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Intra-aortic balloon pump after VA-ECMO reduces mortality in patients with cardiogenic shock: an analysis of the Chinese extracorporeal life support registry

Kexin Wang[1†], Liangshan Wang[1†], Jiawang Ma[1], Haixiu Xie[1], Chenglong Li[1], Xing Hao[1], Zhongtao Du[1*], Hong Wang[1*] and Xiaotong Hou[1*]

Abstract

Background The role of intra-aortic balloon pump (IABP) combined with venoarterial extracorporeal membrane oxygenation (VA-ECMO) in patients with cardiogenic shock (CS) remains unclear. This study investigated the effect of applying IABP for left ventricle (LV) unloading after VA-ECMO on reducing mortality in patients with CS.

Methods Data from 5,492 consecutive patients with CS treated with VA-ECMO between January 2017 and July 2023 were collected from the CSECLS registry. The primary outcome was in-hospital mortality. The secondary outcomes included 30-day mortality, survival on VA-ECMO, and various complications. The association between the application of IABP after VA-ECMO and in-hospital outcomes was assessed.

Results Among 5,492 patients undergoing VA-ECMO (mean age 54.7 ± 15.1 years, 3,917 [71.3%] male), 832 (15.1%) received IABP after VA-ECMO. Before VA-ECMO, a higher incidence of cardiac intervention (13.9% vs. 16.7%) and myocardial infarction (12.0% vs. 14.8%) (all $P < 0.05$) was seen in the IABP after VA-ECMO group. In this cohort, the IABP after VA-ECMO group had a lower in-hospital mortality (52.5% vs. 48.0%, $P = 0.017$) and a higher survival rate on VA-ECMO (75.4% vs. 79.4%, $P = 0.014$). On multivariate modeling, the use of IABP after VA-ECMO was associated with a lower risk of in-hospital mortality (adjusted odds ratio[aOR], 0.823 [95% confidence interval [CI], 0.686–0.987]; $P = 0.035$) and on-support mortality (aOR, 0.828 [95% CI, 0.688–0.995]; $P = 0.044$). However, the use of IABP after VA-ECMO was also associated with an increased incidence of complications, including mechanical (aOR: 1.905, [95% CI, 1.278–2.839]; $P = 0.002$), bleeding (aOR: 1.371, [95% CI, 1.092–1.721]; $P = 0.007$), renal (aOR: 1.252, [95% CI, 1.041–1.505]; $P = 0.017$), and pulmonary (aOR: 1.768, [95% CI, 1.446–2.163]; $P < 0.001$).

Conclusion In this multicenter retrospective study, the use of IABP after VA-ECMO was associated with lower in-hospital mortality in patients with CS. These findings suggest that IABP may offer advantages for LV unloading in patients with CS treated with VA-ECMO, but further validation through randomized controlled trials is warranted to better understand the balance of risks and benefits.

Keywords Intra-aortic balloon pump, Venoarterial extracorporeal membrane oxygenation, Cardiogenic shock

†Kexin Wang and Liangshan Wang have contributed equally to this work.
Zhongtao Du, Hong Wang, and Xiaotong Hou are co-corresponding authors.

*Correspondence:
Zhongtao Du
zhongtaodu@126.com
Hong Wang
914286855@qq.com
Xiaotong Hou
xt.hou@ccmu.edu.cn
[1] Present Address: Center for Cardiac Intensive Care, Beijing Anzhen Hospital, Capital Medical University, Beijing, People's Republic of China

Introduction

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) has been increasingly used to treat cardiogenic shock (CS) over the past few decades [1–3]. However, the mortality rate of patients with CS is approximately 50% [1, 4]. VA-ECMO applies a high afterload to the heart because of the reversed vascular flow, which negatively affects survival [5, 6]. Physiologically, the intra-aortic balloon pump (IABP) appears to assist VA-ECMO by reducing left ventricular (LV) afterload, which may increase coronary blood flow, provide a pulsatile blood supply to improve circulatory status, facilitate myocardial recovery, increase the probability of successful VA-ECMO weaning, and theoretically improve survival in patients with CS [6, 7]. Although some studies have shown that combining VA-ECMO with IABP reduces mortality in patients with CS, in these studies, IABP was not exclusively used for LV unloading after VA-ECMO. The decision-making and objectives for applying IABP before VA-ECMO differed from those for LV unloading, which created some confounding bias [8–13]. Therefore, it is unclear whether the routine initiation of IABP for LV unloading after VA-ECMO is beneficial for patients with CS. To address this uncertainty, this study excluded patients who received IABP before VA-ECMO and aimed to determine the association between the use of IABP for LV unloading after VA-ECMO and outcomes in patients with CS.

Methods

Study design and population

We retrospectively evaluated consecutive patients who underwent VA-ECMO between January 2017 and July 2023 from the Chinese Extracorporeal Life Support (CSECLS) registry, a voluntary database that collects information on VA-ECMO use, complications, and outcomes in adults and children from over 112 centers in China. Data were collected using a standardized electronic reporting sheet submitted via the organization's website. This study was approved by the institutional ethics committee board of the Capital medical university, Beijing Anzhen hospital (2019040X).

Patients with CS undergoing VA-ECMO were screened as shown in Fig. 1. The inclusion criteria for this study were: (1) patients who received VA-ECMO for CS between January 2017 and July 2023 and (2) age greater than 18 years. Patients were excluded if they met any of the following criteria: (1) pregnant, (2) missing data, (3) underwent ECMO mode conversion, (4) central cannulation and other forms of LV unloading, and (5) Patients who received IABP before VA-ECMO.

Outcome and definitions

The primary outcome was in-hospital mortality. Secondary outcomes included 30-day mortality, survival on ECMO (survival 48 h after successful weaning from ECMO), and various complications including mechanical (any of the following: membrane lung oxygenation impairment, tubing rupture, joint cracking, heat exchanger warming malfunction, intubation problems, and thrombosis), bleeding (any of the following: gastrointestinal bleeding, bleeding at intubation, surgery-related bleeding, hemolysis, FHb > 50 mg/dl, and DIC), neurological (any of the following: cerebral hemorrhage, cerebral infarction, seizures, and brain death), renal (any of the following: elevated creatinine and continuous renal replacement therapy), pulmonary (any of the following: pneumothorax, pulmonary hemorrhage, and infection), metabolic (any of the following: glucose < 40 mg/dL, glucose > 240 mg/dL, PH < 7.2, and PH > 7.6), and limb complications (any of the following: distal ischemia, necrosis, fasciotomy techniques, amputation, removal of embolus, and endoluminal stripping).

Statistical analysis

All statistical analyses were performed using SPSS (version 19.0; SPSS Inc., Chicago, IL, USA) and R 4.3.2 (http://www.R-project.org). Patient characteristics were reported as mean values with standard deviation for continuous variables or frequency with proportion for categorical variables. Continuous variables were compared using Student's t-test or the Mann–Whitney U test, while categorical data were analyzed using Fisher's exact test or Pearson's chi-square test. The 30-day survivals was calculated using the Kaplan–Meier method, and the log-rank test was used for comparison between the two groups. $P < 0.05$ was considered statistically significant. In-hospital mortality, on-support mortality, and complication rates were analyzed as dichotomous outcomes

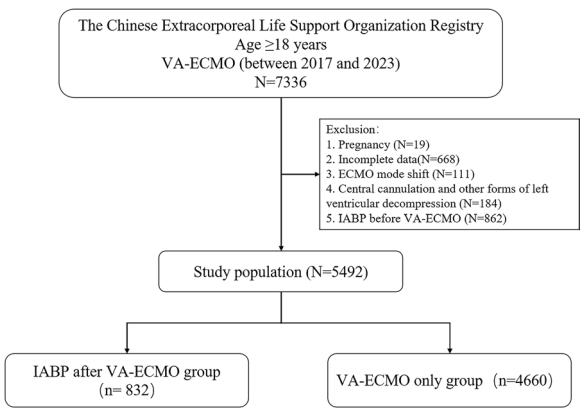

Fig. 1 Study flowchart

and compared using the chi-square test and multivariate logistic regression modeling. The covariates for multivariate modeling included age, gender, body mass index (BMI), comorbid conditions, pre-ECMO cardiac arrest (CA), and vasopressors. For sensitivity analysis, logistic regression models were generated to examine the association between IABP and in-hospital mortality across important subgroups of gender, age, obesity status, pre-ECMO diagnosis, pH levels, pre-ECMO CA, vasopressor use, and large center (more than 30 cases annually). In the presence of missing pH, PaCO2, and PaO2 data (N = 1747), multiple imputation by chained equations were employed to account for missingness. This method was chosen to reduce potential biases caused by incomplete data, under the assumption that data were missing at random. A total of 5 imputed datasets were generated, and the results were pooled to obtain valid estimates of the model parameters. A sensitivity analysis was also performed to ensure that the results remained consistent with and without imputation (Supplemental material). Given the potential for confounding in this observational dataset, the following variables were used to calculate the propensity score to reduce the effects of known possible confounders: gender, age, BMI, medical history (cardiac intervention, myocardial infarction, hypertension, diabetes, hyperlipidemia, heart failure, chronic kidney disease, cirrhosis, and smoking), pre-ECMO CA, pre-ECMO vasopressors, and pre-ECMO mechanical ventilation. Based on these propensity scores, patients treated with IABP after VA-ECMO were matched 1:1 to patients treated with VA-ECMO alone, using the nearest neighbor method. The standardized mean difference for each covariate was calculated in the propensity-matched cohort.

Results

Patient characteristics

The study cohort is detailed in Table 1. A total of 5,492 patients were enrolled in the registry and included in the analysis, of whom 4,660 (84.9%) were treated with ECMO only and 832 (15.1%) were treated with IABP after ECMO. In the total cohort, mean age was 54.7 ± 15.1 years, and 71.3% of the patients were male. The IABP after ECMO group had a higher incidence of cardiac intervention, myocardial infarction, cirrhosis, and smoking history than the ECMO only group ($P = 0.040$, $P = 0.031$, $P = 0.040$, and $P = 0.025$, respectively). Pre-ECMO diagnosis was categorized as myocarditis in 9.9% of the patients, post-cardiotomy cardiogenic shock (PCS) in 9.0%, acute myocardial infarction (AMI) in 24.4%, chronic heart failure in 0.4%, and sepsis in 5%, with no significant differences between the two groups. A total of 43% of the patients had CA before ECMO, and the IABP after ECMO group had a lower rate of CA than the ECMO only group, although this difference was not statistically significant ($P = 0.117$). After propensity matching, baseline characteristics were well balanced (all SMF approached 0) between 832 patients in the IABP after ECMO group and 832 in the ECMO only group (Supplemental Table 1). The use of vasopressors was higher in the IABP after ECMO group than in the ECMO only group ($P = 0.005$), and the use of more than 3 types of vasopressors was more frequent in the IABP after ECMO group ($P < 0.001$). However, a decrease in the type of vasopressor used was more frequent in the IABP after ECMO group (10.6% vs. 7.8%, $P = 0.007$). Additionally, the proportion of patients requiring mechanical ventilation before ECMO was lower in the IABP after ECMO group ($P = 0.021$). The pre-ECMO lactate level was 8.86 ± 7.95 mmol/L in the IABP after ECMO group and 9.11 ± 14.1 mmol/L in the ECMO only group ($P = 0.168$). During ECMO, the lactate levels at 4 h and 24 h were 8.51 ± 6.73 mmol/L and 4.69 ± 4.98 mmol/L, respectively, in the IABP after ECMO group, and 8.47 ± 6.54 mmol/L and 5.06 ± 5.39 mmol/L, respectively, in the ECMO only group. There were no significant differences between the two groups at any time point.

Primary outcome

The IABP after ECMO group exhibited a lower rate of in-hospital mortality than the ECMO only group (48.0% vs. 52.5%, $P = 0.017$) and a higher rate of survival on ECMO (79.4% vs. 75.4%, $P = 0.014$) (Table 2), and the same outcomes were observed in the propensity-matched cohort between the two groups, with low mortality (48.0% vs. 53.6%, $P = 0.024$) and high survival during ECMO (79.4% vs. 74.5%, $P = 0.020$) (Table 3). Additionally, the proportion of patients with lactate level decreasing from 4 to 24 h after ECMO implantation was higher in the IABP after ECMO group (64.8% vs. 59.3%, $P = 0.009$) (Table 1). Multivariate logistic regression modeling revealed an association between the use of IABP after ECMO and a lower risk of in-hospital mortality (adjusted odds ratio[aOR], 0.823 [95% CI, 0.686–0.987]; $P = 0.035$) and on-support mortality (aOR, 0.828 [95% CI, 0.688–0.995]; $P = 0.044$) (Fig. 2). The 30-day mortality risk was lower in patients treated with IABP after ECMO than in those treated with ECMO alone, which is consistent with the results of propensity score matching (Fig. 3). The association between the use of IABP after ECMO and lower in-hospital mortality remained consistent across clinical subgroups. However, the effect is not universal across all subgroups. Significant reductions in mortality were observed in specific groups such as patients aged ≥ 65 (aOR, 0.73 [95% CI, 0.56–0.95]); $P = 0.021$), those with BMI < 28 (aOR, 0.80 [95% CI, 0.68–0.93];

Table 1 Baseline characteristics of patients supported with VA-ECMO stratified by IABP

Variable Mean (SD)/n (%)	Overall (N = 5492)	ECMO only (N = 4660)	IABP after VA-ECMO (N = 832)	*P* value
Age	54.7 (15.1)	54.5 (15.2)	55.5 (14.6)	0.087
Male	3917 (71.3%)	3320 (71.2%)	597 (71.8%)	0.796
weight	67.4 (12.2)	67.3 (12.2)	67.8 (11.9)	0.325
BMI	23.9 (3.63)	23.8 (3.66)	24.0 (3.47)	0.065
Medical history				
Cardiac surgery	325 (5.9%)	277 (5.9%)	48 (5.8%)	0.907
Cardiac intervention	788 (14.3%)	649 (13.9%)	139 (16.7%)	0.040
Myocardial infarction	684 (12.5%)	561 (12.0%)	123 (14.8%)	0.031
Hypertension	2146 (39.1%)	1820 (39.1%)	326 (39.2%)	0.976
Diabetes	1140 (20.8%)	957 (20.5%)	183 (22.0%)	0.363
Hyperlipidemia	600 (10.9%)	500 (10.7%)	100 (12.0%)	0.299
Heart failure	779 (14.2%)	662 (14.2%)	117 (14.1%)	0.956
Neurological disease	343 (6.2%)	290 (6.2%)	53 (6.4%)	0.933
Chronic respiratory diseases	275 (5.0%)	242 (5.2%)	33 (4.0%)	0.159
Chronic kidney disease	199 (3.6%)	176 (3.8%)	23 (2.8%)	0.181
Cirrhosis	51 (0.9%)	49 (1.1%)	2 (0.2%)	0.040
Anticoagulants	560 (10.2%)	465 (10.0%)	95 (11.4%)	0.232
Smoking	1652 (30.1%)	1374 (29.5%)	278 (33.4%)	0.025
Pre ECMO diagnosis				
Myocarditis	545 (9.9%)	459 (9.8%)	86 (10.3%)	0.712
Post-cardiotomy cardiogenic shock	497 (9.0%)	428 (9.2%)	69 (8.3%)	0.447
Acute myocardial infarction	1341 (24.4%)	1139 (24.4%)	202 (24.3%)	0.954
Chronic heart failure	22 (0.4%)	20 (0.4%)	2 (0.2%)	0.620
Sepsis	273 (5.0%)	238 (5.1%)	35 (4.2%)	0.310
Other	2814 (51.2%)	2376 (51.0%)	438 (52.6%)	0.399
Pre-ECMO cardiac arrest	2364 (43.0%)	2027 (43.5%)	337 (40.5%)	0.117
ECPR	1293 (23.5%)	1119 (24.0%)	174 (20.9%)	0.058
Pre-ECMO Hemodynamics				
Heart rate (bpm)	107 (43.5)	107 (43.5)	108 (43.5)	0.763
SBP (mmHg)	75.8 (24.6)	76.1 (24.9)	74.1 (22.9)	0.112
DBP (mmHg)	46.2 (16.6)	46.2 (16.8)	46.0 (15.7)	0.696
MAP (mmHg)	55.9 (18.5)	56.1 (18.7)	55.2 (17.5)	0.555
Pre-ECMO blood gases				
PH	7.22 (0.230)	7.22 (0.234)	7.24 (0.208)	0.014
HCO3(mmol/L)	18.3 (8.37)	18.3 (8.20)	18.6 (9.18)	0.206
PO2 (mmHg)	110 (98.4)	109 (97.6)	117 (102)	0.078
PCO2 (mmHg)	43.7 (25.7)	44.0 (26.4)	42.1 (21.2)	0.029
Lac(mmol/L)	9.07 (13.3)	9.11 (14.1)	8.86 (7.95)	0.168
SaO2(%)	86.6 (18.0)	86.5 (18.1)	87.2 (17.6)	0.353
Pre-ECMO support				
Vasopressors	3627 (66.0%)	3042 (65.3%)	585 (70.3%)	0.005
One type	1326 (24.1%)	1142 (24.5%)	184 (22.1%)	0.150
Two types	1345 (24.5%)	1124 (24.1%)	221 (26.6%)	0.143
Three types	956 (17.4%)	776 (16.7%)	180 (21.6%)	< 0.001
Mechanical ventilation	4484 (81.6%)	3829 (82.2%)	655 (78.7%)	0.021
Blood gases for 4 h during ECMO				
PH	7.33 (0.235)	7.33 (0.223)	7.33 (0.294)	0.186
HCO3(mmol/L)	19.7 (9.05)	19.7 (9.48)	19.7 (6.34)	0.775
PO2 (mmHg)	203 (148)	204 (150)	198 (138)	0.993

Table 1 (continued)

Variable Mean (SD)/n (%)	Overall (N = 5492)	ECMO only (N = 4660)	IABP after VA-ECMO (N = 832)	*P* value
PCO2 (mmHg)	36.2 (15.9)	36.3 (16.5)	35.7 (12.2)	0.167
Lac(mmol/L)	8.48 (6.57)	8.47 (6.54)	8.51 (6.73)	0.749
SaO2(%)	95.9 (9.84)	95.9 (9.72)	96.1 (10.4)	0.958
Blood gases for 24 h during ECMO				
PH	7.40 (0.17)	7.39 (0.17)	7.41 (0.11)	0.066
HCO3(mmol/L)	23.5 (9.08)	23.6 (9.53)	22.7 (5.05)	0.015
PO2 (mmHg)	166 (117)	168 (119)	148 (93.9)	0.019
PCO2 (mmHg)	37.6 (13.6)	37.8 (14.1)	36.6 (9.20)	0.001
Lac(mmol/L)	5.01 (5.34)	5.06 (5.39)	4.69 (4.98)	0.173
SaO2(%)	97.2 (11.1)	97.3 (11.6)	96.4 (7.31)	0.041
Decrease in lactate from 4 to 24 h	3174 (59.9%)	2762 (59.3%)	412 (64.8%)	0.009
During ECMO support				
Vasopressors	3393 (61.8%)	2796 (60.0%)	597 (71.8%)	< 0.001
One type	1360 (24.8%)	1156 (24.8%)	204 (24.5%)	0.894
Two types	1215 (22.1%)	969 (20.8%)	246 (29.6%)	< 0.001
Three types	818 (14.9%)	671 (14.4%)	147 (17.7%)	0.017
Mechanical ventilation	4024 (73.3%)	3401 (73.0%)	623 (74.9%)	0.273
Decrease in types of vasopressors	452 (8.2%)	364 (7.8%)	88 (10.6%)	0.007
Duration of the supports				
ECMO assistance (hour)	104 (203)	104 (215)	108 (112)	0.003
ICU (day)	13.4 (108)	11.9 (23.9)	21.7 (271)	0.010
Mechanical ventilation (h)	189 (407)	188 (399)	195 (449)	0.022
Hospitalization (day)	18.1 (28.5)	18.0 (28.0)	18.3 (31.2)	0.045

Data are presented as mean (SD) or n (%)

BMI, body mass index; ECMO, extracorporeal membrane oxygenation; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure

Table 2 Outcomes between the two groups

Outcomes	Overall (N = 5492)	ECMO only (N = 4660)	IABP after VA-ECMO (N = 832)	*P* value
In-hospital mortality	2846 (51.8%)	2447 (52.5%)	399 (48.0%)	0.017
Survival on ECMO	4176 (76.0%)	3515 (75.4%)	661 (79.4%)	0.014
Complications				
Mechanical	216 (3.9%)	170 (3.6%)	46 (5.5%)	0.013
Bleeding	870 (15.8%)	722 (15.5%)	148 (17.8%)	0.106
Neurological	279 (5.1%)	228 (4.9%)	51 (6.1%)	0.158
Renal	2568 (46.8%)	2160 (46.4%)	408 (49.0%)	0.164
Pulmonary	1177 (21.4%)	945 (20.3%)	232 (27.9%)	< 0.001
Metabolic	2291 (41.7%)	1950 (41.8%)	341 (41.0%)	0.671
Limb	337 (6.1%)	273 (5.9%)	64 (7.7%)	0.051

Data are presented as n (%)

ECMO, extracorporeal membrane oxygenation

$P=0.005$), patients without myocarditis (aOR,0.81 [95% CI, 0.69–0.94]; $P=0.006$), PCS (aOR, 0.80 [95% CI, 0.69–0.94]; $P=0.005$), AMI (aOR, 0.83[95% CI, 0.70–0.98]; $P=0.032$), or sepsis (aOR, 0.85 [95% CI, 0.73–0.99]; $P=0.032$), fewer vasopressors (0–1 type) (aOR, 0.77 [95% CI, 0.63–0.95]; $P=0.015$), and in larger medical centers (aOR, 0.77 [95% CI, 0.63–0.95]; $P=0.016$). No significant interactions were observed between IABP after ECMO and the variables defining the subgroups

Table 3 Outcomes and duration of the supports for the PSM cohort

Variable mean (SD)/n (%)	ECMO only (N = 832)	IABP after ECMO (N = 832)	*P* value
In-hospital mortality	446 (53.6%)	399 (48.0%)	0.024
Survival on ECMO	620 (74.5%)	661 (79.4%)	0.020
Complications			
Mechanical	32 (3.8%)	46 (5.5%)	0.031
Bleeding	114 (13.7%)	148 (17.8%)	0.026
Neurological	43 (5.2%)	51 (6.1%)	0.457
Renal	370 (44.5%)	408 (49.0%)	0.069
Pulmonary	173 (20.8%)	232 (27.9%)	< 0.001
Metabolic	347 (41.7%)	341 (41.0%)	0.803
Limb	50 (6.0%)	64 (7.7%)	0.207
Duration of the supports			
ECMO assistance (hour)	96.5 (99.3)	108 (112)	0.007
ICU (day)	12.5 (24.1)	21.7 (271)	0.061
Mechanical ventilation (hour)	188 (313)	195 (449)	0.133
Hospitalization (day)	17.5 (22.6)	18.3 (31.2)	0.119

PSM, propensity-matched; ECMO, extracorporeal membrane oxygenation

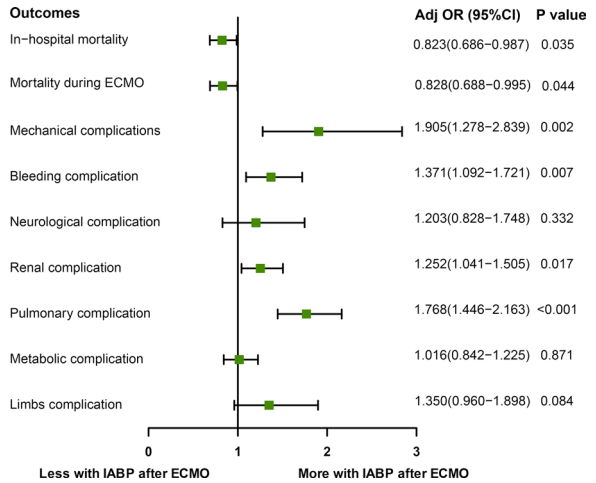

Fig. 2 The relationship between the use of IABP and outcomes Adjusted for age, gender, BMI, comorbid conditions, pre-ECMO cardiac arrest, and vasopressors.

(Fig. 4). These findings are consistent with those of the propensity-matched cohort (Supplemental Fig. 1).

Other outcomes

Mechanical complications ($P=0.013$) and pulmonary complications ($P<0.001$) were more common in the IABP after ECMO group. However, there was an association between the use of IABP after ECMO and increased risks of mechanical complications (aOR, 1.905 [95% CI, 1.278–2.839]; $P=0.002$), bleeding complications (aOR, 1.371 [95% CI, 1.092–1.721]; $P=0.007$), renal complications (aOR, 1.252 [95% CI, 1.041–1.505]; $P=0.017$), and pulmonary complications (aOR, 1.768 [95% CI, 1.446–2.163]; $P<0.001$) on logistic regression analyses (Fig. 2). Additionally, the IABP after ECMO group had a significantly longer duration of ECMO assistance ($P=0.003$), ICU stay ($P=0.010$), mechanical ventilation ($P=0.022$), and hospitalization ($P=0.045$) than the ECMO only group (Table 1). These results were corroborated in the propensity-matched cohort, as shown in the Table 3 and Supplemental Fig. 2.

Discussion

In this large multicenter registry of patients with CS supported by VA-ECMO, we demonstrated that the use of IABP for LV unloading after VA-ECMO significantly reduced both in-hospital and on-support mortality compared to VA-ECMO support alone. The combination of VA-ECMO with IABP improved the circulatory status and may have increased tissue perfusion, as indicated by the higher proportion of patients with decreases in the lactate level and types of vasopressors among patients in the IABP after ECMO group. However, the use of IABP after ECMO was also associated with an increased incidence of complications.

VA-ECMO provides temporary circulatory support for patients with CS; however, its increased LV afterload can lead to LV dilatation, impairing recovery and potentially reducing patient survival [14–17]. To address LV dilatation after ECMO, current strategies for LV unloading include both invasive and noninvasive approaches [15, 18]. Among the invasive methods, IABP and Impella are the most common, with IABP being the most straightforward, simple, and widely used strategy for LV unloading

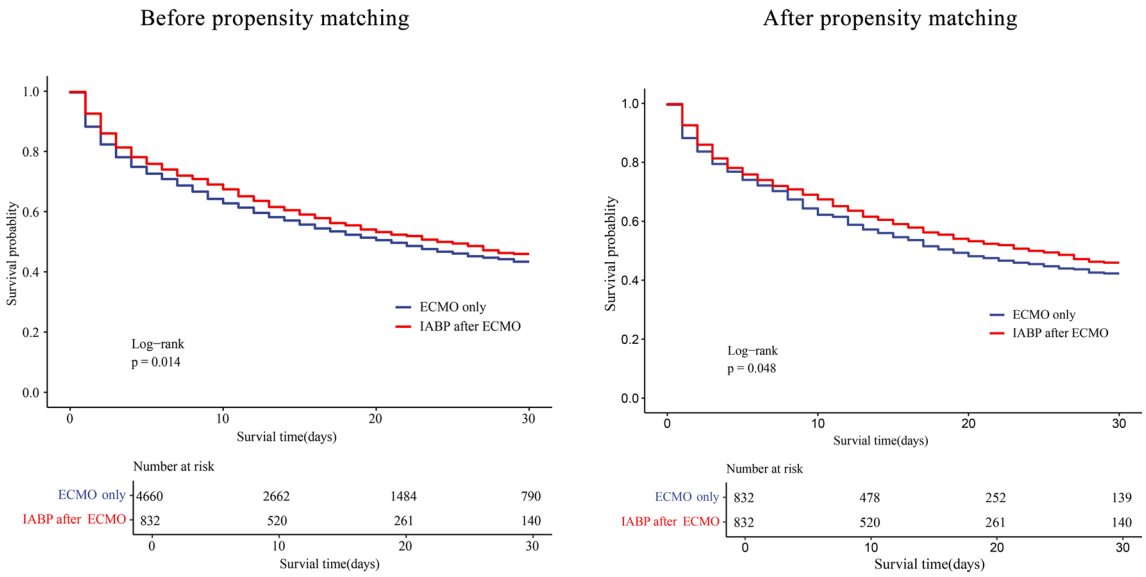

Fig. 3 The curve of survival between the two group

Variable	Number(%)	ECMO only	IABP after ECMO	Adj OR (95%CI)	Mortality	P value	P for interaction
All patients	5492 (100.00)	2447/4660	399/832	0.83 (0.72 ~ 0.97)		0.016	
Gender							0.644
Male	3917 (71.32)	1780/3320	296/597	0.85 (0.71 ~ 1.01)		0.069	
Female	1575 (28.68)	667/1340	103/235	0.79 (0.60 ~ 1.04)		0.093	
Age, years							0.254
< 65	3879 (70.63)	1653/3297	273/582	0.88 (0.74 ~ 1.05)		0.151	
≥ 65	1613 (29.37)	794/1363	126/250	0.73 (0.56 ~ 0.95)		0.021	
BMI							0.102
< 28	4999 (91.02)	2231/4252	350/747	0.80 (0.68 ~ 0.93)		0.005	
≥ 28	493 (8.98)	216/408	49/85	1.21 (0.75 ~ 1.94)		0.429	
Myocarditis							0.120
No	4947 (90.08)	2327/4201	373/746	0.81 (0.69 ~ 0.94)		0.006	
Yes	545 (9.92)	120/459	26/86	1.22 (0.74 ~ 2.03)		0.433	
PCS							0.079
No	4995 (90.95)	2214/4232	357/763	0.80 (0.69 ~ 0.94)		0.005	
Yes	497 (9.05)	233/428	42/69	1.30 (0.77 ~ 2.19)		0.320	
AMI							0.952
No	4151 (75.58)	1873/3521	306/630	0.83 (0.70 ~ 0.98)		0.032	
Yes	1341 (24.42)	574/1139	93/202	0.84 (0.62 ~ 1.13)		0.254	
Sepsis							0.366
No	5219 (95.03)	2302/4422	382/797	0.85 (0.73 ~ 0.99)		0.032	
Yes	273 (4.97)	145/238	17/35	0.61 (0.30 ~ 1.23)		0.168	
PH							0.556
< 7.2	3151 (57.37)	1561/2719	227/432	0.82 (0.67 ~ 1.01)		0.058	
≥ 7.2	2341 (42.63)	886/1941	172/400	0.90 (0.72 ~ 1.12)		0.333	
Pre-ECMO CA							0.605
No	3128 (56.96)	1113/2633	186/495	0.82 (0.67 ~ 1.00)		0.052	
Yes	2364 (43.04)	1334/2027	213/337	0.89 (0.70 ~ 1.13)		0.352	
Vasopressors							0.632
0-1	3191 (58.10)	1320/2760	179/431	0.77 (0.63 ~ 0.95)		0.015	
> 1	2301 (41.90)	1127/1900	220/401	0.83 (0.67 ~ 1.04)		0.100	
Large center							0.323
No	3073 (55.95)	1395/2673	198/400	0.90 (0.73 ~ 1.11)		0.316	
Yes	2419 (44.05)	1052/1987	201/432	0.77 (0.63 ~ 0.95)		0.016	
					0 1 2		
					Less with IABP after ECMO	More with IABP after ECMO	

Fig. 4 Subgroup analyses examining the association between IABP use after ECMO and mortality

[19]. Several studies have directly examined the relationship between VA-ECMO combined with IABP and in-hospital mortality. However, these studies often suffer from biases due to limitations such as small sample sizes and lack of adjustment for baseline characteristics [11, 20–23]. Retrospective analyses of ELSO registry data have indicated that LV unloading is associated with lower in-hospital mortality with strategies including both IABP and percutaneous ventricular assist devices (pVAD). However, most cases of LV unloading in that study escalated from IABP or pVAD to VA-ECMO and occurred before VA-ECMO rather than after VA-ECMO [9]. A study of Japanese national multicenter data on the effects of IABP in patients with CS under VA-ECMO showed a significantly lower 28-day mortality rate in the group receiving both VA-ECMO and IABP. However, the indications for IABP use and its timing in this study were not clearly defined [8]. Similarly, an analysis of the CSECLS registry database found no mortality benefit from combining ECMO with IABP in patients with CS, and that study included cases in which IABP was escalated to VA-ECMO [12]. The lack of consistency in the indications for IABP use and the timing of its application across these studies, along with the fact that not all studies specifically aimed at LV unloading, has left the question of whether IABP should be routinely used for LV unloading after VA-ECMO unresolved. This study specifically excluded cases in which IABP was upgraded to VA-ECMO and clarified the relationship between LV unloading with IABP after VA-ECMO and reduced in-hospital mortality.

Theoretically, IABP reduces LV preload and afterload, increases stroke volume and coronary perfusion, and simultaneously enhances peripheral tissue perfusion, thereby improving patient prognosis [13, 19]. Lactate levels serve as an indirect marker of tissue perfusion and microcirculatory function [24]. Previous studies have highlighted the significance of lactate and lactate clearance as valuable tools for evaluating the effectiveness of ECMO therapy for CS. Notably, lactate clearance following ECMO support is highly associated with in-hospital mortality, particularly in post-cardiotomy patients [25, 26]. In our study, the use of IABP after ECMO resulted in more patients experiencing a decrease in lactate levels and a reduction in the use of vasopressors, which could theoretically be attributed to the role of IABP in improving circulatory status, restoring vital organ perfusion, and enhancing microcirculation in patients with CS [19, 27]. The ability of IABP to increase tissue perfusion, improve microcirculation, reduce lactate levels, and decrease the need for vasopressors further underscores its potential benefits when used alongside VA-ECMO in patients with CS. The survival benefits of IABP after VA-ECMO in our study may be attributed to several key physiological mechanisms. IABP directly reduce LV afterload and improve cardiac efficiency. Additionally, the elevation of diastolic blood pressure induced by the IABP increases coronary blood flow, which aids myocardial recovery. Furthermore, the IABP provides a pulsatile blood supply that improves tissue perfusion and microcirculation, thereby reducing mortality.

A systematic review and meta-analysis reported that neurological, gastrointestinal, and limb-related complications did not significantly differ between patients receiving VA-ECMO with and without concurrent IABP [11]. In the IABP- SHOCK II trial [28], the rate of major bleeding did not differ between patients with AMI-CS treated and not treated with IABP. When VA-ECMO and IABP are used simultaneously, the occurrence of complications such as bleeding may depend more on VA-ECMO management. Earlier studies did not find an increase in complications related to IABP, possibly because of analytical methodological limitations and variability in the detection of adverse events. The data in this study were obtained from a large multicenter registry in China to standardize the definition of adverse events to reduce bias [29, 30]. Mechanical, bleeding, renal, and pulmonary complications are also associated with IABP use. Bleeding may be associated with vascular injury caused by a device that requires additional arterial devices [31]. The higher rate of renal injury may be associated with hemolysis-induced pigment nephropathy [32]. Pulmonary complications are more often observed in patients with pulmonary infections and are mainly associated with the presence of infection-prone features in patients with poor baseline conditions. Currently, the decision to combine VA-ECMO with IABP implantation is complex, and the key parameters for initiating IABP are not clearly defined [33]. The requirement for LV unloading depends on the complex interplay between native right and left heart function, systemic arterial properties, and VA-ECMO blood flow. In addition, the extent of LV unloading varies widely across medical and device therapies, with IABP being the most commonly used therapy for LV unloading in China. The present study found that combined IABP after VA-ECMO was associated with a lower mortality rate, particularly in older patients and those with a lower BMI. Additionally, larger medical centers with more advanced technical expertise appeared to achieve better outcomes with IABP after ECMO, suggesting that center-specific factors may influence the success of the intervention. These results suggested the variability in practices across centers, underscoring the need for further investigation into how institutional factors such as size, experience, and technical capabilities might influence clinical decision-making and patient outcomes. While the use of IABP after VA-ECMO was associated with a lower mortality rate, it also led

more complications. This highlights the need for appropriate patient selection and rigorous management. Future studies are needed to identify the factors that increase or decrease the risk of complications in this setting and can be used to guide decisions regarding IABP use.

Limitation

The main limitation of this study is its observational design, which inherently includes the presence of residual confounders. Despite efforts to mitigate these issues through matching, the inability to exclude all residual and unmeasured confounders remains a challenge. The retrospective nature of data collection also introduces potential issues such as incomplete or missing events. In addition, the CSECLS registry database did not have detailed vasopressor doses or the vasoactive-inotropic score (VIS), and therefore could not directly indicate the role of IABP in VIS. This gap prevents us from directly evaluating the effect of IABP on vasopressor use, which is an important consideration when assessing hemodynamic support strategies. Although complete data on mortality outcomes were available, some variables had missing data, which could have introduced bias into the study results. Despite using multiple imputation to address missing pH, PaCO2, and PaO2 data from 1747 patients, the possibility of bias due to non-random missingness cannot be fully excluded. While sensitivity analyses showed no significant impact of imputation on the results, caution is warranted in the interpretation of findings where data were incomplete. Although we performed a stratified analysis by center size, variations in institutional protocols, physician expertise, and resource availability across centers could have affected the decision to use IABP. Another limitation is that, while patients who received IABP before ECMO were excluded, the specific indications for IABP implantation was physician-decision, whether for LV unloading or routine use, were not clearly defined. Future research should focus on determining the optimal timing for IABP use after ECMO initiation in patients with CS. Additionally, the lack of post-discharge follow-up data in the Chinese registry meant that the study could only assess survival and prognosis during hospitalization. Therefore, future studies should aim to clarify the benefits and long-term prognostic impact of combining IABP with ECMO in patients with CS through comprehensive randomized controlled trials and extended follow-up assessments.

Conclusion

In this large, multicenter cohort study of patients with CS treated with IABP after ECMO was associated with lower mortality but also with more complications than VA-ECMO alone. Although this study supports the use of IABP for LV unloading in patients with CS treated with VA-ECMO, appropriate patient selection and strict management are required to mitigate complications. This study supports the results of randomized controlled trials that evaluated IABP in patients with CS supported with VA-ECMO.

Abbreviations

VA-ECMO	Venoarterial extracorporeal membrane oxygenation
CS	Cardiogenic shock
IABP	Intra-aortic balloon pump
CA	Cardiac arrest
LV	Left ventricular
CSECLS	Chinese extracorporeal life support
PCS	Post-cardiotomy cardiogenic shock
AMI	Acute myocardial infarction
BMI	Body mass index
pVAD	Percutaneous ventricular assist devices
VIS	Vasoactive-inotropic score

Supplementary Information

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Supplementary Material 1.

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Author contributions

KW, LW, JM, HX, CL, XH, and ZD collected and analyzed the patient data. KW and LW performed the statistical analysis. KW, LW, and HW were major contributors in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional ethics committee/review board of the Beijing Anzhen Hospital. Informed consent for demographic, physiological and hospital-outcome data analyses was not obtained because this observational study did not modify existing diagnostic or therapeutic strategies.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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