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Original Article

The effects of hemodynamic monitoring using the PiCCO system on critically ill patients

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Abstract: Objective: We aimed to evaluate the effects of hemodynamic monitoring using the pulse index continuous cardiac output (PiCCO) system with critically ill patients. Methods: In total, 292 patients with primary physiological abnormalities of hypotension (n = 180) or hypoxemia (n = 112) were evaluated. The attending physicians completed a questionnaire before each catheterization. After each catheterization, the attending physicians reviewed each chart to determine the possibility of altering the therapy. Results: In the hypotension subgroup, the attending physicians showed less accuracy in predicting the global end-diastolic index values (23.9%, 43/180), with a significant difference, and more accuracy in predicting the extravascular lung water index values (58.9%, 66/112), without a significant difference from the patients in the hypoxemia subgroup. In the hypotension patients, the lactate clearance rate within 6 h was significantly higher (36.4 ± 9.6 vs 21.3 ± 9.5; *P*<0.0001) when the hemodynamic monitoring led to therapeutic changes. Conclusions: The hemodynamic variables obtained using the PiCCO system improved the accuracy of the bedside evaluations and led to alterations in the therapeutic plans, particularly among the hypotension patients. The therapy changes showed no improvement in the overall mortality but were associated with improved tissue perfusion among the hypotension patients.

Keywords: Hemodynamic variables, mortality, pulse index continuous cardiac output, therapy

Introduction

The accurate assessment of the hemodynamic status is of great importance for critically ill patients experiencing circulatory or respiratory failure. The hemodynamic variables (HV) of critically ill patients are poorly predicted based on their physical examinations, laboratory examinations, and radiographic findings, and the invasive hemodynamic monitoring of pulmonary artery catheterization (PAC) often induces clinically important therapeutic changes [1, 2]. As a substitute for PAC with high validity and correlation, the pulse index continuous cardiac output (PiCCO) system, which has seen widespread use in recent years, has changed the approach to the bedside hemodynamic monitoring of critically ill patients [1, 2].

Our previous study [1] on critically ill patients also documented the HV inaccurately predicted based on careful clinical evaluations. The information obtained by the PiCCO system often leads to a change in therapy, particularly in critically ill patients with hypotension or unknown diagnoses. However, the effect of the PiCCO system on patient outcomes is still unclear.

We hypothesized that the potential benefit of using this technique could only be expected in patients in whom its use led to alterations in the therapeutic plan. We undertook this descriptive study to document the accuracy of bedside clinical evaluations and the frequency of alterations in the therapeutic plans induced by the PiCCO system. Most importantly, we also compared the outcomes of patients with and without therapeutic changes induced by the hemodynamic monitoring.

Patients and methods

Study site and patients

After obtaining written informed consent by legal representatives, 300 consecutive patients (173 women and 127 men) with primary hypotension or hypoxemia were recruited as

Table 1. Definition of the ranges

	CI, l/min/m²	GEDI, ml/m²	SVRI, dyn·s·cm⁻⁵·m²	EVLWI, ml/kg
Low	<3	<680	<1200	≤7
Medium	3-5	680-800	1200-2000	8-12
High	>5	>800	>2000	≥13

CI, mean cardiac index; EVLWI, mean extravascular lung water index; GEDI, mean global end-diastolic index; SVRI, mean systemic vascular resistance index.

the study cohort in our 48-bed general intensive care unit between February 2013 and February 2019. After the exclusion of patients with insufficient data, 292 patients were included. Hypotension was regarded as a systolic blood pressure of <90 mmHg or a decrease of >40 mmHg compared with the baseline. Hypoxemia represented impaired oxygenation with PaO_2/FiO_2 of ≤300.

The inclusion criteria were: Patients admitted to the emergency observation room, emergency rescue room, and the emergency intensive care unit, and patients for whom their clinical data was collected immediately when they entered the emergency department, and the clinical data must be complete, including gender, emergency department number, chief complaint, doctor's diagnosis, admission method, systemic assessment, contact information, and the relevant physiological parameters. At the same time, for the patients in the later stages, the clinical data should include the emergency treatment measures accepted during the emergency department and the patient's whereabouts (hospitalized, transferred or discharged).

The exclusion criteria included the following: (1) Patients <18 years old, (2) patients with significantly acute myocardial infarction, (3) patients who experienced a hemorrhagic shock, (4) patients who were moribund or for whom informed consent could not be obtained, (5) patients with contraindications to catheterization, including overlying infections and arterial grafting, (6) patients with conditions including intracardiac shunts, large aortic aneurysms, significant mitral/tricuspid regurgitation, which were likely to render the PiCCO measurements inaccurate [3], and (7) patients who had undergone repeated PiCCO catheterizations. This study was approved by the China-Japan Friendship Hospital. This study was observational and descriptive; therefore, we did not register it. It also was not randomized and did not have any intervention in the management by the investigators.

Experimental protocols

For the transpulmonary thermodilution-based hemodynamic monitoring, a 4-Fr thermistor-tipped arterial catheter was inserted into the femoral artery of the patients before anesthesia. A double or 3-lumen central venous catheter (Arrow, Reading, PA) was inserted in the internal jugular or subclavian vein. Both pressure transducers were positioned at the midaxillary line level and were zeroed to atmospheric pressure. Three central venous bolus injections (15 mL of cold isotonic saline in each injection) were injected within 7 s for the PiCCO measurement. The value used was the average of three consecutive measurements. All the operations were performed according to the described procedure by the same attending physician. The catheter positions were confirmed in all cases using a standard portable chest x-ray.

Data collection

Before the catheter insertion, the attending physician in charge of the patient obtained information such as the blood pressure, the PaO_2/FiO_2, and the blood lactate concentrations through the arterial line and arterial gases. The attending physician was asked to determine the primary pathophysiological abnormality (hypotension, hypoxemia, or both) and predicted the range of key HVs for the cardiac index (CI), the global end-diastolic index (GEDI), the systemic vascular resistance index (SVRI), and the extravascular lung water index (EVLWI) in addition to all the previous clinical information (**Table 1**). Additionally, the attending physician was also required to document a therapeutic plan based on the predicted hemodynamic profile, selecting from a list of potential therapeutic procedures (**Table 2**).

After the PiCCO catheterization was performed and the actual hemodynamic profile of the patient was determined, the attending physician reviewed the hemodynamic data to evaluate whether there was any possibility of altering the predicted therapy plan for the improvement of the patient's situation. The patients

Table 2. Therapeutic options

	Fluid expansion	Crystalloid infusion
		Colloid infusion
Volume management	Fluid balance	
	Fluid restriction	Diuretic drugs
		Hemodialysis
		Cardiac renal replacement therapies
	Constrictor	Dopamine
		Norepinephrine
	Dilator	Sodium nitroprusside
Vasoactive medication		Nitroglycerin
		Urapidil
		Nicardipine
		Diltiazem
Inotropic agent	Inotropic drug	Cedilanid
		Dobutamine
		Mirinone

were then divided into two subgroups: therapy changed and therapy unchanged. A clinically important change in therapy was prospectively defined as a change in the type of recorded therapeutic plan (i.e., volume management from fluid expansion to restriction, starting the use of inotropic drugs, initiating cardiac renal replacement therapies). No alteration in the anticipated therapy was interpreted as no adjustment to the treatment or just a dosage change of a given drug (i.e., dobutamine from 8 to 10 ug/kg/min, fluid infusion from 200 to 300 ml/h).

To compare the effect of the PiCCO catheter on the improvement of patient outcomes for those patients in whom the catheter led to therapeutic changes with no change in therapy after the catheter insertion, we documented the hemodynamic parameters, the blood lactate concentrations, and the PaO_2/FiO_2 ratios at the following time points: inclusion (T0), 6 h (T6), and 12 h (T12). We calculated the lactate clearance rates at 6 and 12 h. We also recorded the 14- and 28-day mortality rates to document the effect of the PiCCO catheter on the improvement of the patient outcomes.

Statistical analyses

Statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). All the graphical results were drawn using GraphPad Prism8 (Shenzhen Tianruiqi Software Technology Co., Ltd.). χ^2 tests were used to compare the qualitative data, and Fisher's exact probability tests were used for the small sample sizes, where applicable. A *t*-test was used to compare the quantitative data. A *P*-value of 0.05 was considered to indicate statistical significance. All the data are expressed as the mean ± standard deviation.

Results

Characteristics of the patients at baseline

A total of 292 patients including 180 (61.6%) with hypotension and 112 (38.4%) with hypoxemia were enrolled in this study. The patients with hypotension had significantly lower systolic blood pressures and higher heart rates, higher PaO_2/FIO_2 ratios, and higher lactate concentrations than the patients with hypoxemia (**Table 3**).

Complications of catheterization

All the catheters were placed using ultrasound as guidance. Complications attributed to the catheterization were noted in only six cases. Five (1.7%) patients experienced hemorrhage at the femoral arterial puncture site, which could be lessened or stopped by compression. One (0.3%) patient experienced pneumothorax, which required a chest tube insertion at the time of the subclavian vein catheterization. Transient ventricular and atrial arrhythmias were observed in four (1.4%) patients at the time of the cold saline injection but did not require antiarrhythmic therapy. No positive blood cultures or serious infectious complications were documented during the PiCCO catheter retention.

Prediction of key HVs

The attending physicians' accuracy in predicting the four HVs are indicated in **Figure 1**. As shown in **Figure 1**, the ability of the attending physicians in predicting key HVs, except for EVLWI, was poor. The attending physicians were able to predict the EVLWI correctly in 65.8% (192/292) of the cases, which was higher than the other three HVs, with a significant difference. The accuracy in predicting

Table 3. Characteristics of the patients at baseline

	All patients (n = 292)	Patients with hypotension (n = 180)	Patients with hypoxemia (n = 112)	
Age, y	61.5 ± 18.3	65.8 ± 22.1	62.6 ± 13.2	0.1669
Sex, M/F	166/126	112/68	54/58	0.2120
APACHE II score	17.3 ± 5.7	17.9 ± 6.1	17.2 ± 5.4	0.3203
SOFA score	8.6 ± 3.4	9.2 ± 3.6	8.3 ± 3.7	0.0408
Type of patient, n (%)**				
Septic shock	154 (52.7)	147 (81.7)	7 (6.3)	<0.0001
Pancreatitis	25 (8.56)	21 (11.7)	4 (3.6)	0.0162
Congestive heart failure	18 (6.16)	8 (4.4)	10 (8.9)	0.2123
ARDS	95 (32.5)	4 (2.2)	91 (81.3)	<0.0001
Heart rate*	115 ± 24	129 ± 35	109 ± 18	<0.0001
MBP, mmHg**	106 ± 25	81 ± 22	125 ± 17	<0.0001
Lactate, mmol/L**	3.6 ± 1.7	5.1 ± 2.8	2.8 ± 1.1	<0.0001
PaO_2/FiO_2*	251 ± 45	278 ± 55	168 ± 27	<0.0001

*P<0.05, **P<0.01, between the two subgroups at baseline.

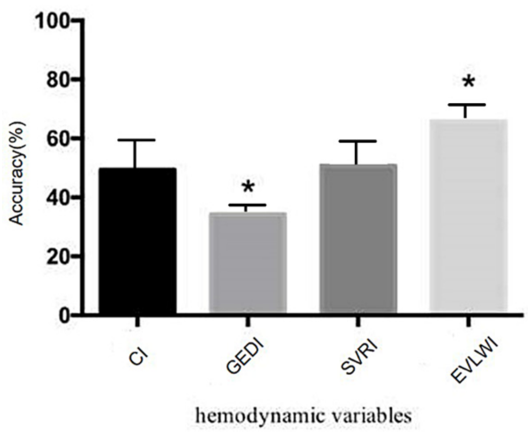

Figure 1. The accuracy in predicting the hemodynamic variables (n = 292). Significant differences between the 2 variables are indicated as *P<0.05.

GEDI (34.2%, 100/292) was significantly lower than the accuracy in predicting CI (49.3%, 144/292) and SVRI (50.7%, 148/292).

In the hypertension subgroup, the attending physicians demonstrated less accuracy in predicting the GEDI (23.9%, 43/180), with a significant difference, and more accuracy in predicting the EVLWI (70.0%, 126/180), without a significant difference from the patients in the hypoxemia subgroup (**Figure 2**).

Change in therapy

The information obtained by PiCCO resulted in a major or minor change in therapy. The incidence of total therapy change was analyzed to determine whether there was any correlation associated with the primary physiological abnormality.

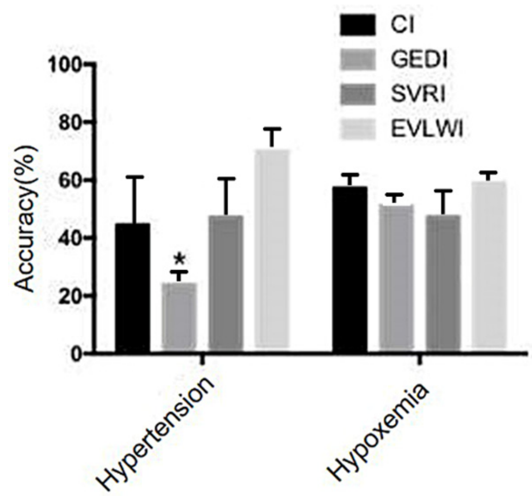

Figure 2. Prediction accuracies of the hemodynamic variables for the hypotension and hypoxemia subgroups (n = 292). Significant differences between the two subgroups are indicated as *P<0.05.

We found that hemodynamic monitoring prompted an alternation in therapy in 55% of the patients, especially those with hypotension (72.2% vs 27.7%, P<0.0001). The attending physicians were most likely to change the volume management (56.8%) according to the first hemodynamic profile (**Figure 3**).

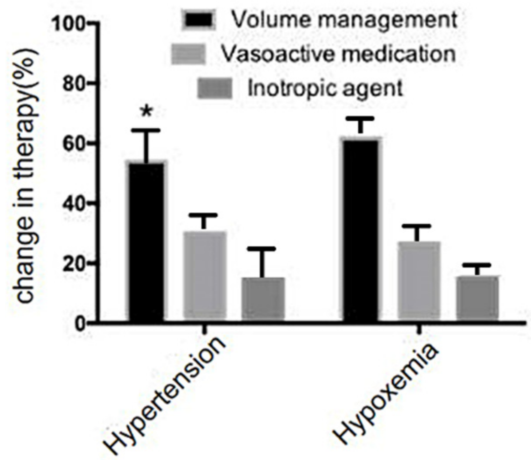

Figure 3. Change in therapy for the hypotension and hypoxemia subgroups (n = 292). Significant differences between the two subgroups are indicated as *P<0.05.

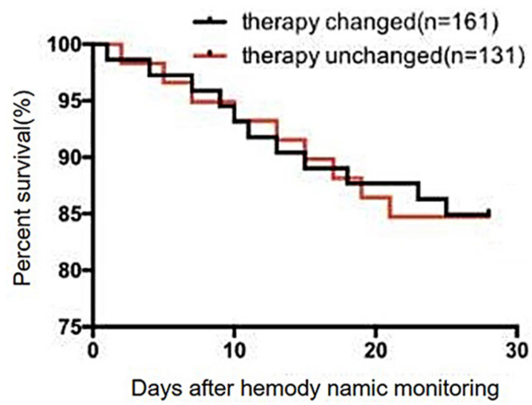

Figure 4. Kaplan-Meier survival analysis in the patients with or without therapeutic changes induced by the hemodynamic monitoring.

Outcome of the therapeutic alternation

We compared the mortality rates of the patients with and without therapeutic changes induced by hemodynamic monitoring (**Figure 4**). We found that there were no differences in the 14-day (9.3% vs 9.2%, P = 0.9634) or the 28-day (18.6% vs 19.1%, P = 0.9220) mortality rates in the patients with catheterization.

We found that, in the patients with hypotension, the lactate clearance rate within 6 h was significantly higher (35.4 ± 10.1 vs 22.5 ± 9.3, P<0.0001) when the hemodynamic monitoring led to therapeutic changes (**Table 4**). In addition, the earlier the treatment was adjusted, the more significant the decrease in the lactate clearance (54.2 ± 8.4 vs 52.9 ± 6.9, P = 0.5105).

In patients with hypoxemia, the PaO_2/FiO_2 ratio before the hemodynamic monitoring was 156 ± 21.7, with no significant difference. After 6 h of monitoring, the PaO_2/FiO_2 ratios in the patients for whom the treatment was changed as a result of the PiCCO monitoring increased significantly (296 ± 27.9 vs 258 ± 21.4, P< 0.0001) compared with those for whom the treatment was not changed (**Table 5**).

Discussion

Pulmonary arterial thermodilution has long been considered the clinical gold standard for the measurement of cardiac output (CO) [4]. Concerns regarding the inherent risks of PAC have driven the development of less invasive devices for the monitoring CO. Of these devices, calibrated arterial pulse-contour analysis as implemented in the PiCCO system (Pulsion Medical Systems, Munich, Germany) has become increasingly popular [5]. The PiCCO system, which provides an accurate assessment of consistent and dynamic hemodynamic status, has gained increasing acceptance in many intensive care units. Furthermore, PiCCO allows for the monitoring of numerous HVs, especially GEDI, which constitutes a reliable indicator of cardiac preload, and EVLWI, which is a sensitive indicator of pulmonary edema. The PiCCO system can provide substantial help in directing immediate and subsequent therapy [6]. However, the benefit of this system has not been clearly demonstrated.

Our study confirms previous observations regarding the inability of physicians to predict HVs obtained by hemodynamic monitoring on the basis of the physical examination and the x-ray findings. Eisenberg et al. [7] found that physician accuracy in predicting the four key HVs of PAC never exceeded 55%, and that after catheterization, planned therapy was altered in 58% of the cases. Steingrub et al. [8] also reported <51% correct predictions of hemodynamic profiles on the basis of clinical experience, which led to the therapeutic alteration of 154 (45%) cases. Similar to our previous study, we also showed the rate of correct predictions for the evaluated key HVs was only close to 50% on average, except for EVLWI, which may

Table 4. The lactate clearance rates when the hemodynamic monitoring led to therapeutic changes

	Patients with hypotension (%) (n = 180)	Therapy changed (%) (n = 130)	Therapy unchanged (%) (n = 50)	*t*	*P* value
6 h	29.6 ± 10.1	36.4 ± 9.6	21.3 ± 9.5	9.479	<0.0001
12 h	56.1 ± 7.5	57.2 ± 9.4	55.9 ± 7.9	0.8668	0.3872

Table 5. Changes in the PaO2/FiO2 ratios when the hemodynamic monitoring led to therapeutic changes

	Patients with hypoxemia (n = 112)	Therapy changed (n = 30)	Therapy unchanged (n = 82)	*t*	*P* value
0 h	156 ± 21.7	147 ± 26.3	158 ± 35.5	1.547	0.1247
6 h	265 ± 25.8	296 ± 27.9	258 ± 21.4	7.647	<0.0001

be easier to evaluate because of the reflection of oxygenation.

Several factors may have accounted for the inaccuracy of the predictions. First, the critically ill patients enrolled were not randomized. Only patients with hypotension and hypoxemia who had not responded to an initial therapy received hemodynamic monitoring. Those who responded favorably to trial therapy did not undergo catheterization. Second, although attending physicians were requested to predict hemodynamic profiles approximately 1 h before the PiCCO insertion, it was likely that the fluid resuscitation or vasopressor support applied before the first hemodynamic measurement, particularly in patients with hypotension, may have significantly affected the predictive ability [9]. Third, most of the patients enrolled had severe disease that involved multiple systems. With a greater appreciation of states of altered ventricular compliance with the hypotension and cardiopulmonary interactions in hypoxemia, it became more complicated and difficult to predict the actual hemodynamic situation provided by the PiCCO catheterization. Fourth, extremely critically ill patients could not express themselves clearly, as most of them (86%) were intubated with mechanical ventilation in a limited supine position. Also, the background noise in the intensive care unit environment may make the accurate characterization of the auscultatory findings extremely difficult [10]. All of these factors are barriers preventing the attending physician from making accurate predictions. In addition, our definition of the prediction range of the four key HVs may be too strict and thus produce a low accuracy prediction rate.

We also found that the hemodynamic monitoring prompted a new therapy in 55% of the patients on the basis of the data obtained using the PiCCO monitoring, especially among those with hypotension (72.3%). The attending physicians were most likely to change the volume management (56.8%) according to the first hemodynamic profile, possibly because of the inaccurate estimates of the GEDI value. As we know, inadequate intravascular volume can result in inadequate CO and tissue hypoperfusion, which are associated with elevated morbidity and mortality [11]. Fluid overload may also result in cardiac failure and subsequent pulmonary edema and hypoxia [12]. Therefore, the optimization of volume management requires an accurate assessment of volume status and fluid responsiveness. As Michard and Teboul [13] have reported, only 40%-72% of critically ill patients who might benefit from the fluid challenge have shown responsiveness to volume expansion. The GEDI parameter has been shown to be extremely useful in evaluating cardiac preload, helping to select patients who might benefit from volume expansion, and avoiding ineffective or even deleterious volume expansion (worsening gas exchange or tissue edema, especially pulmonary edema) in the nonresponding patients, in whom inotropic or vasopressor support should preferentially be used [6]. Our study also showed that the timely alternation of volume management, avoiding volume depletion and overload, may result in adequate CO and tissue perfusion, finally increasing the lactate clearance rate.

As for patients in hypoxemia, the PiCCO system can be used to diagnose and treat hypoxemia by monitoring EVLWI and pulmonary vascular permeability index. The attending physicians seldom changed the established therapeutic options, even when a patient's hemodynamic situation deteriorated. Attending physicians often take the negative fluid balance for granted for the treatment of hypoxemia, which has repeatedly been proven to be associated with improved clinical outcomes [14]. According to the chest x-rays or the auscultations, the EVLWI values can be evaluated more easily than the other values and diuretics or cardiac renal replacement therapies with a higher fluid removal rate will be given. Whatever the exact quantity of EVLWI, the attending physicians lean toward treating such patients using the strategy of negative fluid balance. Of course, the major alternate therapy for such patients may be mechanical ventilation adjustment, including recruitment maneuvers and positive end-expiratory pressure titration, which may lead to an improvement in their oxygenation [15]. Unfortunately, however, our experiment design did not list this type of therapeutic option, which may have led to a lower rate of alternation of therapy.

Interestingly, we found that the attending physicians changed their established therapies in 8% of the cases, even when the key HVs were all correctly predicted. This finding suggests that physician experience and self-confidence played important roles in the number of such changes and that hemodynamic monitoring has an effect on these vital clinical decisions, even when the correct diagnosis is suspected.

Only a few studies have assessed the effect on outcomes of hemodynamic monitoring that led to therapeutic alternation in critically ill patients. One [16] observed no beneficial effect in terms of the mortality rate for medical patients in whom PAC monitoring led to therapeutic alternation. Mimoz et al. [17] were also unable to demonstrate any difference in the mortality rates of critically ill patients in whom a therapy change was induced by the PAC monitoring. In our study, we were also unable to demonstrate any difference in the mortality rate of patients in whom PiCCO monitoring led to a therapy alternation. The reason may be explained as follows: (1) our sample size was small; (2) the acquisition of the hemodynamic monitoring alone does not alter mortality, if it cannot be converted into hemodynamic treatment; (3) the therapeutic alternation judgment was made just after the first measurement of the hemodynamic profile, as it is unethical and impossible to insist on the former treatment afterward; (4) a misinterpretation of the hemodynamic data may lead to an inappropriate therapeutic alternation and therefore potentially influence the mortality rates; and (5) the patient's treatment algorithm is not merely based on the PiCCO variables, such as the anti-infectious strategy; the mechanical ventilation adjustment will have an unavoidable effect on the mortality rates. Nevertheless, in patients with hypotension, the lactate clearance rate was significantly higher when the hemodynamic monitoring led to therapeutic changes. That indicated, at least in this subgroup of patients, that a change in therapy prompted by the PiCCO monitoring was associated with sufficient tissue perfusion, which may have led to an improved prognosis [18].

Randomized studies [19, 20] comparing patients managed with and without the PiCCO catheter may be the best way to substantiate the benefit of the invasive hemodynamic monitoring. However, there are limitations to our studies. First, it is unethical to ignore hemodynamic monitoring for an extremely critically ill patient when he or she experiences circulatory or respiratory failure. Furthermore, it would be difficult to conduct a randomized trial using the expensive PiCCO catheter, which is not yet covered by medical insurance in China. Lastly, hemodynamic management differentiates based on the clinical experience and hemodynamic understanding of the attending physician. The same PiCCO values may be interpreted with opposite results, which could then result in contradictory treatment.

Our study demonstrated the inaccuracy of prediction for HVs based on the clinical evaluation, which largely lead to alterations in the therapeutic plan, particularly in patients with hypotension. This change in therapy showed no improvement on overall mortality but was associated with improved tissue perfusion in patients with hypotension.

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Disclosure of conflict of interest

None.

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