Values of the Bedside Ultrasound Measurement of Aortic Peak Flow Velocity Variability Combined with PLR in Predicting the Volume Responsiveness in Patients with Septic Shock

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Abstract

The value of the bedside ultrasound measurement of aortic peak flow velocity variability ($\Delta Vpeak_{AO}$) combined with passive leg raising test (PLR) in predicting the volume responsiveness was investigated in patients with septic shock. Eighty two patients with septic shock admitted in our hospital from January 2018 to January 2021 were selected. $\Delta Vpeak_{AO}$ values before and after PLR and after volume loading test (VE) were measured by a bedside ultrasound instrument. The $\Delta Vpeak_{AO}$ values were calculated and the stroke volume (SV) was monitored, and according to the changes of SV after VE, the patients were divided into a response group ($\Delta SV \geq 15\%$) and a non-response group ($\Delta SV < 15\%$). The results showed that the SV and $\Delta Vpeak_{AO}$ in the response group were lower than those in the non-response group after PLR and VE ($P < 0.05$), the SV and $\Delta Vpeak_{AO}$ in the response group after PLR and VE were higher than those before PLR ($P < 0.05$), and the $\Delta Vpeak_{AO}$ in the response group was higher than that in the non-response group after PLR ($P < 0.05$). The ROC analysis showed that the best cut-off point of $\Delta Vpeak_{AO}$-PLR was 11.09%, and the sensitivity was 88.24%, the specificity was 91.67% and the area under the curve (AUC) was 0.866. These results indicate that the bedside ultrasound measurement of $\Delta Vpeak_{AO}$ combined with PLR can effectively predict the volume responsiveness of patients with septic shock, with a guiding value in fluid resuscitation therapy.

Keywords: *Sepsis, shock, volume responsiveness, bedside ultrasound, variability in aortic peak flow velocity (∆vpeakao), passive leg raising (PLR)*

I. Introduction

Septic shock is one of the main factors for the death of critically ill patients, and it has bee reported that there are millions of septic patients and 25% ~ 30% of them die from septic shock in the world every year [1]. The stimulation of systemic inflammatory response syndrome and the severe tissue hypoxia may cause the damage of endothelial cells, the destruction of vascular tension, and the dysfunction of multiple organs in patients with septic shock [2]. Fluid resuscitation is used for the treatment of septic shock in clinic to improve the patient's tissue perfusion and maintain the balance of oxygen supply and demand [3]. However, the ideal effect of volume loading test (VE) can not be achieved in some patients, and a volume overload or insufficiency can damage organs to cause some cardiopulmonary complications, further aggravating the patient's conditions [4,5]. Therefore, an accurate assessment of volume responsiveness plays an important role in the fluid resuscitation of septic shock patients [6].

At present, bedside ultrasound is used to detect aortic peak flow velocity variability ($\Delta Vpeak_{AO}$) to judge the volume responsiveness, with the characteristics of non-invasion, rapidness and easiness to operate and repeatable monitoring [7]. In addition, passive leg raising test (PLR) can be used to evaluate the effect of fluid resuscitation, in which the volume responsiveness can be evaluated safely and reversibly, and the results can not be affected by

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other factors, such as spontaneous breathing and arrhythmia [8]. However, the predictive effect of bedside ultrasound measurement of $\Delta Vpeak_{AO}$ combined with PLR in the volume responsiveness is still unclear in patients with septic shock. In view of this, 82 patients with septic shock in our hospital were selected to explore the value of bedside ultrasound of $\Delta Vpeak_{AO}$ combined with PLR in predicting the volume responsiveness in septic shock.

II. Materials and Methodology

2.1 Clinical data

With the approval of the Ethics Committee of Longhua District Central Hospital of Shenzhen, 82 patients with septic shock admitted to Longhua District Central Hospital of Shenzhen from January 2018 to January 2021 were selected, including 48 males and 34 females, with an average age of 57.93 ±9.17 years (20~75 years). There were 51 cases with abdominal infection, 23 cases with lung infection and 8 cases with an infection in other sites, and the acute physiology and chronic health evaluation Ⅱ (APACHE Ⅱ) scores were 15.08 ± 2.37, and the Glasgow Coma Scores (GCS) were 6.82 ±0.96.

Inclusion criteria: patients diagnosed as septic shock based on the diagnostic criteria of septic shock in The Third International Consensus Definitions for Sepsis and Septic Shock [9]; those with 18~28 APACHE Ⅱ scores and 4~10 GCS, and those aged at 20~75; those with a tissue hypoperfusion; all the family members signed the informed consent.

Exclusion criteria: Patients with chest surgery, emphysema, etc. who could not receive a chest ultrasound examination; those complicated with other pulmonary infectious diseases; those with a severe cardiac dysfunction; pregnant women; patients with arrhythmia; those with a severe coagulation dysfunction.

2.2 Methods

Bedside electrocardiographic monitoring was performed in all patients, and their heart rate (HR), mean arterial pressure (MAP) and central venous pressure (CVP) were recorded. The patients were placed in semi-reclining position before PLR, with their upper bodies raised by 45°. The $\Delta Vpeak_{AO}$ values were measured with a Mindray UMT-200 bedside ultrasound instrument (SonoSite Company, USA). The $\Delta Vpeak_{AO}$ values were calculated according to the following equation: $\Delta Vpeak_{AO}$ = (Vpeakmax - Vpeakmin)/ [(Vpeakmax - Vpeakmin)/2] ×100%. The velocity-time integral (VTI) of aortic valve was measured in the apical five chamber view and the diameter of aortic ring (D) was measured in the parasternal left ventricular long axis view, and the stroke volume (SV) was calculated according to the equation: $SV = VTI \times \pi(D/2)^2$. Durinf VE, 500 mL of normal saline were given the patients within 15 min at a constant velocity, in which the above indexes were monitored, and according to the changes of SV after VE, the patients were divided into two groups, a response group ($\Delta SV \geq 15\%$) and a non-response group ($\Delta SV < 15\%$). During PLR, the patients was in supine position with their both lower limbs raised by 45°for the measurement of the above indexes. The ultrasound measurement was completed by the same group of physicians, and the average value of three consecutive measurements in three breathing cycles was recorded.

2.3 Observation indexes

① The basic data of patients were compared between the two groups; ② The hemodynamic parameters were compared between the two groups; ③ The $\triangle Vpeak_{AO}$ values after PLR were compared between the two groups; ④ The value of bedside ultrasound measurement of $\triangle Vpeak_{AO}$ combined with PLR in predicting the volume responsiveness was analyzed in patients with septic shock.

2.4 Statistical analysis

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SPSS 22.0 was used for statistical analysis. After the normality test, the measurement data were expressed as “mean ± *s*”, and *t* test was used for testing the significance of difference in the average between the two groups. The measurement data measured repeatedly were analyzed by repeated measures analysis of variance (ANOVA), the comparison of two samples was performed by *LSD-t* test, and the count data were expressed as “%” and tested by χ^2 test, in which the calibration was required if the theoretical frequency was 1~5. The value of the bedside ultrasound measurement of $\triangle Vpeak_{AO}$ combined with PLR in predicting the volume responsivenes of patients with septic shock was evaluated based on the operating characteristic curve (ROC) of subjects. A value with $P < 0.05$ was considered to be significant in statistics.

III. Data Analysis

3.1 Comparison on basic data between two groups

There was no significant difference in the gender, age, infection site, APACHE II score and positive end expiratory pressure (PEEP of patients between the two groups ($P > 0.05$), as shown in Table 1.

Table 1 Comparison on basic data between two groups

Group	*n*	Gender male/female	Age (year)	Infection site Abdominal cavity	lung	others	APACHE Ⅱ score	PEEP (cmH_2O)
Non-response	34	19/15	57.78±9.05	21	10	3	15.31±2.26	5.86±0.93
Response	48	29/19	58.13±9.26	30	13	5	14.85±2.48	5.77±0.87
t/χ^2 value	-	0.169	0.170	0.005	0.053	0.019	0.858	0.448
P value	-	0.681	0.865	0.946	0.817	0.890	0.393	0.655

Note: PEEP: positive end-expiratory pressure.

3.2 Comparison on hemodynamic parameters between two groups

There was no significant difference in the heart rate, mean arterial pressure and central venous pressure at the different time points between the response group and non-response group ($P > 0.05$), SV and $Vpeak_{AO}$ of patients in the response group were lower than those in the non-response group after PLR and VE ($P < 0.05$), while SV and $Vpeak_{AO}$ of patients after PLR and VE were higher than those before PLR in the response group ($P < 0.05$), as shown in Table 2.

Table 2 Comparison on hemodynamic parameters between two groups

Index	Time	Non-response group (*n*=34)	Response group (n=48)	*T* value	*P* value
Heart rate (times/min)	Before PLR	107.54±14.75	105.38±12.62	0.712	0.479
	After PLR	105.67±13.18	103.77±11.83	0.683	0.496
	After VE	103.83±11.39	102.42±11.15	0.559	0.578
	F value	0.674	0.747		
	P value	0.512	0.476		
MAP (mmHg)	Before PLR	72.86±11.94	69.57±10.36	1.330	0.187
	After PLR	75.15±13.06	72.66±13.18	0.846	0.400
	After VE	77.25±14.13	73.15±13.67	1.320	0.191
	F value	0.959	1.159		

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	P value	0.387	0.317		
CNP (cmH_2O)	Before PLR	7.65±1.03	7.34±0.92	1.430	0.157
	After PLR	7.88±1.27	7.52±0.98	1.448	0.151
	After VE	8.04±1.35	7.75±1.30	0.979	0.330
	F value	0.872	1.739		
	P value	0.421	0.179		
SV (mL)	Before PLR	77.16±12.35	64.73±9.56	5.135	<0.001
	After PLR	79.84±13.92	77.60±12.67[a]	0.726	0.470
	After VE	81.59±14.68	80.43±14.28[a]	0.358	0.721
	F value	0.904	22.120		
	P value	0.408	<0.001		
$Vpeak_{AO}$ (cm/s)	before PLR	108.32±15.63	96.54±13.41	3.658	<0.001
	After PLR	112.09±16.88	111.73±16.26[a]	0.097	0.923
	After VE	114.65±18.27	115.80±19.52[a]	0.263	0.793
	F value	1.198	19.753		
	P value	0.306	<0.001		

Note: compared with pre-PLR, [a]$P < 0.05$; MAP: mean arterial pressure; CNP: central venous pressure; SV: stroke volume; VE: volume loading test.

3.3 $\Delta Vpeak_{AO}$ after PLR

As shown in Table 3, the $\Delta Vpeak_{AO}$ of patients in the response group was significantly higher than that in the non-response group ($P < 0.05$).

Table 3 $\Delta Vpeak_{AO}$ after PLR

Group	*n*	$\Delta Vpeak_{AO}$ (%)
Non-response	34	8.15±1.34
Response	48	12.93±2.07
T value	-	11.814
P value	-	<0.001

3.4 Analysis of the bedside ultrasound measurement of $\Delta Vpeak_{AO}$ combined with PLR in predicting the volume responsiveness in septic shock

ROC analysis showed that the optimal cutoff point of bedside ultrasound measurement of $\Delta Vpeak_{AO}$ combined with PLR for predicting the volume responsiveness in septic shock was 11.09%, and the sensitivity was 88.24%, the specificity was 91.67% and the area under the curve (AUC) was 0.866, as shown in Table 4 and Figure 1.

Table 4 Value of bedside ultrasound measurement of $\Delta Vpeak_{AO}$ combined with PLR in predicting the volume responsiveness in septic shock

Index	Optimal cutoff point	Sensitivity	Specificity	AUC	95% *CI*
$\Delta Vpeak_{AO}$	11.09%	88.24%	91.67%	0.866	0.797~0.946

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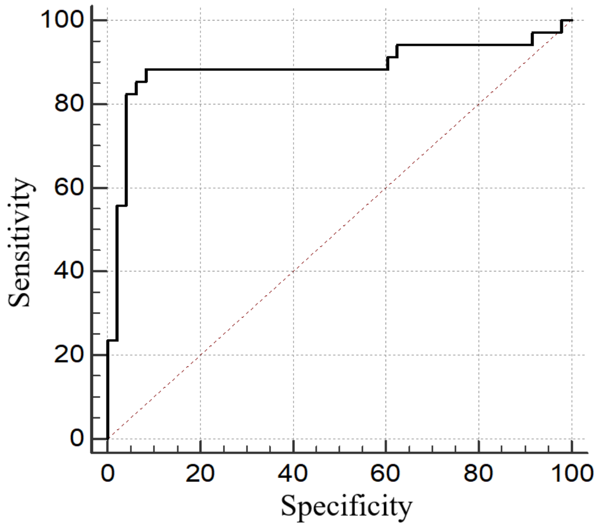

Fig 1: ROC of bedside ultrasound measurement of △$Vpeak_{AO}$ combined with PLR in predicting the volume responsiveness in septic shock

3.5 Discussion

Septic shock is a common disease in intensive care unit, characterized by acute onset, severe conditions and many pathogenic factors, and can lead to the damage and system function decline of multiple organs [10]. In septic shock patients, the vascular bed is in a state of stress due to infections, leading to the insufficiency of effective circulating blood volume, and the effective tissue perfusion can be ensured by fluid resuscitation in clinic [11, 12]. However, patients without response to the fluid resuscitation are often complicated with some serious conditions, such as tissue edema, pulmonary edema, heart failure, seriously threatening the health of patients [13]. Therefore, an effective prediction of volume responsiveness in septic shock patients is of great significance for their prognosis.

The results showed that SV and △$Vpeak_{AO}$ in the response group were lower than those in the non-response group after PLR and VE, SV and △$Vpeak_{AO}$ in the response group after PLR and VE were higher than those before PLR, and △$Vpeak_{AO}$ in the response group was higher than that in the non-response group after PLR. The ROC analysis showed that the optimal cutoff point of bedside ultrasound measurement of △$Vpeak_{AO}$ combined with PLR was 11.09%, and the sensitivity was 88.24%, the specificity was 91.67% and the AUC was 0.866, suggesting that bedside ultrasound measurement of △$Vpeak_{AO}$ combined with PLR can effectively predict the volume responsiveness in patients with septic shock. Volume responsiveness is the response ability of septic shock patients to a rapid volume expansion, reflecting the preparation level of preload [14]. Bedside ultrasound technology can accurately measure the cardiac function and hemodynamic parameters of patients with septic shock, with the characteristics of simple operation and strong repeatability, the measurement of △$Vpeak_{AO}$ by a bedside ultrasound can reflect the dependence of the body's circulatory system on preload, and the dynamic monitoring of SV and △$Vpeak_{AO}$ can effectively predict the volume responsiveness of patients with septic shock [15, 16]. A preload redistribution method can be employed in PLR to simulate VE, and the measurement of the patients can be completed in an automatic sickbed and not affected by spontaneous breathing [17]. In addition, by raising the lower limbs of patients, the volume of blood in the systemic circulation can be increased reversibly, the backflow can be increased by 150~300 mL, and the right ventricular preload can be increased, better predicting the volume responsiveness [18]. Xue *et al*. [19] reported that PLR combined with △$Vpeak_{AO}$ measurement could effectively predict the volume responsiveness of severe sepsis patients with a preserved spontaneous respiratory mechanical ventilation, which is consistent with the results of this study. However, the great variability of SV in patients with arrhythmia can affect the evaluation of volume responsiveness, so the patients with arrhythmia were excluded in the selection of cases in this study. In addition, the individual variation in tidal volume may also affect the changes of ultrasound indicators, and for the prediction of volume responsiveness in patients with septic shock, various hemodynamic parameters should be strictly detected and a comprehensive evaluation should be made according to the severity of the patient's conditions, so as to take the best treatment plan and try not to miss the optimal treatment opportunity [20, 21]. Therefore, an active fluid replacement therapy is necessary for septic shock patients with volume responsiveness, and in those without volume responsiveness, their specific conditions still need to be strictly evaluated, in which whether a fluid overload causes a hemodynamic instability and a diuretic treatment is required should be considered.

IV. Conclusion

Bedside ultrasound measurement of $\Delta Vpeak_{AO}$ combined with PLR can effectively predict the volume responsiveness of septic shock patients, with a guiding value in the treatment of fluid resuscitation. However, the selection of cases in this study was limited, and the results may be biased. The follow-up study still needs to expand the sample to further confirm the results. In clinical treatment, other hemodynamic indexes and ultrasound indexes should be combined to provide a more accurate prediction scheme for the prediction of volume responsiveness in septic shock patients.

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