

Intra-aortic balloon pump impacts the regional haemodynamics of patients with cardiogenic shock treated with femoro-femoral veno-arterial extracorporeal membrane oxygenation

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Abstract

Aims To investigate the impact of intra-aortic balloon pump (IABP) on the regional haemodynamics of patients with severe cardiogenic shock undergoing femoro-femoral veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

Methods and results From July 2017 to April 2018, a total of 39 adult patients with cardiogenic shock receiving both IABP and ECMO for circulatory support were enrolled consecutively in a university-affiliated cardiac surgery intensive care unit. The blood flow rates (BFRs) of the bilateral femoral artery (IABP side: iFA, ECMO side: eFA) and carotid artery (left: LCA, right: RCA) and the velocity time integral (VTI) of aortic root were assessed by ultrasonography and compared when IABP was on and off. Seventeen of 39 (43.6%) patients survived to discharge, and 29 (74.4%) survived on ECMO. A total of 172 pairs of data (IABP on and off) were collected in this study, measured on the median of 2.0 (1.0, 4.5) days after patients received VA-ECMO. The BFR on both sides of FA (iFA: 176.4 ± 104.5 vs. 152.2 ± 139.8 mL/min, $P < 0.01$; eFA: 299.3 ± 279.9 vs. 242.4 ± 258.8 mL/min, $P < 0.01$) and the aortic VTI (10.1 ± 4.4 vs. 8.5 ± 4.4 cm, $P < 0.01$) decreased significantly when turning the IABP off, while the BFR on both sides of CA remained unchanged (LCA: 555.7 ± 326.9 vs. 578.6 ± 328.0 mL/min, $P = 0.27$; RCA: 550.0 ± 331.1 vs. 533.0 ± 303.5 mL/min, $P = 0.30$). The LCA BFR dramatically increased after turning the IABP off (296.8 ± 129.7 vs. 401.4 ± 278.1 mL/min, $P = 0.02$) in patients with cardiac stunning (defined as pulse pressure ≤ 5 mmHg). However, there was no significant difference in LCA BFR between IABP-On and IABP-Off (359.6 ± 105.4 mL/min vs. 389.6 ± 139.3 mL/min, $P = 0.31$) in patients with cardiac stunning receiving a higher ECMO blood flow (> 3.5 L/min).

Conclusions Concomitant IABP used in patients undergoing femoro-femoral VA-ECMO was associated with increased aortic VTI and BFR in bilateral FA. The change in CA BFR depended on cardiac function. A decreased LCA BFR was observed in patients with cardiac stunning when IABP was turned on, which might be compensated by a higher ECMO blood flow. Further study is needed to confirm the relationship between BFR and extremities and neurological complications.

Keywords Extracorporeal membrane oxygenation; Intra-aortic balloon pump; Cardiogenic shock; Regional haemodynamics

Received: 3 December 2021; Revised: 14 April 2022; Accepted: 6 May 2022

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Introduction

Cardiogenic shock is associated with a high mortality rate of up to 50%.¹ Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is a temporary mechanical circulatory support device that has been increasingly used to treat cardiogenic shock in recent decades.^{2–4} However, VA-ECMO increases left ventricular (LV) afterload attributable to retrograde aortic perfusion, especially in femoro-femoral VA-ECMO. This could slow myocardial recovery or damage the myocardium and negatively affect survival.^{5,6} An intra-aortic balloon pump (IABP) is one of the logical approaches to decompress the LV and has been widely used.⁷

However, the role of IABP in providing additional circulatory support and LV decompression in patients with concomitant VA-ECMO is controversial.^{7–10} In addition, there are several safety concerns. First, IABP may increase the occurrence of vascular complications.^{9,11} Lower extremity ischaemia is an independent risk factor for patients undergoing VA-ECMO.^{12,13} A distal perfusion cannula was introduced to improve the blood supply in the femoral artery obstructed by the ECMO cannula but was rarely applied on the IABP side.¹⁴

Second, IABP was reported to change the blood flow in the bilateral middle cerebral arteries detected by transcranial Doppler.¹⁵ Cerebral blood flow decreased when IABP was concomitantly used in patients with a pulse pressure less than 10 mmHg (the patients experienced cardiac stunning) but increased in patients with a pulse pressure greater than 10 mmHg. This may theoretically lead to cerebral ischaemia and ischaemic stroke when the patient has poor cardiac function during VA-ECMO support. In an animal model of cardiac arrest, a decreased carotid flow velocity was observed in addition of IABP to femoro-femoral VA-ECMO, but without significance.¹⁶

Additionally, the haemodynamic effect of concomitant IABP in LV unloading is controversial. In a study investigating IABP's effects on macrocirculation and microcirculation in cardiogenic shock patients supported by VA-ECMO, there were no differences in velocity-time integral and cardiac output measured by echocardiography when IABP was on, off, or restarted, despite the changes in LV dimension and pulmonary artery-occlusion pressure measured by pulmonary artery catheter.¹⁷

However, to date, no study has carefully evaluated IABP's impact on the regional haemodynamics of patients with severe cardiogenic shock undergoing femoro-femoral VA-ECMO assessed by ultrasonography. This study will evaluate the changes in blood flow in the femoral artery (FA), the carotid artery (CA), and the aorta in cardiogenic shock patients undergoing VA-ECMO when IABP is concomitantly used.

Methods

Study design and setting

This single-centre, prospective, observational study, conducted between July 2017 and April 2018 in the Center for Cardiac Intensive Care, Beijing Anzhen Hospital, Capital Medical University, was approved by the hospital's institutional ethics committee (approval number 2017074X). Informed consent was obtained from all patients or their surrogates.

Patients

This study enrolled patients (aged ≥ 18) with cardiogenic shock consecutively, defined as the following: (i) systolic blood pressure < 90 mmHg for 30 min, a mean arterial pressure < 65 mmHg for 30 min, or a requirement for vasopressors to achieve a blood pressure 90 mmHg; (ii) pulmonary congestion or elevated left ventricular filling pressure; and (iii) signs of impaired organ perfusion with at least 1 of the following indications: altered mental status; cold, clammy skin; oliguria; or increased serum lactate despite optimized supportive measures, such as IABP and inotropes. These patients received both VA-ECMO and IABP for cardiogenic shock in the intensive care unit or intraoperatively in the operating room for circulatory instability during or immediately after weaning from cardiopulmonary bypass in the primary cardiac procedure. Patients were excluded if any one of the following was present: inability to maintain stable ECMO flow or ECMO or IABP duration less than 24 h.

Extracorporeal membrane oxygenation and intra-aortic balloon pump management

Patients in this study underwent ECMO implantation via peripheral cannulation through the femoral route with the cutdown method. The 15 Fr or 17 Fr returning cannula was chosen according to the diameter of the femoral artery. A distal leg perfusion cannula was routinely introduced to prevent lower extremity ischaemia. The detailed ECMO management protocol was described in a previous study by the authors.¹⁸

The IABP was installed before or after VA-ECMO implantation. In all of these patients, the IABP catheter used was a 7.5-F, 40 mL balloon Percor STAT-DL catheter (Datascope Corp, Fairfield, NJ) connected to a Datascope portable computerized console (Datascope), placed using a percutaneous insertion technique via the femoral artery. We positioned the distal tip of the balloon catheter in the descending thoracic aorta 2 cm distal to the origin of the left subclavian artery. The catheter position was confirmed by a chest X-ray. Balloon inflation was triggered by the R wave of the electro-

cardiogram. The balloon was inflated just before the diastolic notch of the arterial pressure waveform and deflated before ventricular systole. The electrocardiogram-triggered IABP was set to a 1:1 assist mode and 100% balloon augmentation during VA-ECMO support.

Study protocol and data collection

The effects of IABP on regional haemodynamics were observed when the IABP was on and off. After measuring baseline data from the bilateral CA, FA, and aorta during IABP counterpulsation, the IABP was turned off for 15 min. When stable circulation was achieved, the relevant data were measured again. When measurements were taken, patients were given adequate analgesia and were sedated following the routine clinical practice. Catecholamine infusion, ECMO, and mechanical ventilation settings were kept constant during all protocol stages, with no fluid loading.

In this study, a Vivid-i portable ultrasound system (GE Health care, Milwaukee, WI) was used to perform vascular and cardiac ultrasonography. The ultrasonography measurements were conducted on each ECMO day by two certificated doctors in the team. A blood flow Doppler signal was obtained and analysed in real time, and the blood flow rate (BFR) was measured in mL/min as a product of the mean blood flow velocity (by the integral method) and the arterial cross-sectional area. The BFRs of the left CA (LCA), right CA (RCA), and bilateral FA (at the distal end of the insertion site of IABP or the ECMO distal perfusion cannula, iFA, or eFA) were obtained. The velocity time integral (VTI) of the aortic root was measured by transthoracic echocardiography via apical five-chamber sectioning. The mean arterial pressure, pulse pressure, heart rate, and ECMO flow rate were also recorded during every ultrasonography measurement.

The following data were recorded: age, sex, co-morbidities, LV ejection fraction (LVEF) on admission, cardiac procedure, indication for ECMO support, IABP timing, survival to discharge, survival on ECMO, lower extremity ischaemia (need surgical intervention), and neurological complications (ischaemic or haemorrhagic stroke confirmed by computed tomography).

Statistical analysis

Continuous variables are presented as the mean (standard deviation) or median (interquartile range), and two-group comparisons were performed with Student's *t*-test. The paired Student's *t*-test was used when comparing the BFR and aortic VTI before and after turning off the IABP. When analysing the regional haemodynamics, the data were stratified by pulse pressure (cardiac stunning group [Group N]: pulse pressure ≤ 5 mmHg when IABP standby, and

cardiac nonstunning group [Group P]: pulse pressure > 5 mmHg when IABP standby) and ECMO flow rate (high ECMO flow [Group H]: ECMO blood flow > 3.5 L/min, and low ECMO flow [Group L]: ECMO blood flow ≤ 3.5 L/min) at measurement. All statistical calculations were performed with IBM SPSS Statistics (version 26.0. Armonk, NY: IBM Corp).

Results

Patients

From July 2017 to April 2018, a total of 39 patients receiving both peripheral femoral VA-ECMO and IABP concomitantly were enrolled. The mean age of the patients was 59.8 ± 9.47 years, and there were 31 men (79.5%). Thirty-eight patients received circulatory support following the cardiac procedure, and one received circulatory support for acute myocardial infarction without cardiac intervention. The cardiac procedures included coronary artery bypass grafting (CABG) (22), CABG combined with valvular procedures (8), percutaneous coronary intervention (3), valvular procedure (3), and heart transplantation (2).

Twenty-nine patients (74.4%) were successfully weaned from ECMO, and 17 patients (43.6%) were discharged and survived. Twelve patients died after ECMO weaning (seven for multiorgan failures and five for cardiac failure). In the 17 patients who survived to discharge, IABPs were all withdrawn after ECMO decannulation (4.0 ± 2.1 days). Of the 12 patients who died after ECMO weaning, only four patients withdrew from IABP. The average ECMO and IABP durations were 156.3 ± 128.8 and 222.9 ± 114.9 h, respectively. The average ICU length of stay was 12.3 ± 7.0 days. The detailed patient characteristics are shown in *Table 1*.

Intra-aortic balloon pump impacting regional haemodynamics

A total of 172 pairs of data (IABP on and off) were collected in this study. The data were measured over a median of 2.0 (1.0, 4.5) days after patients received VA-ECMO. There was no statistically significant difference in MAP (IABP-On 81.9 ± 17.3 mmHg vs. IABP-Off 82.0 ± 17.9 mmHg, $P = 0.81$) or HR (IABP-On 87.0 ± 15.0 vs. 87.1 ± 15.0 /min, $P = 0.22$) before and after turning the IABP off. The change in regional haemodynamics is shown in *Table 2*. The BFR on both sides of the FA and the aortic VTI decreased significantly when turning the IABP off (*Figure 1*).

Table 1 Characteristics of the 39 patients

Variable	Value
Age, mean \pm SD (years)	59.8 \pm 9.47
Male, <i>n</i> (%)	31 (79.5%)
Body surface area, mean \pm SD (m ²)	1.7 \pm 0.44
Co-morbidity, <i>n</i> (%)	
Hypertension	23 (59%)
Diabetes	12 (31%)
Femoral artery stenosis	12 (30.8%)
Peripheral vascular disease	29 (74.4%)
LVEF on admission, mean \pm SD (%)	51.3 \pm 13.4
ECMO indications, <i>n</i> (%)	
Unable to disconnect from CPB	12 (30.8%)
Cardiogenic shock	22 (56.4%)
ECMO under cardiopulmonary resuscitation, <i>n</i> (%)	5 (12.8%)
IABP timing	
Implanted before ECMO	30 (76.9%)
Implanted after ECMO	9 (23.1%)
Outcomes	
Survival to discharge, <i>n</i> (%)	17 (43.6%)
Survival ECMO, <i>n</i> (%)	29 (74.4%)
Complications	
Lower extremity ischaemia	2 (5.1%) ^a
Neurological complications	4 (10.3%) ^b

^aThe two cases were both IABP related lower extremity ischaemia. One happened after the patient weaned from ECMO. In the other patient, we introduced a femoral distal perfusion catheter in the IABP side.

^bThree cases of ischaemic stroke and one haemorrhagic stroke confirmed by computer tomography.

LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

Subgroup analysis

The measured data were divided into Group N (*n* = 22) and Group P (*n* = 150) based on pulse pressure (pulse pressure 1.4 \pm 2.0 mmHg in Group N vs. 30.1 \pm 17.4 mmHg in Group P, *P* < 0.01) observed when IABP was off (Table 3). The change in regional haemodynamics in each subgroup was the same as that in the total sample except for the LCA BFR. The LCA BFR dramatically increased after turning the IABP off (296.8 \pm 129.7 vs. 401.4 \pm 278.1 mL/min, *P* = 0.02).

Then, the measured data were divided into Group H (*n* = 47) and Group L (*n* = 103) based on ECMO blood flow

(ECMO blood flow 3.7 \pm 0.3 in Group H vs. 2.9 \pm 0.5 in Group L, *P* < 0.01) (Table 4). The iFA BFR and aortic VTI decreased after turning the IABP off in both groups. There was no change in the eFA BFR in Group H.

To investigate the increase in the LCA BFR in Group N after turning the IABP off, the LCA BFR in Group N was compared by high (>3.5 L/min, Group NH, *n* = 9) and low (\leq 3.5 L/min, Group NL, *n* = 13) ECMO blood flow (3.7 \pm 0.2 vs. 2.8 \pm 0.5, *P* < 0.01) (Figure 2). In Group NH, there was no statistically significant difference in bilateral CA BFR between IABP-On and IABP-Off (359.6 \pm 105.4 mL/min vs. 389.6 \pm 139.3 mL/min in LCA, *P* = 0.31; 320.2 \pm 101.7 mL/min vs. 266.0 \pm 97.0 in RCA, *P* = 0.14). However, in Group NL, the LCA BFR was lower when the IABP was on than when the IABP was off (253.4 \pm 130.6 mL/min vs. 409.5 \pm 349.7 mL/min, *P* = 0.04), and there was no statistically significant difference in the RCA BFR (360.5 \pm 216.4 mL/min vs. 454.2 \pm 334.2 mL/min, *P* = 0.05).

Discussion

This study assessed the regional haemodynamic effect of IABP on patients undergoing femoro-femoral VA-ECMO by ultrasonography and indicated that IABP was associated with increased aortic VTI and bilateral FA BFR. The change in CA BFR depends on patient condition and ECMO blood flow rate. This is an important finding to explain how blood flows are distributed in the systemic circulation of patients who received ECMO and IABP concomitantly for circulatory support.

Intra-aortic balloon pump has been used for decades to supply partial circulatory support for patients with severe heart failure. It can increase coronary blood flow by balloon inflation during the diastolic period and decrease the cardiac afterload by rapid deflation at the end of the diastolic period to create a vacuum in the aorta. Although IABP remains the predominant device of choice in cardiogenic shock patients, its effect on patient mortality has been questioned.^{1,19} ECMO is widely used in managing cardiac shock since it provides both circulatory and respiratory support, rapid access, and

Table 2 IABP impacting on regional haemodynamics

Variable	IABP-On	IABP-Off	<i>P</i> value
MAP, mean \pm SD (mmHg)	81.9 \pm 17.3	82.0 \pm 17.9	0.81
HR, mean \pm SD (/min)	87.0 \pm 15.0	87.1 \pm 15.0	0.22
CA BFR, mean \pm SD (mL/min)			
LCA	555.7 \pm 326.9	578.6 \pm 328.0 ^a	0.27
RCA	550.0 \pm 331.1	533.0 \pm 303.5	0.30
FA BFR, mean \pm SD (mL/min)			
eFA	299.3 \pm 279.9 ^b	242.4 \pm 258.8 ^b	<0.01
iFA	176.4 \pm 104.5	152.2 \pm 139.8	<0.01
VTI, mean \pm SD (cm)	10.1 \pm 4.4	8.5 \pm 4.4	<0.01

MAP, mean arterial pressure; HR, heart rate; CA, carotid artery; BFR, blood flow rate; LCA, left carotid artery; RCA, right carotid artery; FA, femoral artery; eFA, femoral artery on the ECMO side; iFA, femoral artery on the IABP side; VTI, velocity time integral.

Figure 1 Diagram of the impact of an intra-aortic balloon pump (IABP) on the regional haemodynamics of patients with cardiogenic shock treated with femoro-femoral veno-arterial extracorporeal membrane oxygenation (VA-ECMO). The blood flow rates (BFRs) on both sides of the femoral artery and the aortic velocity time integral decreased significantly when the IABP was turned off (regarded as the absence of IABP), while the BFRs on both sides of the carotid artery remained unchanged. The retrograde blood flow toward the aortic arch from ECMO (ECMO_{upper}) might theoretically be partially blocked by the IABP balloon. RCA right carotid artery, LCA left carotid artery, iFA femoral artery on the IABP side, eFA femoral artery on the ECMO side, VTI velocity time integral, ECMO_{upper} ECMO flow to the upper body.

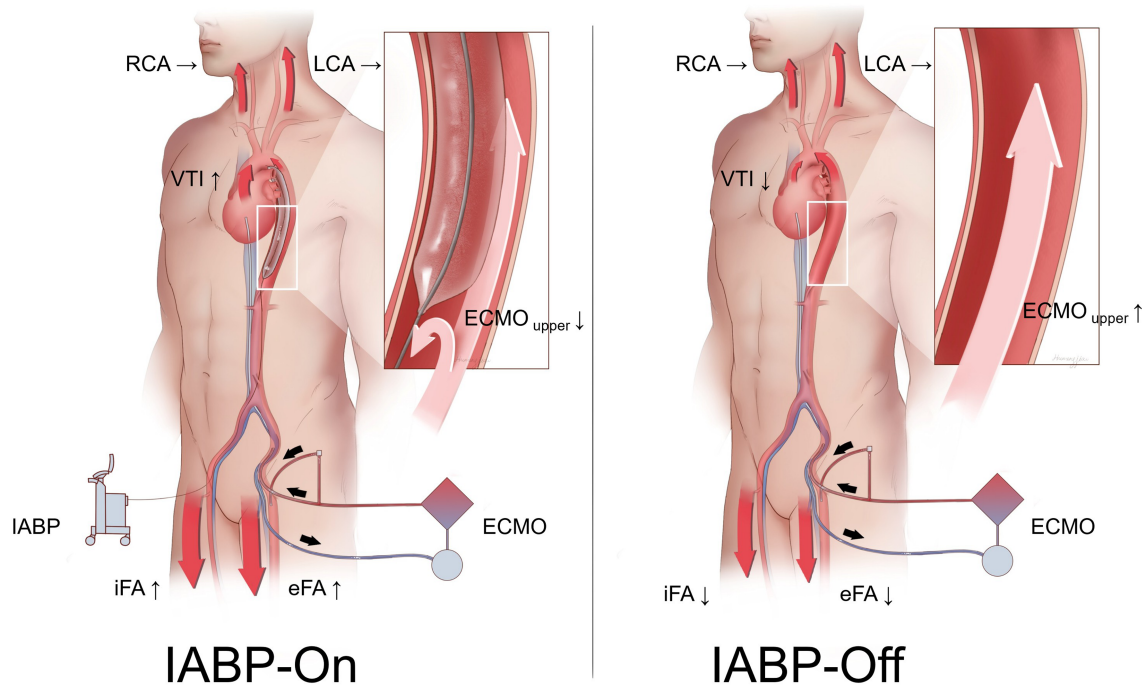


Table 3 IABP impacting on regional haemodynamics by cardiac stunning (N) and nonstunning (P)

Variable	Group N (n = 22)			Group P (n = 150)		
	IABP-On	IABP-Off	P value	IABP-On	IABP-Off	P value
MAP, mean ± SD (mmHg)	75.5 ± 12.5	74.9 ± 13.3	0.68	82.8 ± 17.7	83.1 ± 18.3	0.72
HR, mean ± SD (/min)	87.6 ± 14.2	87.7 ± 14.2	0.34	83.0 ± 19.3	83.2 ± 19.0	0.41
CA BFR, mean ± SD (mL/min)						
LCA	296.8 ± 129.7	401.4 ± 278.1	0.02	594.8 ± 330.0	605.3 ± 327.5 ^a	0.64
RCA	344.0 ± 176.4	377.2 ± 276.4	0.32	581.0 ± 338.2	556.5 ± 301.3	0.17
FA BFR, mean ± SD (mL/min)						
eFA	182.5 ± 166.2 ^b	173.4 ± 241.5 ^b	0.76	317.1 ± 289.7 ^b	253.0 ± 260.6 ^b	<0.01
iFA	103.3 ± 63.5	59.9 ± 42.0	0.01	187.1 ± 105.2	165.7 ± 144.0	0.01
VTI, mean ± SD (cm)	5.7 ± 3.1	2.8 ± 1.5	0.16	10.6 ± 4.3	9.0 ± 4.2	<0.01

^aThere was a significant blood flow rate between left and right carotid artery.

^bThere was a significant blood flow rate between the femoral arteries in the ECMO side and the IABP side.

MAP, mean arterial pressure; HR, heart rate; CA, carotid artery; BFR, blood flow rate; LCA, left carotid artery; RCA, right carotid artery; FA, femoral artery; eFA, femoral artery on the ECMO side; iFA, femoral artery on the IABP side; VTI, velocity time integral.

nearly full cardiac output.⁴ However, in patients with poor LV contractility, VA-ECMO is associated with an increase in LV afterload, worsening LV performance, and pulmonary congestion, which has been suggested by several studies.^{5,20–22}

Intra-aortic balloon pump is an alternative method to achieve LV unloading. In this study, a higher VTI was observed when turning the IABP on. This is consistent with a previous simulation study showing that IABP reduces LV afterload and thus increases cardiac output.²³ However, a study

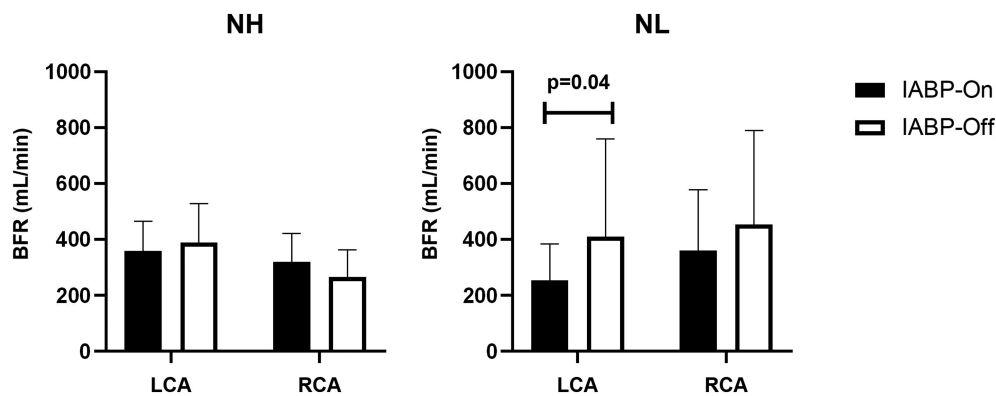
assessing IABP's effect on microcirculation during ECMO did not find a difference in aortic VTI and cardio output after switching the IABP off and on.¹⁷ This could be caused by the delayed measuring period, 6.3 ± 5.9 days after ECMO was inserted and 4.7 ± 4.4 days after IABP was inserted. We performed the measurement a median of 2.0 (1.0, 4.5) days after patients received VA-ECMO, which might reflect the timing benefit from LV unloading. Compared with Impella™ or LV venting, additional intra-aortic balloon pumping only

Table 4 IABP impacting on regional haemodynamics by high (H) and low (L) ECMO blood flow

Variable	Group H (n = 47)			Group L (n = 103)		
	IABP-On	IABP-Off	P value	IABP-On	IABP-Off	P value
MAP, mean ± SD (mmHg)	75.5 ± 15.9	74.3 ± 16.0	0.13	83.8 ± 17.3	84.4 ± 17.8	0.51
HR, mean ± SD (/min)	92.6 ± 13.1	92.6 ± 12.9	0.88	84.9 ± 15.1	85.0 ± 15.1	0.15
CA BFR, mean ± SD (mL/min)						
LCA	498.2 ± 274.1	527.2 ± 322.2	0.17	578.1 ± 343.7	598.5 ± 329.4	0.46
RCA	521.7 ± 347.2	347.2 ± 272.7	0.39	560.9 ± 325.5	549.2 ± 307.3	0.51
FA BFR, mean ± SD (mL/min)						
eFA	219.4 ± 254.8 ^a	210.9 ± 353.3	0.72	330.8 ± 284.0 ^a	254.9 ± 210.9 ^a	<0.01
iFA	146.8 ± 88.6	118.6 ± 97.7	<0.01	187.5 ± 108.2	164.8 ± 151.0	0.02
VTI, mean ± SD (cm)	11.8 ± 3.2	8.8 ± 3.8	<0.01	9.7 ± 4.6	8.3 ± 4.6	<0.01

^aThere was a significant blood flow rate between the femoral arteries in the ECMO side and the IABP side.

MAP, mean arterial pressure; HR, heart rate; CA, carotid artery; BFR, blood flow rate; LCA, left carotid artery; RCA, right carotid artery; FA, femoral artery; eFA, femoral artery on the ECMO side; iFA, femoral artery on the IABP side; VTI, velocity time integral.

Figure 2 Blood flow rates (BFRs) in the bilateral carotid arteries in patients with cardiac stunning (pulse pressure ≤ mmHg) stratified by ECMO flow rate (high ECMO flow [group NH]: > 3.5 L/min, and low ECMO flow [group NL]: ≤ 3.5 L/min). LCA left carotid artery, RCA right carotid artery.

marginally decreased cardiac loading through a closed-loop, real-time computer model of the human cardiovascular system.²³ However, a retrospective analysis of the Japanese national inpatient database including 604 patients who received IABP combined with ECMO and 1,064 patients who received ECMO alone suggested that IABP combined with ECMO was associated with improved mortality (HR 0.74, $P < 0.001$) and successful weaning from ECMO.¹⁰ The clinical benefit from concomitant IABP usage is still controversial.^{7,8}

In addition, vascular complications are one of the safety concerns of concomitant IABP usage. A single-center retrospective observational study indicated a higher incidence of fasciotomy in the IABP plus ECMO group than in the ECMO alone group.⁹ However, whether limb fasciotomy is related to IABP is unknown. In this study, there were 2 cases of lower-extremity ischaemia, both related to IABP cannula. One occurred after the patient was weaned from ECMO. In the other case, we introduced a femoral distal perfusion catheter on the IABP side. Assessed by ultrasonography, concomitant IABP was associated with higher FA BFR on both the ECMO and IABP sides. This may be due to the IABP balloon

obstructing retrograde blood flow from femoro-femoral VA-ECMO, thereby increasing blood flow to the lower extremities. Our results are consistent with the findings from a numerical model of aortic haemodynamics.²⁴ This model suggested that there was a higher velocity distribution in the femoral artery of the IABP side when turning the IABP on. In the subgroup analysis of our study, this effect was the same as the total measurements. We also found that the eFA BFR was always higher than the iFA BFR regardless of when the IABP was turned on because the distal leg perfusion cannula on the ECMO side was implanted routinely.

The effect of concomitant IABP on CA was more complex. In all 172 measurements, the results indicated no significant changes in bilateral CA BFR before and after turning the IABP off. To explain this phenomenon, retrograde blood flow toward the aortic arch from ECMO (ECMO_{upper} in Figure 1) was introduced theoretically, although it could hardly be measured by ultrasonography. The CA BFR was from two sources: blood ejected from the heart and ECMO_{upper}. When the IABP was turned on, the VTI increased according to the result, and the ECMO_{upper} might be partially blocked by the

IABP balloon and decrease. As a consequence, the CA BFR is unchanged. However, when the heart was in stunned status (Group N), the increase in VTI could not compensate for the decrease in ECMO_{upper} when the IABP was turned on. Then, the CA BFR decreased, especially in the LCA, which is far away from the aortic root.

To further investigate the change in LCA affected by ECMO_{upper} during cardiac stunning, the CA BFR in Group N was compared based on high and low ECMO flow. The LCA BFR was affected by IABP in the low ECMO flow group but not in the high ECMO flow group. However, the measurement sample in the subgroup was limited.

A previous animal model study showed that the carotid flow velocity was similar when IABP-Off and IABP-On were used.¹⁶ That study also measured the blood flow in the coronary artery, which has been rarely measured in human patients, suggesting that concomitant IABP in femoro-femoral VA-ECMO worsens the blood flow in the coronary artery caused by balloon blockade. However, that study used a cardiac arrest model whose pathophysiology was different from the situation in cardiogenic shock. The results in the present study were similar to our previous research,¹⁵ in which we measured cerebral blood flow (CBF) in the bilateral middle cerebral arteries by transcranial Doppler. The mean CBF (sum of bilateral CBF) was higher in VA-ECMO alone than in VA-ECMO combined with IABP support during cardiac stunning. The addition of IABP to VA-ECMO support significantly increased the mean CBF when the heart had improved systolic function. However, in the present study, the left and right sides of CA were differentiated, and the cardiac function was evaluated by echocardiography simultaneously. Yet evidence of the relationship between CBF and the incidence of ischaemic stroke during ECMO is lacking. Further study is needed to better define the management strategy of cerebral perfusion and to prevent neurological complications.

Study limitations

The present study has several limitations. First, the sample size was limited. Although it was enough to detect the difference in BFR, a few patients developed extremities and neurological complications, which did not allow us to analyse the association between BFR and complications. Especially, there were three ischaemic strokes and one haemorrhagic stroke in this cohort. The incidence (nearly 10%) of neurological com-

plications was higher than the average level (6.2% in our center in the past 5 years). A larger sample size is required to investigate the IABP's effect on neurological complications. In the subgroup analysis, the specific clinical condition made it difficult to achieve a similar number of measurements in each subgroup. And most of the population were postcardiotomy patients, whose physiological profile and vasodilatory nature was different from other types of cardiogenic shock, such as chronic decompensated heart failure, acute unrevascularized myocardial infarction, and so on. The IABP's effect on regional haemodynamics in various phenotypical profiles of cardiogenic shock should be investigated in further study.

Second, functional variables were not measured in the present study, such as near-infrared spectroscopy or side-stream dark-field (SDF) imaging, to evaluate the tissue microcirculation, which requires a longer washout period and may lead to haemodynamic instability when the IABP is turned off. In addition, BFR in the renal artery, abdominal trunk, and other locations reflecting abdominal organ perfusion was not assessed but will be evaluated in a subsequent study.

Conclusions

Concomitant IABP used in patients undergoing femoro-femoral VA-ECMO was associated with increased aortic VTI and BFR in bilateral FA. The change in CA BFR depended on cardiac function. A decreased LCA BFR was observed in patients with cardiac stunning when IABP was turned on, which might be compensated by a higher ECMO blood flow. Further study is needed to confirm the relationship between BFR and extremities and neurological complications.

Conflict of interest

None declared.

Funding

This work was supported by the National Key Research and Development Program of China (2016YFC1301001, to X.H.).

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