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Intra-aortic balloon pump combined with mechanical ventilation for treating patients aged > 60 years in cardiogenic shock: Retrospective analysis

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Abstract

Objective: To examine if mechanical ventilation with positive end-expiratory pressure (PEEP) combined with intra-aortic balloon pump (IABP) provided a better outcome than IABP alone for the treatment of cardiogenic shock after acute myocardial infarction in patients aged > 60 years.
Methods: This was a retrospective analysis of data from patients in cardiogenic shock, refractory to pharmacological therapy and treated at a geriatric coronary care unit.
Results: Sixty-two patients were eligible for study inclusion: 33 received IABP alone; 29 received IABP combined with mechanical ventilation. Patients in the IABP + mechanical ventilation group had lower mean arterial blood pressure (BP), systolic BP and partial pressure of oxygen compared with the IABP group, indicating worse cardiac and pulmonary function. In addition, higher rates of pulmonary infection and renal insufficiency were observed in the IABP + mechanical ventilation group than in the IABP group. A statistically significant improvement of left ventricular function before and after treatment was observed in the IABP + mechanical ventilation group, but not in the IABP group. Pulmonary infection and renal insufficiency were risk factors for all-cause in-hospital mortality; successful revascularization was a negative risk factor. There was no between-group difference in survival.
Conclusion: Mechanical ventilation with an appropriate level of PEEP appears to enhance the beneficial effects of IABP on left ventricular function for patients in cardiogenic shock.

Keywords

Cardiogenic shock, intra-aortic balloon pump, artificial respiration, treatment outcome, complications, geriatric patients

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Introduction

Cardiogenic shock is a life-threatening complication that occurs in ~10% of patients following acute myocardial infarction (MI).[1] Increasing and widespread use of coronary revascularization has led to a decrease in the incidence of cardiogenic shock, although mortality remains high in affected patients (40–60%).[2] Mechanical circulatory support mechanisms may also help patients in cardiogenic shock to achieve initial haemodynamic stabilization with a subsequent improved clinical outcome.[2] For nearly 50 years, the intra-aortic balloon pump (IABP) has been used with inotropic drugs and fluid resuscitation as adjunctive mechanical support for patients in cardiogenic shock.[3]

A meta-analysis of 16 studies demonstrated a reduced mortality following IABP utilization.[4] However, the beneficial effects of IABP strongly depend on the type of reperfusion therapy used. For example, another meta-analysis showed that patients undergoing thrombolysis and IABP had an 18% mortality risk reduction, whereas, in patients undergoing a primary percutaneous coronary intervention, IABP was associated with a 6% mortality risk increase.[5] Interestingly, in the IABP-SHOCK II trial (which is the largest randomized controlled clinical study involving patients with cardiogenic shock), IABP did not significantly reduce 30-day mortality compared with controls.[6] These data corroborate other findings from extended follow-up at 6 and 12 months.[7] Notably, in these studies, no significant differences between the IABP and control groups were obtained with respect to stroke rates, peripheral ischaemic complications, bleeding, sepsis, inflammation (i.e., C-reactive protein [CRP]) and tissue oxygenation [i.e., serum lactate] indices). Nevertheless, IABP is considered by many physicians to be the gold standard treatment for cardiogenic shock.[8]

Noninvasive or invasive mechanical ventilator support is required for patients with acute left ventricular failure (a condition that may result in cardiogenic shock).[9] Indeed, mechanical ventilation with positive end-expiratory pressure (PEEP) has been associated with improved haemodynamic measurements and superior clinical outcomes in patients in cardiogenic shock.[10,11] However, studies assessing the clinical outcome and safety of IABP in conjunction with mechanical ventilation for the treatment of cardiogenic shock are rare. Therefore, the purpose of this study was to examine if mechanical ventilation combined with IABP provided a better outcome than IABP alone for the treatment of cardiogenic shock after acute MI in patients aged > 60 years.

Patients and methods

Study population and design

This was a retrospective analysis of data collected between January 1, 2005 and December 31, 2013 at the Geriatric Coronary Care Unit, General Hospital of Chinese People's Liberation Army, Beijing, China. Inclusion criteria were: (1) aged > 60 years; (2) diagnosis of ST-segment elevation myocardial infarction (STEMI); (3) STEMI complicated by cardiogenic shock; 4) cardiogenic shock refractory to pharmacological therapy including dopamine, noradrenaline, and/or fluid administration, tailored to each individual patient. Patients were excluded if they had a contraindication to IABP such as severe peripheral vascular disease, aortic regurgitation, aortic dissection or aortic aneurysm.

Demographic variables and other baseline characteristics, clinical outcomes and complications were collected from patients' records. Written informed treatment consent was obtained from the patients or their relatives at hospital admission. This study was approved by the Ethics Committee of General Hospital of Chinese People's Liberation Army in Beijing, China. The need for individual study inclusion consent was waivered by the committee because of the retrospective nature of the study.

IABP therapy. At our centre, an IABP was used in patients with cardiogenic shock persisting for >30 min after fluid replacement and despite the administration of pharmacological therapy (i.e., maximum doses of morphine, nitrates, diuretics, dopamine and noradrenaline). A 7.5- or 8-Fr IABP catheter [30 or 40 ml, Datascope, NJ, USA] was placed percutaneously via the femoral artery using the Seldinger technique.[12] The tip position was verified by chest radiography. The duration of IABP support was dependent on the patient's haemodynamic stability. The counter-pulsation timing was 1: 1 immediately after IABP placement. At the time of discontinuation, the IABP counter-pulsation timing was progressively reduced from 1: 1 to 1: 2, then to 1: 4 and finally to standby before IABP removal.

Mechanical ventilation therapy. The indication for mechanical ventilation at our centre was refractory hypoxaemia, with arterial partial pressure of oxygen (PaO_2) <60 mmHg and arterial oxygen saturation (SaO_2) <90% despite high-flow supplemental oxygen therapy (>6 l/min) via a reservoir mask, and/or partial pressure of carbon dioxide ($PaCO_2$) >45 mmHg. Patients were intubated with cuffed endotracheal tubes (internal diameter 7.5–8.5 mm, Teleflex, NC, USA). The head of the patient's bed was positioned at 45°. Pressure support ventilation (Dräger Evita 4® Lubeck, Germany) was provided initially with a tidal volume of 8–10 ml/kg and a respiratory rate (RR) of 15–20 breaths per min (bpm), and then synchronized intermittently. Pressure support ventilation was then adjusted to 14–20 cmH_2O and a PEEP of 4–10 cmH_2O for all patients. Mechanical ventilation was gradually withdrawn as the patient improved, as evidenced by RR = 14–16 bpm and $SpO_2 > 95\%$ under fraction of inspired oxygen (FiO_2) < 0.35 and pressure support ventilation < 10 cmH_2O.

Monitoring clinical parameters

Arterial blood PaO_2, $PaCO_2$ and pH were measured using an arterial blood gas analyser (cobas® b 221, Mannheim, Germany). Left ventricular ejection fraction (LVEF) was measured using a cardiac ultrasound system (Acuson Aspen™, Munich, Germany) according to conventional methods before and after treatment with IABP or IABP + mechanical ventilation.

Study outcomes and definitions

The study endpoint was the incidence of all-cause, in-hospital death that occurred during treatment or after IABP removal and weaning from mechanical ventilation. Cardiogenic shock was defined as a systolic blood pressure (BP) < 90 mmHg secondary to cardiac dysfunction, with clinical signs of hypoperfusion (oliguria, cold extremities, and altered mental status).[13,14] Acute MI was defined as elevated serum creatine kinase levels (at least three times the upper limit of normal range) with chest pain or ST-T deviation on the electrocardiogram. Pulmonary infection was defined as the occurrence of a new and persistent radiographic infiltrate, with temperature >37.5°C and white blood cell count $\geq 10 \times 10^9$/l. Renal insufficiency was defined as an absolute increase of serum creatinine by ≥0.5 mg/dl from baseline values.[15] Successful revascularization was defined as an improvement in blood flow through the coronary artery after revascularization compared with that before a percutaneous coronary intervention or the patient having a successful coronary artery bypass graft.

Statistical analyses

Continuous variables were expressed as mean ± SD. Categorical data were presented as *n* or *n*%. Student's *t*-test, X^2-analysis or Fisher's exact tests were used to compare the treatment groups (i.e., IABP or IABP + mechanical ventilation group) as appropriate. A Cox regression model was applied to determine the hazard ratio (HR) associated with overall in-hospital deaths. Risk factors (i.e., age, sex, hypertension, diabetes, previous MI, IABP + mechanical ventilation, pulmonary infection, renal insufficiency and success of revascularization) were added into the model in a forward stepwise approach. HR, 95% confidence interval (95% CI), and *P*-value were reported for each variable. Kaplan–Meier survival curves were plotted according to different groups and between-group differences were assessed with the log-rank test. A *P*-value of < 0.05 was considered statistically significant.

Results

Clinical characteristics of patients

Of the 62 patients included in the study, 33 had received an IABP, and 29 an IABP in combination with mechanical ventilation based on clinical need. There were no statistically significant between-group differences in terms of age, sex distribution, hypertensive status, diabetes mellitus frequency, history of previous MI, location of MI, in-hospital mortality and success of revascularization (all comparisons $P > 0.05$) (Table 1). However, statistically significantly higher pulmonary infection (62.1% vs. 36.4%) and renal insufficiency (58.6 vs. 30.3%) rates were observed in the IABP + mechanical ventilation group compared with the IABP group ($P < 0.05$) (Table 1).

Patients in the IABP + mechanical ventilation group had statistically significantly lower mean arterial BP, systolic BP and

Table 1. Clinical characteristics of 62 patients aged > 60 years in cardiogenic shock and treated with IABP or IABP and mechanical ventilation.

Characteristic	IABP group n = 33	IABP + MV group n = 29	Statistical significance
Age, years	71.1 ± 7.9	74.4 ± 8.9	P = 0.125
Sex, male/female	28/5	22/7	P = 0.372
Hypertension	24 (72.7)	18 (62.1)	P = 0.370
Diabetes mellitus	12 (36.4)	12 (41.4)	P = 0.408
Previous MI	8 (27.3)	13 (44.8)	P = 0.087
AMI-anterior	14 (42.4)	18 (62.1)	P = 0.122
AMI-inferior	10 (30.3)	7 (24.1)	P = 0.587
In-hospital mortality	16 (48.5)	19 (65.5)	P = 0.177
Successful revascularization	18 (54.5)	14 (48.3)	P = 0.622
Pulmonary infection	12 (36.4)	18 (62.1)	P = 0.043
Renal insufficiency	10 (30.3)	17 (58.6)	P = 0.025

Values are shown as mean ± SD, *n* or *n* (%).
IABP, intra-aortic balloon pump; MV, mechanical ventilation; MI, myocardial infarction; AMI, acute myocardial infarction.

Table 2. Cardiac and pulmonary function data at baseline and after treatment for 62 patients aged > 60 years in cardiogenic shock, treated with IABP or IABP and mechanical ventilation.

Parameters	IABP group $n = 33$	IABP + MV group $n = 29$	Statistical significance
MAP, mmHg	58.9 ± 6.2	53.2 ± 3.9	$P = 0.045$
SBP, mmHg	73.4 ± 6.1	68.2 ± 3.5	$P < 0.001$
HR, bpm	120.0 ± 9.6	120.1 ± 9.2	$P = 0.863$
pH	7.25 ± 0.4	7.04 ± 0.6	$P < 0.001$
PaO_2, mmHg	83.5 ± 5.0	49.9 ± 5.1	$P < 0.001$
$PaCO_2$, mmHg	38.9 ± 8.3	41.6 ± 7.7	$P = 0.198$
LVEFb, %	42.0 ± 3.9	36.4 ± 5.2	$P < 0.001$
LVEFa, %	44.1 ± 4.9	43.8 ± 5.4	$P = 0.801$

Values are shown as mean ± SD.
IABP, intra-aortic balloon pump; MV, mechanical ventilation; MAP, mean arterial pressure; SBP, systolic blood pressure; HR, heart rate; LVEFb, left ventricular ejection fraction before treatment; LVEFa, left ventricular eject fraction after treatment; PaO_2, partial pressure of oxygen; $PaCO_2$, partial pressure of carbon dioxide.

PaO_2 compared with patients in the IABP group (Table 2). In the IABP + mechanical ventilation group, LVEF statistically significantly increased from 36.4 ± 5.2% before treatment to 43.8 ± 5.4% after treatment ($P < 0.001$); in the IABP group there was a nonsignificant increase (from 42.0 ± 3.9% to 44.1 ± 4.9%) ($P = 0.059$) (Table 2 and Figure 1).

Independent predictors of mortality

In-hospital mortality in the IABP + mechanical ventilation group was 65.5%, while in the IABP group the 30-day cumulative survival was 51.5% (Table 1). Although the IABP group had better survival than the IABP + mechanical ventilation group (i.e., 48.5% vs 34.5%), there was no difference in the in-hospital mortality between the two groups (log rank test; $P = 0.29$) (Figure 2).

Pulmonary infection ($P = 0.041$) and renal insufficiency ($P = 0.011$) were significant risk factors for all-cause, in-hospital mortality (Table 3). Age, sex, hypertension, diabetes mellitus, previous myocardial infarction, IABP + mechanical ventilation were not associated with all-cause in-hospital mortality (all $P > 0.05$). In addition successful revascularization was a significant negative risk factor for in-hospital mortality ($P = 0.029$).

Discussion

This retrospective analysis sought to examine if IABP combined with mechanical ventilation provided a better outcome at our centre (in terms of all-cause in-hospital mortality) than IABP alone, for the treatment of cardiogenic shock after acute myocardial infarction in patients aged > 60 years. The IABP + mechanical ventilation group tended to present with more severe cardiogenic shock than the IABP group, as demonstrated by a lower mean arterial BP, systolic BP and a greater incidence of Type 1 respiratory failure. Type 1 respiratory failure is defined as $PaO_2 < 60$ mmHg and the mean ± (SD) PaO_2 for the IABP + mechanical ventilation group was 49.9 ± 5.1.

Nevertheless a significant improvement of left ventricular function, as measured by LVEF, was observed in the IABP + mechanical ventilation group following the procedure. By contrast, no difference was

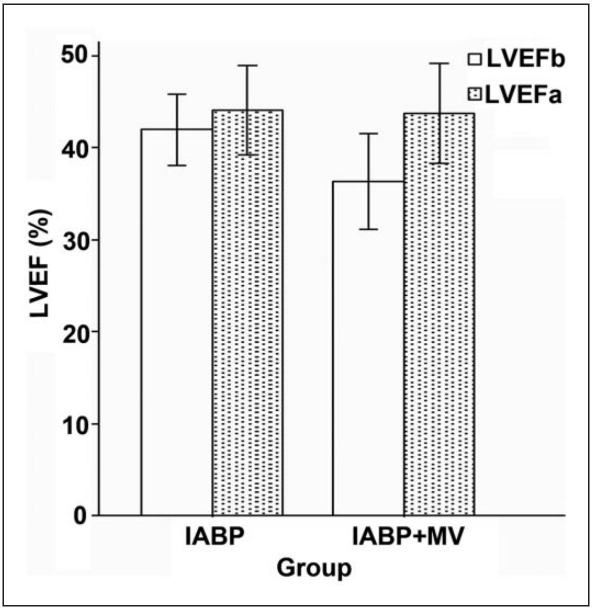

Figure 1. Left ventricular ejection fraction (LVEF) before and after treatment.
Comparison of LVEF before and after the procedures showed a statistically significant improvement in left ventricular function in the IABP + mechanical ventilation group ($n = 29$; $P < 0.001$). IABP: intra-aortic balloon pump, MV: mechanical ventilation, LVEFb: left ventricular ejection fraction before treatment, LVEFa: left ventricular ejection fraction after treatment.

observed in left ventricular function before and after treatment in the IABP group. In addition, there were significantly more cases of pulmonary infection and renal insufficiency in the IABP + mechanical ventilation group than the IABP group; analysis showed that these two conditions were significant risk factors for all-cause in-hospital mortality. However, there was no between-group difference in 30-day survival rates.

In patients with fragile haemodynamic status, such as those assessed in this study, inappropriate ventilation settings can have severe deleterious effects. Indeed, mechanical ventilation is often referred to as a double-edged sword for patients in cardiogenic shock.[16] Mechanical ventilation with PEEP is universally used in patients who have cardiogenic shock.[17] However, some investigations have shown that PEEP exerts unfavourable haemodynamic effects such as decreased venous blood return which increases right ventricular afterload, decreases left ventricular filling pressure and depresses cardiac output and overall organ perfusion.[18] Nevertheless, moderate levels of PEEP appear to be well tolerated in severe left ventricular dysfunction and cardiogenic shock, and may provide some haemodynamic benefits.[19] Therefore, clinicians should be aware that PEEP can be used for clinical benefits, but high levels should be avoided to minimize the potential side-effects.

A significant improvement in left ventricular function was observed in the IABP + mechanical ventilation group. IABP is the most commonly used intervention for cardiogenic shock:[20] it decreases the left ventricular afterload, increases the diastolic coronary arterial perfusion pressure and promotes a redistribution of the

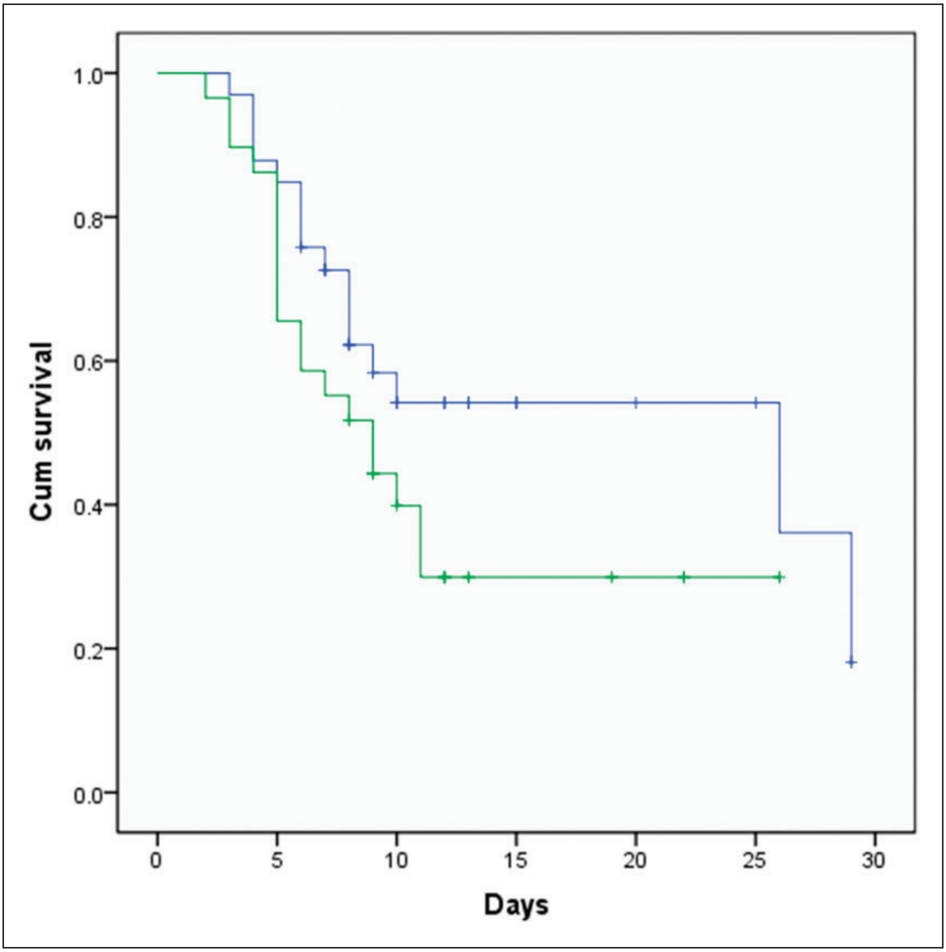

Figure 2. Although the IABP group tended to show better 30-day cumulative (cum) survival than the IABP + mechanical ventilation group, there was no significant between-group difference in in-hospital mortality (log-rank test; $P = 0.29$). Blue line: IABP group, Green line: IABP + MV group. IABP: intra-aortic balloon pump, MV: mechanical ventilation, cum: cumulative. The colour version of this figure is available at: http://imr.sagepub.com

coronary blood flow towards the ischaemic myocardium.[21] In addition, an appropriate level of PEEP can improve cardiac output by decreasing the left ventricular afterload and preload.[22,23] Mechanical ventilation also triggers the respiratory muscles that, during pulmonary oedema, generate more work and absorb a large proportion of the cardiac index.[24] Finally, we feel that mechanical ventilation improves pH and oxygenation, thereby offering a good chance of myocardial survival.

Survival rates observed in this study (i.e., 34.5% and 48.5% for IABP and IABP + mechanical ventilation groups, respectively) did not corroborate other research, which found rates of 28% and 80% for the IABP and IABP + mechanical ventilation groups, respectively.[19] As stated above, pulmonary infection and renal insufficiency were the

Table 3. Independent predictors of in-hospital mortality for 62 patients aged > 60 years in cardiogenic shock, treated with IABP or IABP and mechanical ventilation.

Factor	HR	95% CI	Statistical significance*
Age	1.299	0.917, 1.023	$P=0.254$
Sex	0.758	0.608, 3.637	$P=0.384$
Hypertension	0.635	0.327, 1.603	$P=0.425$
Diabetes mellitus	0.001	0.464, 2.210	$P=0.975$
Previous MI	0.779	0.648, 3.138	$P=0.378$
IABP + MV	0.005	0.413, 2.279	$P=0.944$
Pulmonary infection	4.186	1.038, 5.640	$P=0.041$
Renal insufficiency	6.425	1.365, 11.405	$P=0.011$
Successful revascularization	4.759	0.163, 0.908	$P=0.029$

*Cox regression analysis

HR, hazard ratio; CI, confidence interval; MI, myocardial infarction; IABP, intra-aortic balloon pump; MV, mechanical ventilation.

main complications reported in the IABP + mechanical ventilation group in this study from our centre and they were significant risk factors for all-cause, in-hospital mortality. Therefore, it is likely that the beneficial effects of improved left ventricular function on in-hospital mortality produced by the combination therapy were counteracted by the high incidence of pulmonary infection and renal insufficiency in this group of patients.

The high incidence of pulmonary infection observed in the IABP + mechanical ventilation group suggests that infections develop more easily with this intervention. Indeed, low cardiac output has been reported to be detrimental to the immune system in patients with cardiogenic shock.[25] In addition, ventilator-associated pneumonia (VAP), which occurs >48 h after intubation and mechanical ventilation,[26] is the most common nosocomial infection in the intensive care unit (incidence of 8–28%) in patients receiving mechanical ventilation via intubation.[27] Therefore, we postulate that IABP + mechanical ventilation may promote an increase in pulmonary infections, in patients in cardiogenic shock. Prevention and early treatment of pulmonary infections are therefore both important in patients receiving IABP + mechanical ventilation.

Renal insufficiency is reportedly related to organ hypoperfusion in patients in cardiogenic shock.[28] In the present study, patients in the IABP + mechanical ventilation group had more severe cardiogenic shock than patients in the IABP group, which may have accounted for the higher incidence of renal insufficiency in this group. Approximately 7% of patients undergoing percutaneous coronary intervention experience renal insufficiency, a condition which is strongly associated with in-hospital mortality.[29] Therefore, the management of renal insufficiency is one of the main cornerstones in the treatment of cardiogenic shock. Urine production should be measured and in cases of acute renal failure with clinical signs of uraemia, hydropic decompensation, metabolic acidosis and refractory hyperkalaemia, continuous renal replacement therapy should be initiated early.[30]

In agreement with previous findings, [31] the present study showed that successful revascularization was a negative risk factor for all-cause in-hospital mortality. Although early revascularization is increasingly performed, revascularization rates remain unsatisfactory.[32] Clinicians should recognize the benefits of revascularization even if the associated risks are high, especially in patients >60 years old.

The present study had several limitations. Firstly, it was a single-centre, nonrandomized, retrospective study. Nevertheless, randomized clinical trials in cardiogenic shock are difficult to perform and are often more costly than trials in other clinical conditions. [33] Therefore, a randomized study in this critically ill population may not be feasible.[21] In addition, because of the retrospective nature of the study, some variables could not be evaluated, including the mid-term survival rate. Secondly, the patients in the IABP + mechanical ventilation group had more abnormalities at baseline compared with those in the IABP group. This may have made it difficult to assess the real added value of mechanical ventilation and may have affected the study outcome. Indeed, the rate of successful revascularization in both treatment groups was lower than what could be expected for STEMI.[31] This may have been attributable to the poor condition of the patients, since this present study included patients in cardiogenic shock who were refractory to pharmacological therapy. Finally, the sample size was limited because at our centre only a small number of cases of cardiogenic shock received IABP or IABP + mechanical ventilation therapy. Therefore, further multicentre, randomized, prospective studies with larger sample sizes are needed to confirm our findings.

To conclude, our study showed that mechanical ventilation with an appropriate PEEP appears to enhance the beneficial effects of IABP on left ventricular function for patients in cardiogenic shock. However, IABP and mechanical ventilation did not decrease in-hospital mortality. The IABP + mechanical ventilation group of patients had greater rates of pulmonary infection and renal insufficiency than the IABP group: factors which were shown to be risk factors for all-cause, in-hospital mortality.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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