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U-shaped prognostic value of left ventricular-arterial coupling in septic patients: a prospective study

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Abstract

Background Ventricular-arterial coupling (VAC) has garnered increasing interest in critical care. The prognostic significance of left ventricular-arterial coupling (LVAC) in this context remains a topic of debate.

Objective This study aimed to explore the association between LVAC and patient outcomes in sepsis.

Methods Patients with sepsis or septic shock admitted to the intensive care unit (ICU) were included. LVAC was evaluated using the arterial elastance (Ea)/left ventricular end-systolic elastance (Ees) ratio. Prognostic indicators, including 30-day mortality, length of ICU stay, mechanical ventilation (MV), changes in delta lactate levels, and oxygen index were also collected.

Results A total of 388 patients were enrolled in this study. A U-shaped relationship was observed between LVAC and 30-day mortality, with an optimal LVAC value of 1.19 identified. For LVAC values above 1.19, the odds ratio (OR) for 30-day mortality was 1.07 (95% confidence interval [CI] 1.01–1.14). Below this threshold, OR was 0.85 (95% CI 0.73, 0.99). Similarly, in the curve for ICU-free days, a β value of − 8.64 (95% CI − 16.53, − 0.76) was noted for LVAC values over 1.26. For ventilator-free time, the kink point was 1.24, with significant β values on both sides of this threshold [− 226.49 (95% CI − 411.59, − 41.38) and 147.67 (95% CI 12.40, 282.93), respectively].

Conclusions This study established U-shaped associations between LVAC and various clinical outcomes in septic patients. Optimizing LVAC could potentially enhance patient prognosis. Given the slight variations in optimal LVAC values across different patient populations, individualized LVAC titration may be beneficial in improving clinical outcomes.

Keywords Echocardiography, Left ventricular-arterial coupling, Prognosis, Sepsis, Septic shock

Introduction

The concept of ventricular-arterial coupling (VAC) has been acknowledged for decades, yet it has only recently gained significant attention in critical care [1, 2]. Hemodynamic abnormalities are ubiquitous among critically ill patients. Sepsis and septic shock, as classic conditions in the intensive care unit (ICU), exhibit distinct characteristics. Moreover, septic cardiomyopathy is notably prevalent in patients with sepsis and septic shock [3, 4]. Commonly in septic shock, there is a loss of peripheral vasomotor tone and cardiac dysfunction,

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primarily characterized by impaired left ventricular (LV) performance, leading to abnormal ventricular-arterial interaction [5].

Initial resuscitation strategies for septic patients, such as volume expansion and vasopressor infusion, invariably modify the heart's preload and afterload, potentially affecting its intrinsic contractility [4]. This alteration in vasomotor tone and left ventricular contractility can lead to abnormal left ventricular-arterial coupling (LVAC), which is the main cause for hemodynamic homeostasis imbalance. The LVAC can be calculated as the arterial elastance (Ea)/left ventricular end-systolic elastance (Ees) ratio. A noninvasive method based on echocardiography has been proved to reliably evaluate the Ea/Ees in critically ill patients [2]. However, prior studies have reported inconsistent findings regarding the association between LVAC and the prognosis of septic patients [6, 7]. Consequently, this study aims to explore the associations of LVAC with the short-term outcomes of septic patients.

Patients and methods

Study population

This observational study was conducted from November 2019 to September 2023 in the ICU of a tertiary hospital. All adult septic patients were screened for enrollment within 24 h of admission.

Sepsis was defined as life-threatening organ dysfunction resulting from a dysregulated host response to infection. Septic shock was defined as sepsis accompanied by persisting hypotension necessitating vasopressors to maintain a mean arterial pressure (MAP) of 65 mmHg or higher, and a serum lactate level exceeding 2 mmol/L, despite adequate volume resuscitation [8].

Patients were excluded for any of the following reasons: absence of echo examination; inadequate echocardiographic images; a history of chronic hear t failure; an acute coronary syndrome event within the previous week; atrial fibrillation rhythm characteristics; left ventricular outflow tract (LVOT) obstruction, defined as an instantaneous LVOT pressure gradient of at least 30 mmHg [9]; prosthetic valves or significant valvular diseases, such as severe mitral, aortic, or tricuspid stenosis or regurgitation; moderate to severe chronic pulmonary hypertension; or withholding of life support.

This study was conducted in compliance with the Declaration of Helsinki and was approved by the ethics committee of our institution (Approval No. ZS-2166). Informed consent was obtained from the patients' next of kin.

Echocardiography

As a critical ultrasound center in China, we implemented a protocol for all patients admitted to our intensive care unit. Echocardiograms were conducted within 24 h of ICU admission and were repeated during subsequent days in the ICU as needed based on clinical needs. In this study, echo images were captured using an echocardiograph (Mindray M9/M11, Shenzhen, China) with a 2.5-MHz phased-array probe by two specific physicians (H Zhang and Q Zhang) who possessed significant experience. The images were saved for offline analysis, and electrocardiograms were continuously recorded during the examination. Three cardiac cycles were analyzed and averaged.

LVAC was calculated as Ea/Ees. Ees was determined using the noninvasive single-beat method (described elsewhere), employing invasively measured blood pressure, echocardiography-derived left ventricular ejection fraction (LVEF), stroke volume (SV), and several timing intervals (pre-ejection period, total systolic period). The pre-ejection period was the interval between R wave and flow onset, and the total systolic period was the interval between R wave and end-flow (Fig. 1) [10]. Ea was calculated using the formula: systolic blood pressure × 0.9/SV. LVEF was ascertained using a modified biplane Simpson's method from the apical two- and four-chamber views. The LVOT velocity–time integral (VTI) was obtained by positioning the sample volume at the LVOT approximately 0.5 cm below the aortic valve using pulsed Doppler imaging at the apical three- or five-chamber view [11]. SV was calculated using the following formula: $SV = \pi \times (\text{LVOT diameter}/2)^2 \times \text{LVOT-VTI}$. Additionally, the cardiac index (CI) was determined as SV × HR/Body Surface Area.

Other parameters collected

Demographic information, including the Sequential Organ Failure Assessment (SOFA) score, diagnosis, and comorbidities, was collected at the time of diagnosis for all patients. Additionally, we recorded each patient's heart rate (HR), MAP, central venous pressure (CVP), total fluid volume, and vasopressor use at the time of the echo examination. Arterial blood lactate levels were collected both at diagnosis and 6 h post-diagnosis.

Outcomes

The primary outcome measured was 30-day mortality. Secondary outcomes encompassed the length of ICU stay, mechanical ventilation time (MVt), delta lactate (the difference in lactate levels between 6 and 0 h), and the oxygen index (PaO_2/FiO_2). Considering the potential influence of censoring for death on the relationship between LVAC and ICU duration and ventilation time, we utilized ICU-free days and ventilator-free time as metrics to mitigate the impact of mortality on clinical results [12]. These were calculated as follows: 30 (day)

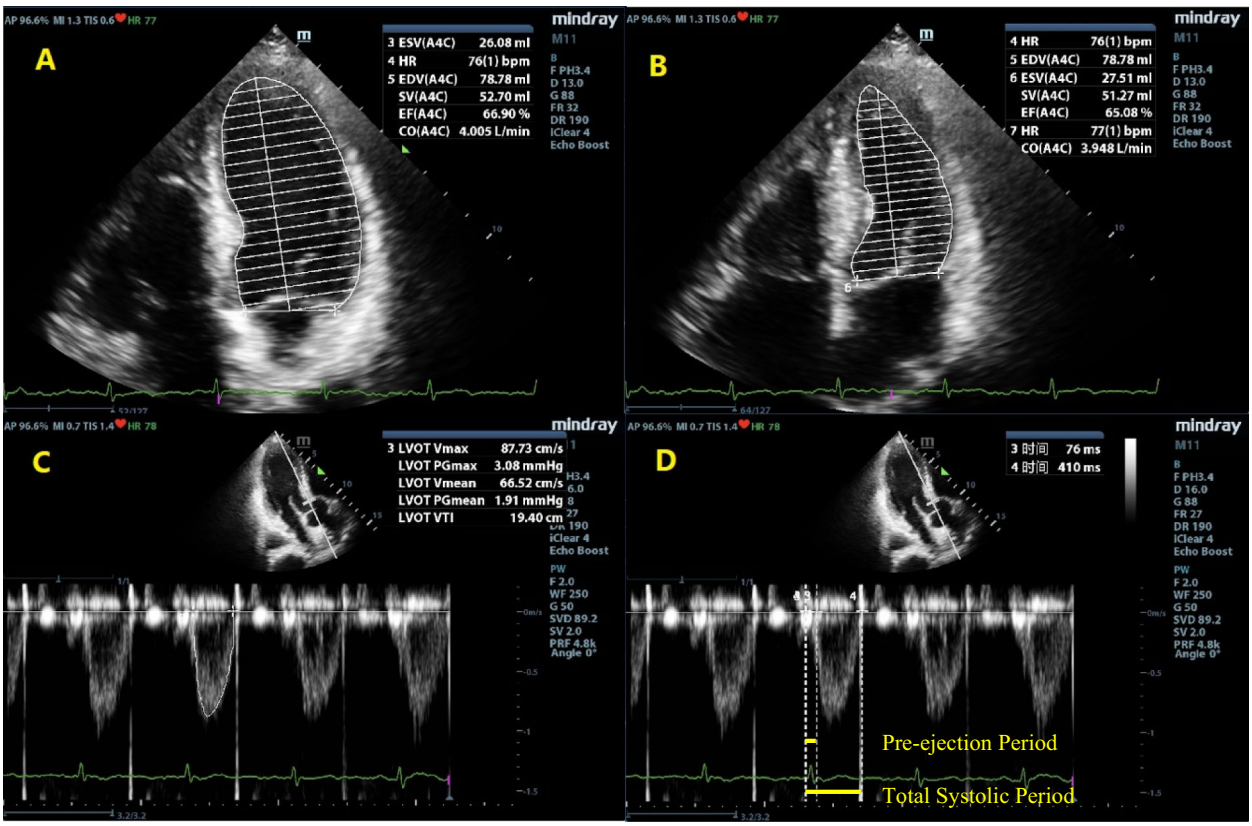

Fig. 1 Echocardiographic measurements for LVEF, LVOT-VTI, and timing intervals for LVAC estimation. **A** and **B** Measurement of LVEF using the Simpson method through an apical four-chamber view. **C** Measurement of LVOT-VTI using PW Doppler from an apical three-chamber view. **D** Measurement of pre-systolic and total systolic periods, necessary for the estimation of single-beat Ees. LVEF: Left ventricular ejection fraction, LVOT-VTI: Left ventricular outflow tract velocity–time integral, LVAC: Left ventricular assistive contraction, PW Doppler: Pulsed-wave Doppler, Ees: End-systolic elastance

minus the number of days in the ICU or 720 (hours) minus the duration of mechanical ventilation. In cases where the patient's outcome was death, both metrics were recorded as 0.

Statistical analyses

We performed the statistical analysis using EmpowerStats (http://www.empowerstats.com) and R software, version 4.2.0 (http://www.R-project.org/). Continuous variables are expressed as either mean ± SD or median with interquartile range. The normality of continuous values' distribution was evaluated using the Kolmogorov–Smirnov test. Categorical variables are presented as frequencies and percentages. Spearman's correlation coefficients were calculated to assess the relationships between variables. To mitigate the effect of collinearity, indicators were added based on Spearman's results. The Generalized Additive Mix Model was used for analysis. Smooth curves were used to quantify the results. A two-tailed $P < 0.05$ was considered statistically significant in all analyses. Subgroup analyses were performed for patient cohorts diagnosed with sepsis or septic shock. For univariate analysis of ICU mortality, we used Generalized Estimating Equations. We assessed intraobserver and interobserver variabilities in LVEF, and LVOT-VTI in 20 randomly selected patients, employing intraclass correlation coefficients (ICCs). An ICC greater than 0.8 indicated excellent agreement. A two-tailed $P < 0.05$ was considered significant.

Results

As shown in Fig. 2, a total number of 502 patients met the criteria for sepsis and septic shock diagnosis. Ultimately, 388 patients were included in this study. Their general characteristics are detailed in Table 1. Of these participants, 63.9% were male and 63.4% were diagnosed with septic shock. The average age was 62.5 years. Mechanical ventilation was administered to 86.1% of the patients. The median ventilator-free time and ICU-free days were 662.5 h and 24 days, respectively. The 30-day mortality rate was 15.5%, indicating that 60 out of 388 patients died within 30 days.

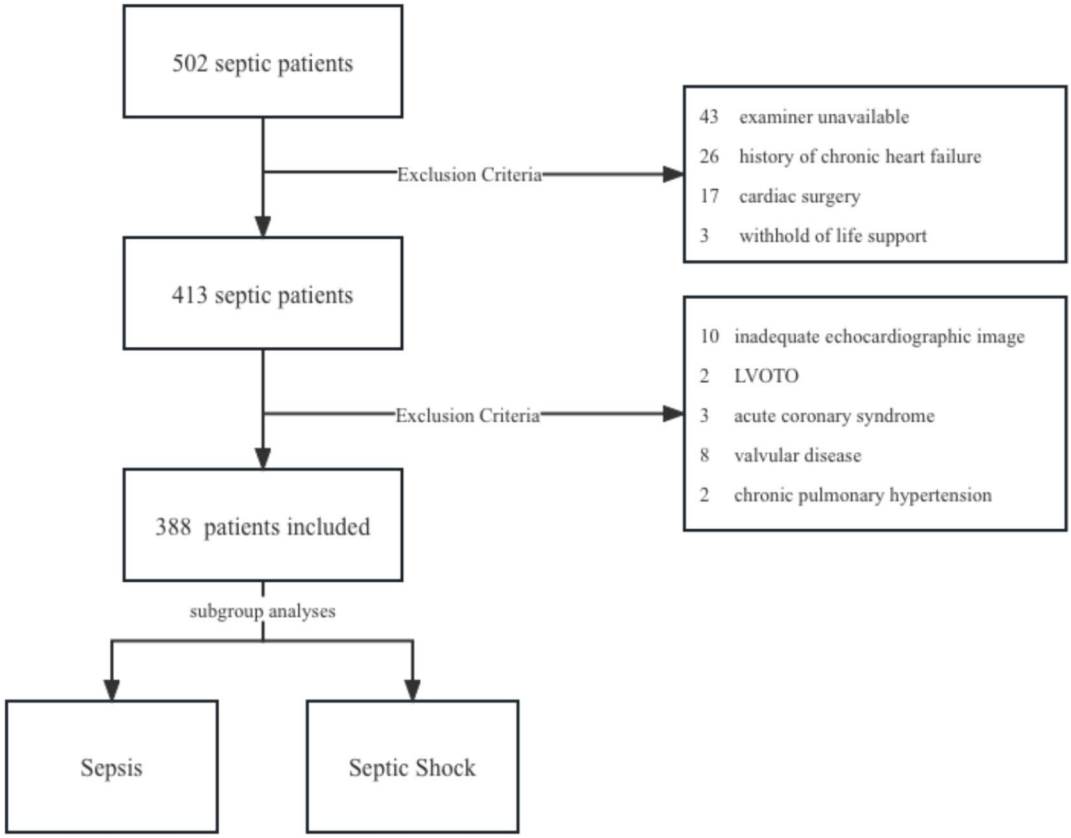

Fig. 2 Flow chart of the study. LVOTO: Left ventricular outflow tract obstruction

Table 1 Demographic characteristics and outcomes of the study population

N = 388	*N* (%)	Mean ± SD	Min.	25th	50th	75th	Max.
Age		62.5 ± 16.8	16	52	64	73	98
Gender							
Male	248 (63.9%)						
Female	140 (36.1%)						
Diagnosis							
sepsis	142 (36.6%)						
Shock	246 (63.4%)						
MVt	334 (86.1%)						
Ventilator-free time (hours)			0	515.5	662.5	708.0	720
ICU-free days			0	10.8	24	27	30
Mortality							
Yes	60 (15.5%)						
No	328 (84.5%)						

MVt: Mechanical Ventilation Time

Table 2 presents the distribution of ICU parameters. The majority of the SOFA and APACHE II scores were notably high. In 75% of patients, SOFA scores ranged from 9 to 20, whereas APACHE II scores were between 15 and 26. The maximum NE dosage reached 3.0 μg/(kg*min), although most patients required NE support at dosages below 0.5 μg/(kg*min). In terms of MV, the PEEP varied from 0 to 15 cmH_2O, plateau pressure

Table 2 Distribution of ICU parameters

	N	Min.	25th	50th	75th	Max.
SOFA	361	1	9	11	13	20
APACHE II	361	3	15	20	25	26
NE	374	0.0	0.1	0.2	0.4	3.0
PEEP	356	0	5	6	8	15
Pplat	341	0	13	17	20	39
TV	284	80	380	410	460	700
HR	387	41	80	91	104	143
MAP	388	51	77	85	90	127
CVP	359	0	5	7	9	22
LVEF	388	19	50	60	67	83
LOVT-VTI	384	6.4	14.0	16.9	19.7	31.0
Ea	388	0.9	1.6	1.9	2.4	7.4
Ees	388	0.6	1.3	1.6	2.1	6.79
LVAC (Ea/Ees)	388	0.3	0.9	1.2	1.5	4.7
CI	360	1.1	2.5	3.0	3.8	8.0
Lac 0 h	351	0.6	1.4	2.2	3.9	28.0
Lac 6 h	336	0.4	1.2	1.9	3.0	30.0
PaO_2/FiO_2	351	57.8	215.5	270.0	331.5	516.0

SOFA: sequential organ failure assessment; APACHE: acute physiology and chronic health evaluation; NE: norepinephrine; PEEP: positive end-expiratory pressure; Pplat: plateau pressure; TV: tidal volume; HR: heart rate; MAP: mean arterial pressure; CVP: central venous pressure; LVEF: left ventricular ejection fraction; LVOT-VTI: left ventricular outflow tract velocity–time integral; Ea: arterial elastance; Ees: left ventricular end-systolic elastance; LVAC: left ventricular-arterial coupling; CI: cardiac index; Lac: lactate; PaO_2/FiO_2: oxygen index

(Pplat) from 0 to 39 cmH_2O, and tidal volume (TV) from 80 to 700 mL. The PaO_2/FiO_2 ranged from 57.8 to 516.0. Under NE administration, the MAP was between 51 and 127 mmHg, and the CVP varied from 0 to 22 mmHg. The ventricular-arterial coupling indicator, Ea/Ees, ranged from 0.3 to 4.7. Half of the study population maintained a normal lactate (Lac) six hours after disease diagnosis.

The Spearman correlation coefficients are presented in Table 3. In calculating Ees, we utilized LVEF and LVOT-VTI, while LVAC represented the ratio of Ea to Ees. Consequently, only LVAC was included in the analyses. We excluded any pair of variables exhibiting collinearity following Spearman correlation analysis. Considering the potential of NE as a mortality risk factor, closely associated with Ea/Ees, it was incorporated into the final regression model alongside age and gender.

Figure 3 and Table 4 depict the U-shaped correlation between LVAC and outcomes. The lowest 30-day mortality was observed in patients with an LVAC value of 1.19. A decrease in LVAC correlates with increased mortality. Specifically, for LVAC values greater than 1.19, the odds ratio (OR) for 30-day mortality was 1.07, with a 95% confidence interval (CI) of 1.01–1.14. Conversely, for LVAC values below 1.19, the OR was 0.85 (95% CI 0.73, 0.99). It should be noted that these ORs reflect each 0.1 change in LVAC. In the ICU-free days curve, when LVAC exceeded 1.26, the β value was -8.64 (95% CI − 16.53, − 0.76). Regarding ventilator-free time, the kink point was 1.24. The β values were statistically significant regardless of whether LVAC is above (-226.49 [95% CI − 411.59, − 41.38]) or below (147.67 [95% CI 12.40, 282.93]) the kink point. U-shaped curves were also evident for delta lactate and oxygen index, although these were not statistically significant.

In the subgroup analyses, we observed U-shaped curves for both the sepsis and septic shock groups in terms of ventilator-free time (Fig. 4). Additionally, in the sepsis group, the mortality data presented wavy lines. However, such U-shaped curves were not consistently evident across other secondary outcomes. Table 5 displays the specific kink values for each curve. In the sepsis group, a linear correlation was identified for ICU-free days and delta lactate, prompting us to perform a multivariate analysis. The β values were found to be − 3.86 (95% CI − 8.82, 1.11) and − 0.32 (95% CI − 1.00, 0.35), respectively. A similar linear relationship was observed for PaO_2/FiO_2 in the septic shock group, with a β value of − 6.45 (95% CI − 43.68, 30.78).

The analysis of interobserver variability revealed minimal differences in the measurement of LVEF and LVOT-VTI. Specifically, the ICCs for LVEF and LVOT-VTI were 0.885 (95% CI 0.735–0.953) and 0.905 (95% CI 0.739–0.963), respectively.

Table 3 Spearman correlations among ICU parameters

	SOFA	APACHE II	NE	Pplat	VT	HR	MAP	CVP	LVAC (Ea/Ees)	CI	Lac 0 h	Lac 6 h	PaO_2/FiO_2	PEEP
SOFA	1.00													
APACHE II	0.41*	1.00												
NE	0.41*	0.25*	1.00											
Pplat	0.24*	0.09	0.25*	1.00										
VT	-0.04	-0.08	0.03	− 0.04	1.00									
HR	0.19*	0.11*	0.31*	0.03	0.10	1.00								
MAP	0.00	− 0.06	− 0.17*	0.02	0.03	− 0.02	1.00							
CVP	0.31*	0.07	0.31*	0.34*	0.11	0.28*	0.06	1.00						
LVAC (Ea/Ees)	0.14*	0.16*	0.05	0.02	0.02	0.18*	− 0.02	0.04	1.00					
CI	0.06	− 0.13*	− 0.04	− 0.10	0.25*	0.33*	0.14*	0.04	− 0.27*	1.00				
Lac 0 h	0.35*	0.27*	0.34*	0.18*	0.02	0.23*	0.09	0.23*	0.06	0.09	1.00			
Lac 6 h	0.40*	0.29*	0.43*	0.23*	0.01	0.24*	0.04	0.29*	0.03	0.03	0.79*	1.00		
PaO_2/FiO_2	− 0.35*	− 0.18*	− 0.17*	− 0.29*	− 0.06	− 0.08	− 0.09	− 0.22*	− 0.10	− 0.08	− 0.20*	− 0.22*	1.00	
PEEP	0.28*	0.11*	0.24*	0.68*	0.15*	0.08	0.05	0.36*	0.05	− 0.08	0.24*	0.28*	− 0.37*	1.00

SOFA: sequential organ failure assessment; APACHE: acute physiology and chronic health evaluation; NE: norepinephrine; PEEP: positive end-expiratory pressure; Pplat: plateau pressure; TV: tidal volume; HR: heart rate; MAP: mean arterial pressure; CVP: central venous pressure; LVEF: left ventricular ejection fraction; LVOT-VTI: left ventricular outflow tract velocity–time integral; Ea: arterial elastance; Ees: left ventricular end-systolic elastance; LVAC: left ventricular-arterial coupling; CI: cardiac index; Lac: lactate; PaO_2/FiO_2: oxygen index

* denotes statistical significance

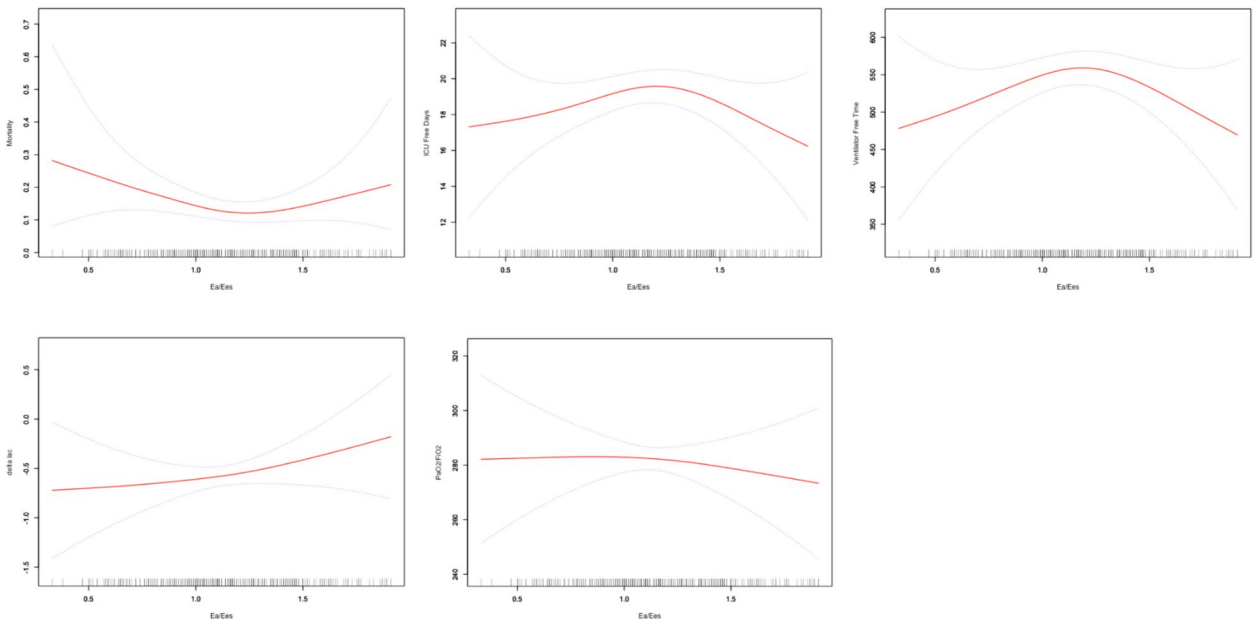

Fig. 3 U-shaped relationship between LVAC (Ea/Ees) and outcomes. Adjusted for age, gender, and NE. Delta lac: Calculated as lac 6 h − lac 0 h; PaO_2/FiO_2: Oxygen index

Discussion

To the best of our knowledge, this study is the first to assess the correlation between LVAC and outcomes in adult septic patients. We found that LVAC functions as a double-edged sword, exhibiting U-shaped curves for all outcomes. This means that both high and low LVAC were associated with poorer outcomes in septic patients, impacting both primary and secondary outcomes, although some effect values were statistically insignificant.

Table 4 Effect value for U-shaped relations between LVAC (Ea/Ees) and outcomes

Outcome	Mortality	ICU-free days	Ventilator-free time	Delta lac	PaO_2/FiO_2
K	1.19	1.26	1.24	1.25	1.22
< K	**0.85 (0.73, 0.99)**	4.85 (– 0.50, 10.20)	**147.67 (12.40, 282.93)**	– 0.54 (– 1.68, 0.60)	25.59 (– 30.43, 81.61)
> K	**1.07 (1.01, 1.14)**	**– 8.64 (– 16.53, – 0.76)**	**– 226.49 (– 411.59, – 41.38)**	1.45 (– 0.17, 3.06)	– 52.89 (– 122.32, 16.54)

"K" represents the kink for the U curve

Adjusted for age, gender, and NE. Values with $P < 0.05$ are highlighted in bold

Delta lac is calculated as lac 6 h – lac 0 h; PaO_2/FiO_2: oxygen index

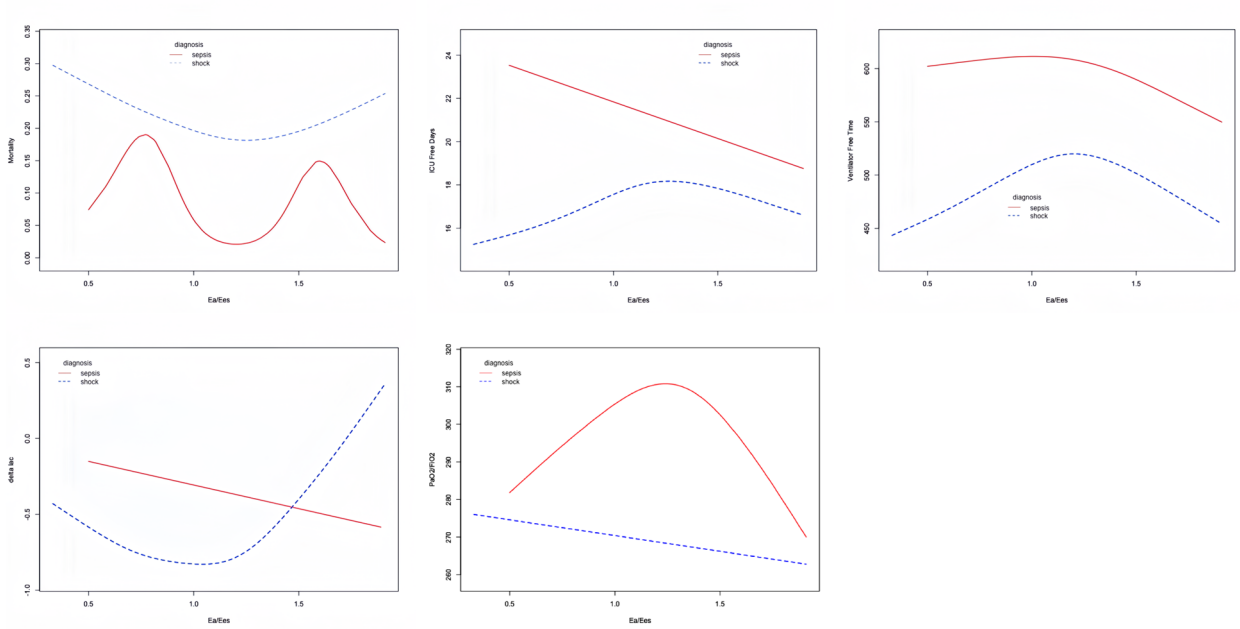

Fig. 4 Subgroup analyses of the relationship between LVAC (Ea/Ees) and outcomes in sepsis and septic shock. Adjusted for age, gender, and NE

Table 5 Effective estimates for subgroup analyses

Outcome		Sepsis	Septic shock
Mortality	(K)	1.15	1.24
	< K	0.69 (0.45, 1.08)	**0.84 (0.70, 0.99)**
	> K	1.16 (0.83, 1.63)	**1.19 (1.01, 1.39)**
ICU-Free Days	(K)		1.24
	< K	Linear effect	6.07 (– 0.75, 12.89)
	> K		– 6.13 (– 16.64, 4.39)
Ventilator-Free Time	(K)	1.12	1.22
	< K	223.16 (– 44.07, 490.39)	159.22 (– 17.79, 336.24)
	> K	**– 221.52 (– 412.70, – 30.35)**	– 195.76 (– 449.10, 57.58)
Delta lac	(K)		1.18
	< K	Linear effect	– 1.00 (– 2.75, 0.74)
	> K		**2.47 (0.33, 4.62)**
PaO_2/FiO_2	(K)	1.35	
	< K	73.09 (– 23.28, 169.47)	Linear effect
	> K	**– 160.64 (– 313.13, – 8.15)**	

Adjusted for age and gender. Values with $P < 0.05$ are highlighted in bold

Optimal vasomotor tone and left ventricular contractility are crucial to maintaining hemodynamic stability, indirectly affecting the outcomes. Our study concluded that an LVAC value of 1.19 was associated with the lowest mortality rate. Although previous studies did not reach the same conclusions, some of their findings do support our results. For instance, Dugar et al. recently found a U-shaped association between LVEF and in-hospital mortality in sepsis and septic shock. Both LV systolic dysfunction (LVEF < 25%) and hyperdynamic LVEF (LVEF ≥ 70%) were independently associated with significantly higher in-hospital mortality [13]. However, a previous meta-analysis revealed that LV systolic dysfunction was neither a sensitive nor a specific mortality predictor in sepsis patients [14], and another study reported that sepsis patients with depressed LVEF did not show a prognostic relationship [15]. Despite the contentious nature of these findings, clinical interventions in sepsis-induced cardiomyopathy (SIC) in both hypo- and hyperdynamic states appear to improve survival rates. Patients with low EF require supportive therapy to maintain sufficient cardiac output, while circulatory hyperdynamics, indicated by high EF, are considered an early-stage manifestation of sepsis [16]. A downregulated response might prevent SIC from progressing into an LV systolic dysfunction state [17]. The use of beta-blockers and dexmedetomidine has been proven to improve patient outcomes [18–21].

Based on the aforementioned research focusing on heart contractility, an increasing number of studies have concentrated on the correlation between vasomotor tone and left ventricular contractility, which is LVAC. While LVEF can partially reflect LVAC, they are not identical; LVAC demonstrates more variability than LVEF [22]. VA decoupling has been observed in the early stages of sepsis in both survivors and nonsurvivors [6]. Patients with a hyperdynamic state, potentially characterized by normal or reduced LVAC, may exhibit higher mortality compared with those having normal or hypodynamic cardiac function [23]. Another study highlighted that LVAC is associated with 30-day mortality in septic patients (HR = 2.57, 95% CI 1.29–5.13) [7]. This disparity may be attributed to the latter study's focus on elderly patients, who are more likely to have chronic LV dysfunction. In their study, LVEF was 47.5% in survivors and 43% in nonsurvivors, significantly lower than in our study. Furthermore, research on nonsepsis patients with LV dysfunction has also identified an association between LVAC and long-term prognosis. Bonnie et al. reported a correlation between LVAC and long-term prognosis in chronic heart failure patients [24]. Trambaiolo et al. found that baseline LVAC was associated with one-year mortality in patients with myocardial infarctions [25].

Few studies have focused on the correlation between LVAC and secondary outcomes. Zhou et al. found that optimizing LVAC can enhance lactate clearance rate compared with usual care ($P = 0.038$). However, their findings did not conclusively establish that optimizing LVAC affects the length of ICU stays or MVt [26]. Our study demonstrated that optimizing LVAC could not only improve lactate clearance but also maximize ICU-free days and ventilator-free time. Additionally, LVAC was found to influence the oxygen index in our study, with optimal LVAC corresponding to the maximum oxygen index. MV and hemodynamic states are closely connected. During MV, inflammation biomarkers significantly increase, particularly when the driving pressure exceeds 10 mmHg [27]. This inflammation status, associated with both hyperdynamic and hypodynamic states of the heart, consequently affects LVAC. Similarly, the interaction between cardiac and pulmonary functions can affect cardiac performance [28]. In the context of sepsis and septic shock, LVAC is notably linked to both oxygen delivery and consumption [29]. Disruptions in homeostasis can also lead to alterations in lung function, thereby affecting the oxygen index. Other parameters, such as tissue perfusion, may be affected by disturbances in normal oxygen delivery, potentially explaining changes in lactate clearance rates. To optimize LVAC, it is crucial for physicians to consider routine therapies that may disrupt this balance. For example, norepinephrine can worsen LVAC by increasing Ea without a corresponding change in Ees. Conversely, dobutamine's opposite effect on Ea and Ees might also negatively impact LVAC [6].

In subgroup analyses, the distinction between sepsis and septic shock patients becomes evident. Although the optimization points differed slightly in mortality outcomes, patients with septic shock exhibited significantly higher 30-day mortality risks at the same LVAC value. In the septic shock group, the risk of death escalates regardless of whether the LVAC is above or below 1.24. Therefore, to improve prognosis, it is necessary for clinicians to optimize LVAC. In terms of ICU-free days, a U-shaped trend was observed in the septic shock group, although not statistically significant. It was apparent that the septic shock group experienced fewer ICU-free days compared with the sepsis group. A similar pattern emerged in ventilator-free time. Despite the slight differences in mortality optimization points between the groups, the curves were nearly parallel, with the sepsis group showing significantly higher ventilator-free time at the same LVAC. In the sepsis group, delta lactate showed no significant relevance as most patients did not exhibit elevated lactate levels. Only those with lower LVACs affected the length of ICU stay, indicating

a greater importance of cardiac function. Conversely, in the septic shock group, the delta lactate curve maintained a U shape. Septic shock patients present more complex conditions in terms of the oxygen index. As illustrated in Fig. 3, the oxygen index linearly declines with increasing LVAC. In septic shock patients with elevated LVAC, cardiac inability to overcome vascular resistance leads to increased intraventricular pressure. This pressure extends through the mitral valve to the left atrium and pulmonary circulation, elevating pulmonary hydrostatic pressure. During septic shock, endothelial barrier disruption and enhanced vascular permeability contribute to increase lung water, adversely affecting lung function [30]. This phenomenon offers a plausible explanation for the observed changes in oxygen index with increasing LVAC. However, further research is necessary to elucidate why the curves differ markedly between the sepsis and septic shock groups, potentially focusing on variations in vascular permeability.

Our study presents some limitations. First, it is a single-center prospective study. Although certain correlations were identified, larger-scale validation is necessary to substantiate these findings. The presence of U-shaped curves was apparent, yet not all demonstrated statistical significance. Being part of a larger, nationwide multi-center prospective study, there is potential for more extensive exploration in future research. Second, echocardiography was only performed at the time of diagnosis. Given that LVAC may vary as the disease progresses, this could influence the final outcomes. Consequently, conducting repeated measurements during different critical periods might yield varying results. Third, several findings, particularly in the septic shock group, remain unclarified. Therefore, more comprehensive studies, including fundamental research focused on septic shock patients, are imperative.

Conclusion

Our study demonstrates that LVAC serves as a critical prognostic marker in patients with sepsis. We observed a U-shaped correlation between LVAC levels and patient outcomes, suggesting that both higher and lower LVAC values may adversely affect 30-day mortality. Similar U-shaped patterns emerged in terms of the length of ICU stay, MVt, delta lac, and the oxygen index. Optimizing LVAC levels might offer a way to enhance patient prognosis. Given that the optimal LVAC might vary among different patient categories, individualized LVAC titration for each patient could potentially improve clinical outcomes.

Abbreviations

CI	Confidence intervals
CVP	Central venous pressure
Ea	Arterial elastance
Ees	Left ventricular end-systolic elastance
ICC	Intraclass correlation coefficient
ICU	Intensive care unit
HR	Heart rate
Lac	Lactate
LVEF	Left ventricular ejection fraction
LVAC	Left ventricular-arterial coupling
LVOT	Left ventricular outflow tract
MAP	Mean arterial pressure
MV	Mechanical ventilation
NE	Norepinephrine
OR	Odds ratio
Pplat	Plateau pressure
PEEP	Positive end-expiratory pressure
SOFA	Sequential organ failure assessment
SV	Stroke volume
TV	Tidal volume
VTI	Velocity–time integral

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Author contributions

H. L. designed the study, performed the statistical analysis, and drafted the manuscript. H. Z. conceived and designed the study, obtained and interpreted data, performed the statistical analysis, and co-drafted the manuscript. S. L. revised the manuscript. Q. Z. obtained data and revised the manuscript. X. W. revised the manuscript. All authors have read and approved the final manuscript.

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Data availability

All datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of Peking Union Medical College Hospital, Beijing, China (Approval No. ZS-2166). Written informed consent was obtained from the next of kin of each patient.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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