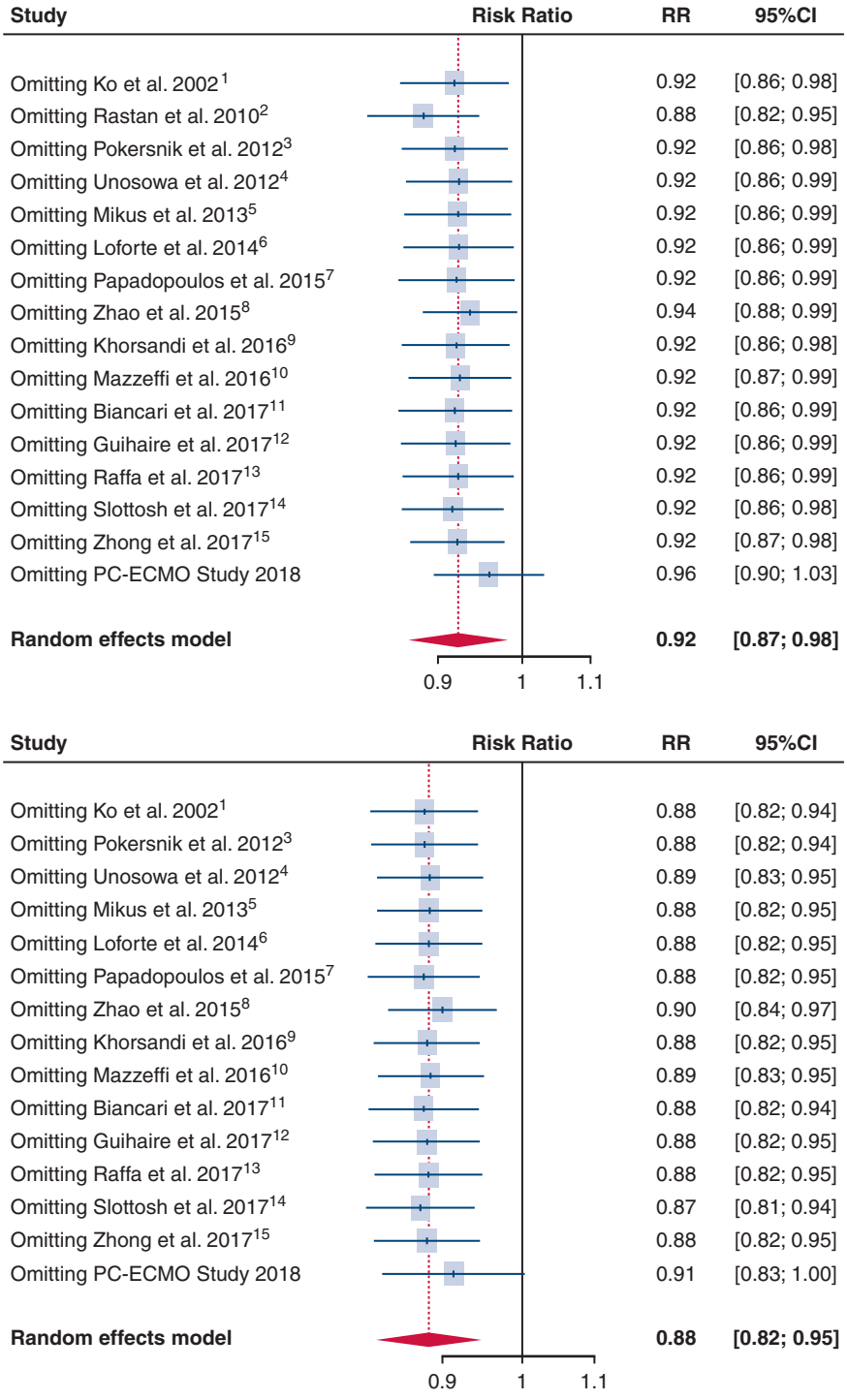



**FIGURE E7.** Leave-one-out meta-analysis (influence analysis) on in-hospital/30-day mortality (*upper panel*), and leave-one-out meta-analysis for sensitivity analysis on in-hospital/30-day mortality after exclusion of the study of Rastan et al,[E2] (*lower panel*). Pooled estimates are calculated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

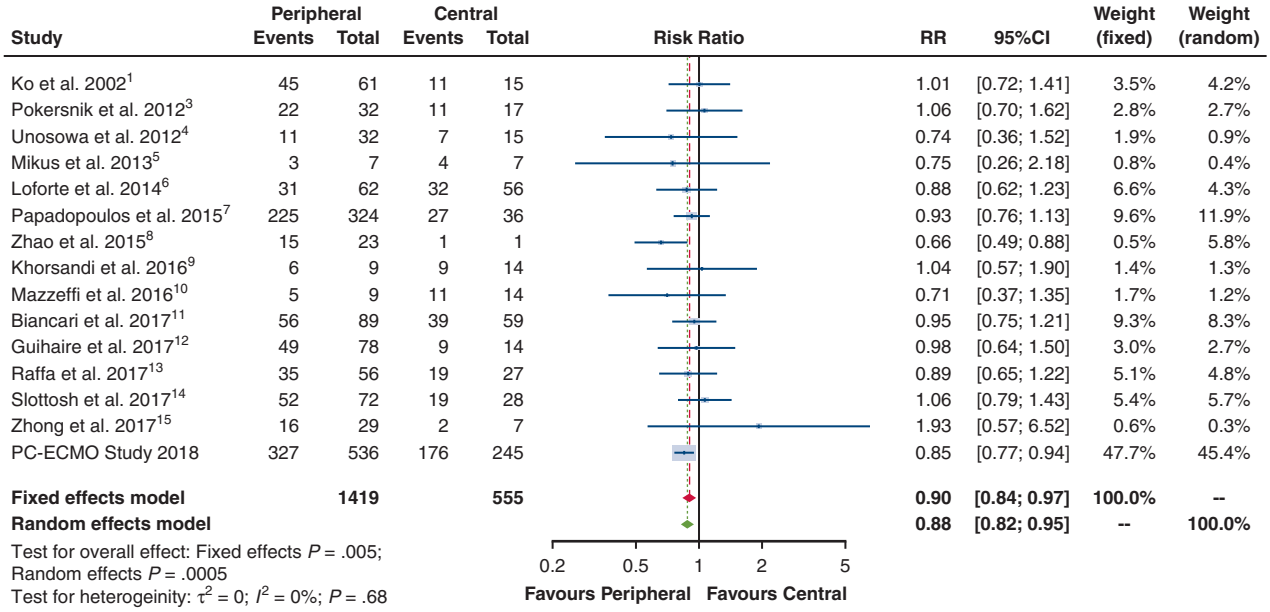



**FIGURE E8.** Forest plots with unadjusted risk estimates for in-hospital/30-day mortality in patients who underwent peripheral versus central extracorporeal membrane oxygenation. *RR*, Risk ratio; *CI*, confidence interval.

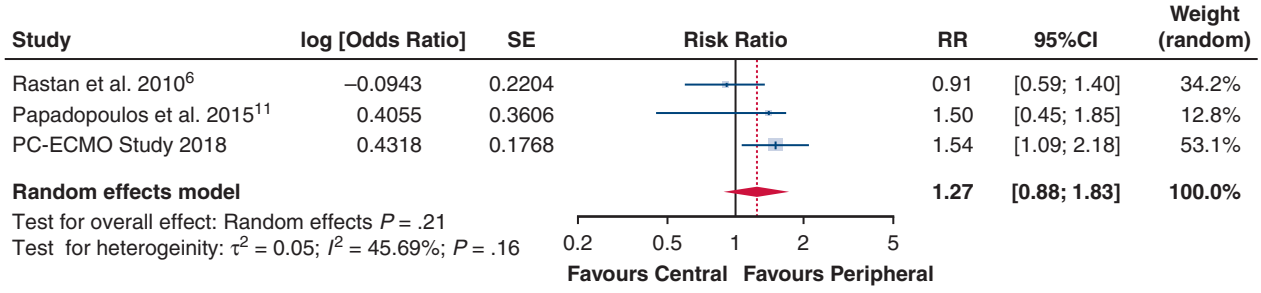
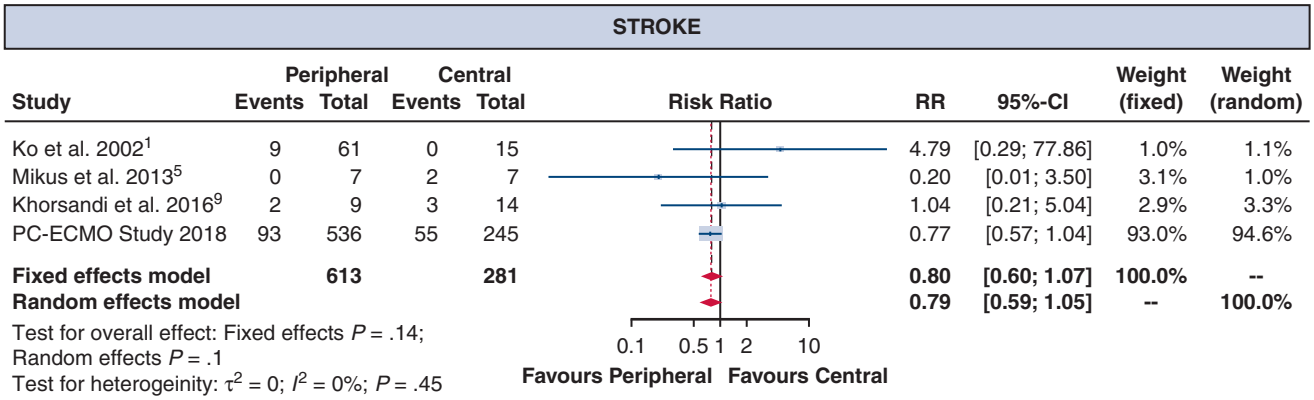
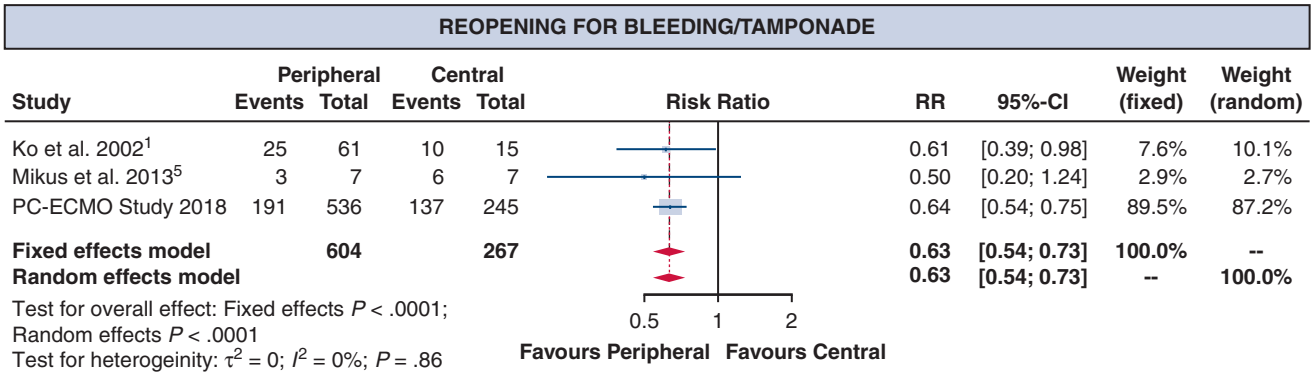



**FIGURE E9.** Forest plot with adjusted risk estimates for in-hospital/30-day mortality in patients who underwent peripheral versus central extracorporeal membrane oxygenation. *SE*, Standard error. *RR*, risk ratio; *CI*, confidence interval.



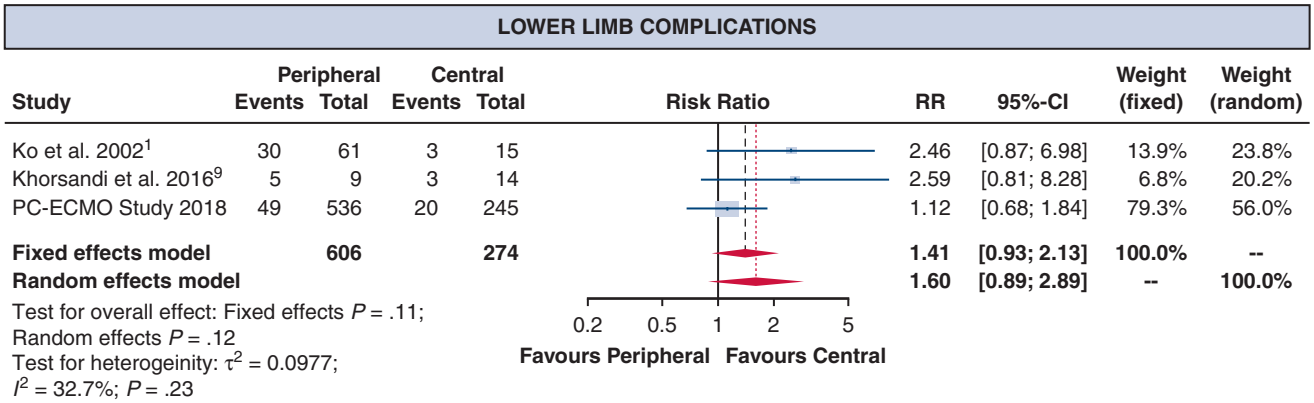




**FIGURE E10.** Forest plots with unadjusted risk estimates for stroke (*top*), reopening for bleeding/tamponade (*central*), and lower-limb complications (*bottom*) in patients who underwent peripheral versus central arterial extracorporeal membrane oxygenation cannulation. *RR*, Risk ratio; *CI*, confidence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

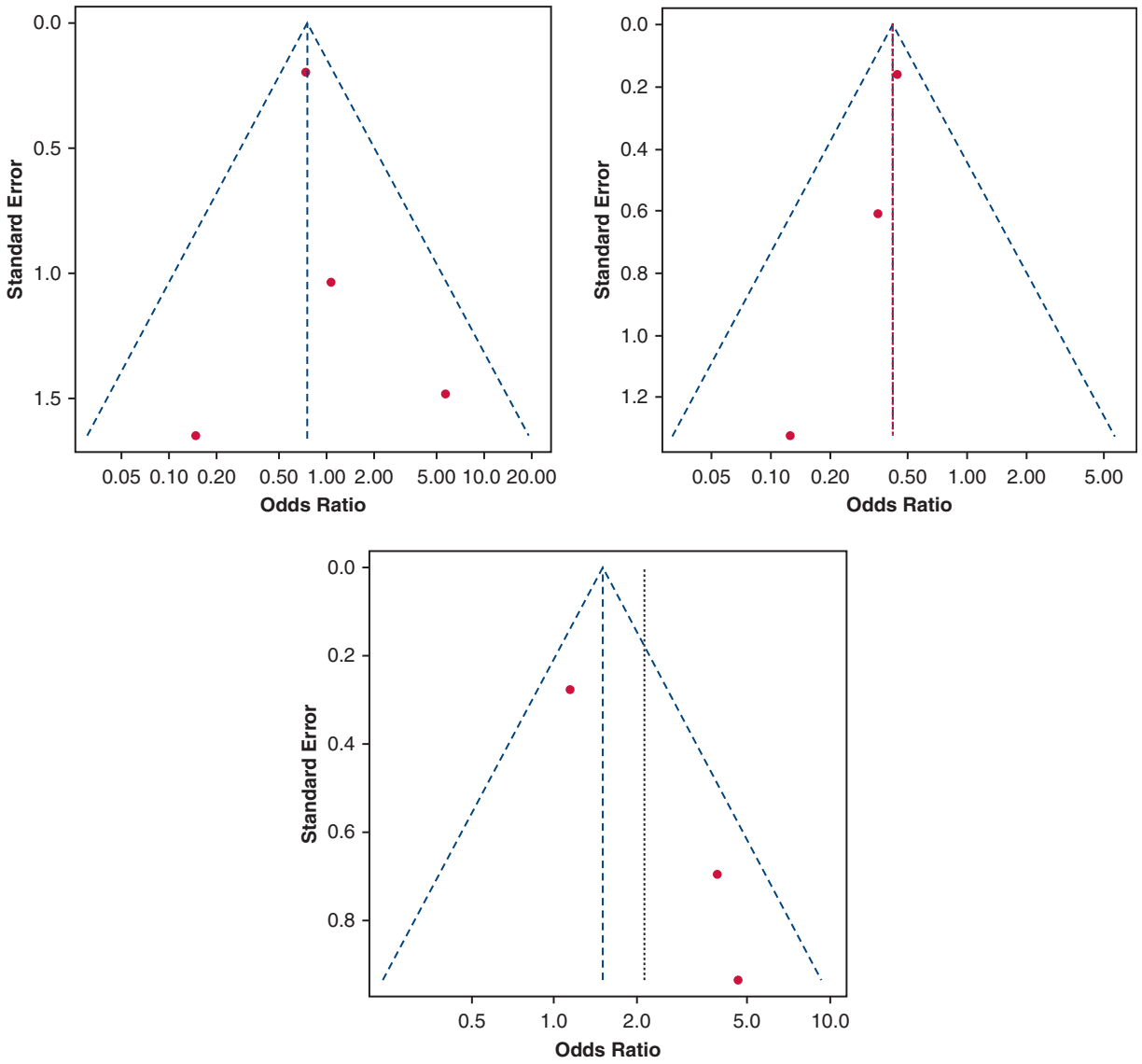



**FIGURE E11.** Funnel plots showing the absence of publication bias in secondary outcomes, stroke (*top left*), reopening for bleeding/tamponade (*top right*), and leg complications (*bottom*).

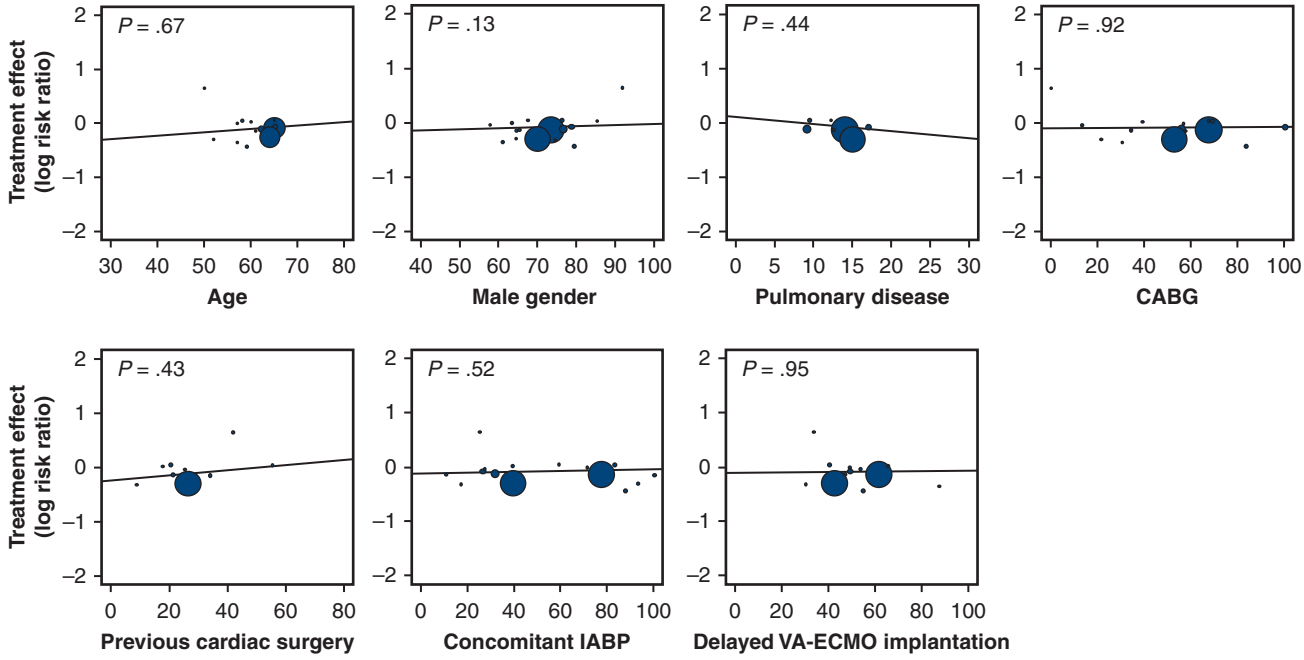



**FIGURE E12.** Meta-regression bubble plots showing the effect of age, sex (proportion of male patients), pulmonary disease, previous cardiac surgery, proportion of patients undergoing CABG, IABP, and delayed VA-ECMO implantation on cannulation site (peripheral versus central VA-ECMO), and in-hospital/30-day 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 | 1 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 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 | 3 |
| | | (b) Describe any methods used to examine subgroups and interactions | 3 |
| | | (c) Explain how missing data were addressed | 3 |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy | – |
| | | (e) Describe any sensitivity analyses | 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 | 3 |
| | | (b) Give reasons for nonparticipation at each stage | 6 |
| | | (c) Consider use of a flow diagram | – |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 3 |
| | | (b) Indicate number of participants with missing data for each variable of interest | 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 | 3,4 |
| | | (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 | – |
| 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, Appenedix 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<br>VA-ECMO after HTx/VAD<br>VV-ECMO |
| Comparator | VA-ECMO cannulation site | No comparison between peripheral versus central VA-ECMO |
| Outcomes | Primary: in-hospital/30-d mortality<br>Secondary (postoperative): re-exploration for bleeding/tamponade; CVA; RRT/dialysis; GI complications; limb ischemia; sepsis; successful ECMO weaning | – |
| Study design | Clinical randomized trials<br>Controlled before-and-after studies<br>Prospective and retrospective cohort studies<br>Cross-sectional studies<br>Case–control studies | Repeat publications of the same analysis or dataset<br>Conference abstracts<br>Editorials and opinion pieces<br>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 | Other |
| 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 | | |
| Silvetti 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 |
| Teman 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*, postcardtomy 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 | | |
|---|---|---|---|
| | Peripheral VA-ECMO, n = 536 patients | Central VA-ECMO, n = 245 patients | *P* value |
| 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 cardia 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**

| | 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 | | | |
| Variable | 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**

| | 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 | | | |
| Variable | 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**

| | 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 | | | |
| Variable | 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**

| | 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 | | | |
| Variable | 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**

| | 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 | | | |
| Variable | 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 | | |
|---|---|---|---|
| | Peripheral VA-ECMO, n = 536 patients | Central VA-ECMO, n = 222 patients | *P* value |
| 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 | | |
|---|---|---|---|
| | Peripheral VA-ECMO, n = 536 patients | Central VA-ECMO, n = 222 patients | *P* value |
| 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 | | |
|---|---|---|---|
| | Peripheral VA-ECMO, n = 536 patients | Central VA-ECMO, n = 222 patients | *P* value |
| 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, | 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 cardia 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**

| | 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 | | | |
| Variable | 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**

| | 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 | | | |
| Variable | Mean | SD | Mean | SD | Mean difference | Variance ratio | KS | Mean | SD | Mean | SD | Mean difference | Mean difference threshold | Variance ratio | KS |
| 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**

| | 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 | | | |
| Variable | 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 cardia 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**

| | Newcastle-Ottawa Scale[E78] | | | Cochrane risk of bias analysis[E79] | | | | | USPSTF |
|---|---|---|---|---|---|---|---|---|---|
| Study (author/year) | Selection | Comparability | Outcome | Selection bias | Performance bias | Detection bias | Attrition bias | Reporting bias | design-specific quality criteria[E80] |
| 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 |
| Slottosch 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.