Accuracy of Combining End-Tidal Carbon Dioxide and Pulse Pressure Variability Measurements in Predicting Fluid Responsiveness During Passive Leg Raising Test in Septic Shock Patient

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Research

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Abstract

Background

It is essential to assess the patients' volume responsiveness before fluid infusion in patients with circulatory failure. The hypothesis is that the combining of end-tidal carbon dioxide ($EtCO_2$) and pulse pressure variability (PPV) measurements can non-invasively predict fluid responsiveness during passive leg raising (PLR) test.

Methods

Pulse indicates continuous cardiac output, right radial artery blood pressure, and $EtCO_2$ were monitored in 71 septic shock patients with mechanical ventilation. A standard PLR test was performed; cardiac index (CI), arterial pressure, stroke volume variability (SVV), PPV, and $EtCO_2$ were measured before and after the PLR test. Patients with an increase in CI greater than 15% after the PLR test were defined as fluid responders. Receiver-operating characteristics (ROC) curve analysis was carried out to assess the predictive performance of the measured parameters.

Results

PPV, $\triangle EtCO_2$ and $\triangle EtCO_2$ variation ratio ($\triangle EtCO_2$%) in fluid-responders were significantly greater than those in the non-responders. The AUC of $\triangle EtCO_2$% was 0.884 (95% CI, 0.785 to 0.948) with a cut-off value of > 5.88%; yielded a sensitivity of 91.89% (95% CI, 78.1–98.3%) and aspecificity of 76.47% (95% CI, 58.8–89.3%). The AUC of PPV was 0.852 (95% CI, 0.748 to 0.925) with a cut-off value of > 10%; yielded a sensitivity of 81.1% (95% CI, 64.8–92%) and specificity of 79.41% (95% CI, 62.1–91.3%). The AUC of PPV-$\triangle EtCO_2$% combination was 0.942 (95% CI, 0.86 to 0.984) with a cut-off value of > 0.666; yielded a sensitivity of 83.8% (95% CI, 68–93.8%) and aspecificity of 94.1% (95% CI, 80.3–99.3%). The AUC of PPV-$\triangle EtCO_2$% combination was significantly greater than either $\triangle EtCO_2$% or PPV.

Conclusion

The combination of PPV and $\triangle EtCO_2$ can better predict fluid responsiveness during PLR.

Background

The first-line treatment for patients with circulatory failure is volume therapy. Optimized adjustment of intravascular volume and cardiac preload is essential for improving cardiac output (CO) and tissue perfusion[1]. However, only 50% of hemodynamically unstable critically ill patients in the intensive care unit (ICU) are volume-responsive[2]. It is essential to assess the patients' volume responsiveness before fluid administration, since excessive fluid load may lead to heart failure, prolonged mechanical ventilation duration and ICU stay, reduced oxygen delivery, and increased risk of mortality[3].

The passive leg raising (PLR) test can transfer blood from the legs and abdomen to the heart cavity via posture changes, and its effect is similar to endogenous fluid supplementation[4]. The advantage of the PLR test is that it is still valuable for detecting preload responsiveness in the situations that the application of dynamic hemodynamic indicators is limited (e.g., strong spontaneous breathing, low tidal volume ventilation, arrhythmia, etc.)[5–14]. However, the disadvantage of the PLR test is that it needs to measure CI directly. At present, the gold standard for assessing volume responsiveness is still to observe changes in cardiac index (CI) or stroke volume (SV) before and after volume loading tests, which requires a thermodilution catheter in place. Another way to measure CI or SV is bedside echocardiography, where the non-invasive nature of echocardiography is also attractive. However, echocardiography requires skilled operators, and continuous estimation for it cannot be made[15, 16].

Studies have shown that the end-tidal carbon dioxide ($EtCO_2$) depends on cellular metabolism and the CO_2 content transported by venous blood flow (which equals to CO at steady status), and is also related to the ability of the lungs to remove CO_2. Therefore, in patients with stable breathing, The $EtCO_2$ mainly depends on cardiac output[17–19]. It has been shown that a change of end-tidal carbon dioxide partial pressure ($\triangle PetCO_2$) ≥ 2 mmHg during PLR determines whether there is volume reactivity[20, 21]. However, the absolute value of this number is too small, which means it is prone to errors. Studies have shown that pulse pressure variability (PPV) can be used to accurately predict volume responsiveness. We can obtain the PPV value by continuously monitoring the radial artery blood pressure. We hypothesis that the combination of PPV and $\triangle EtCO_2$% can non-invasively predict volume responsiveness in septic shock patients.

Methods

Patients

This prospective study was approved on January 23rd, 2018, by the Ethics Committee of Fujian Provincial Hospital (Approval # K2018-01-23). The study was registered on December 26th, 2019, at the Chinese Clinical Trial Registry (ChiCTR1900028210). Written informed consent was obtained from each patient's next of kin.

The inclusion criteria were: 1) Patients diagnosed septic shock according to the Sepsis 3.0 definition[21]; 2) Age ≥ 18; 3) blood pressure and heart rate of the enrolled patients fluctuated less than 10% within 15 min before the start of the study, with relatively stable hemodynamics. The exclusion criteria were: 1) preliminary judgment at the end of the disease, may die within 24 hours; 2) patients with contraindications for the use of pulse indicating continuous cardiac output (PiCCO) monitoring; 3) patients with intra-aortic balloon counter-pulsation or artificial membrane pulmonary oxygenation.

Study design and measurements

All patients with septic shock were treated in accordance with the relevant guidelines[21]. Characteristics and demographic data of the study population were recorded. Patients were intubated and treated with sufentanil and midazolam, with a Richmond agitation-sedation scale (RASS) maintained at -3. Patients were kept with no spontaneous breathing, and with a tidal volume greater than 8 ml/kg, and PEEP was at a constant value.

Hemodynamic monitoring was performed with the PiCCO catheter (PC 4000, PULSION, Feldkirchen, Germany). Invasive blood pressure was also monitored with catheterization of the right radial artery. Heart rate (HR) was measured via electrocardiograph monitor; central venous pressure (CVP) was measured via the right subclavian venous catheter; CI, stroke volume variability (SVV) was measured via the PiCCO catheter; pulse pressure variability (PPV), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and pulse pressure (PP) was measured via the right radial artery catheter. $EtCO_2$ was continuously measured by using a sidestream infrared gas analyzer connected to the patient's monitor (M2741A, PHILIPS, Amsterdam, Netherlands).

For the PLR test, the first step was to raise the head of the bed by 45 degrees; patients were kept in the semi-recumbent position for one minute. At baseline, we obtained the first set of measurements, including HR, CVP, CI, SVV, PPV, SBP, DBP, MAP, PP, and $EtCO_2$. The second step was to elevate both legs at 45 degrees, and the trunk was placed in a horizontal position. The postural change was performed by using the automatic motion of the bed[4]. The second set of measurements was obtained.

Statistical analysis

Patients with an increase in CI ≥ 15% after PLR test were defined as fluid responders (R). Patients with a change of < 15% were defined as non-responders (NR).

Statistical analysis was performed using SPSS statistical software (ver. 25.0, IBM, NY, USA) and MedCalc software (ver. 18.2.1, Mariakerke, Belgium). Continuous variables were tested for normal distribution (Kolmogorov–Smirnov test) and were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR), as appropriate. Comparison between the two groups was performed by *t*-test or Mann-Whitney *U* test, as appropriate. Categorical variables were expressed as frequency (percentage), and the comparison between the two groups was performed by Chi-square test or Fisher exact test.

The combination of $EtCO_2$ and PPV was performed by using a logistic regression model which involved both $EtCO_2$ and PPV as co-variables (use "enter" as the method of variable selection), and the software would then output a predict value. We used this predict value as a "score" of a combination of $EtCO_2$ and PPV. Receiver-operating characteristic (ROC) curves were constructed to determine the performance of each variable in predicting volume responsiveness. The Hanley–McNeil test was used to compare the areas under the ROC curves[22]. Correlations were tested by the Pearson method. All reported p values are two-sided, and a $p < 0.05$ was considered significant.

Results

Patients' characteristics

From January to May 2020, 71 patients were included. All patients successfully completed the PLR test. There were 37 fluid responders (52.11%) and 34 non-responders (47.88%). Patients' characteristics were summarized in Table 1.

Table 1
Characteristics and demographic data of study population (n = 71)

	Responders (n = 37)	Non-responders (n = 34)	*p* value
Age (yr)	57 [44, 69]	51 [45, 69.3]	0.734
Lactate (mmol / L)	8 [5.3, 12]	6 [5, 11]	0.164
APACHEII	15 [9, 21.5]	18 [10, 21]	0.904
SOFA	8.1 ± 3.5	8.9 ± 3.5	0.364
Male (%)	25 (67.57)	24 (70.59)	0.783
Infection site			
Pneumonia	13	14	0.123
Abdominalcavity	17	16	0.234
Bloodstream	10	9	0.512
Others	2	1	0.432
Underlingdiseases			
CAD	14	10	0.215
Hypertension	10	8	0.139
Diabetes	23	22	0.458

Values are expressed mean ± standard deviation (SD) or as median [25–75% interquartile range, IQR], as appropriate;

APACHEII: Acute Physiologic and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; CAD: Coronary Atherosclerotic heart Disease;

Values are expressed as mean ± SD, median (25th to 75th percentile) or absolute numbers, as appropriate.

Effects of the PLR maneuver

The SVV, PPV, △SBP, △PP, △$EtCO_2$ and △$EtCO_2$ variation ratio (△$EtCO_2$%) of responder were all greater than that in the non-respond patients (Table 2). The responders had a greater △EtCO2% than the non-responders (10.39% ± 3.66% *vs.* 2.97% ± 5.08%, $p < 0.001$). The responders also had a greater PPV than the non-responders (15.78% ± 6.87% *vs.* 7.71% ± 4.03%, $p < 0.01$).

Table 2
Effects of PLR on hemodynamic variables and end-tidal carbon dioxide

	Responders (n = 37)	Non-responders (n = 34)	*p* value
Before PLR			
HR (b.p.m)	99.11 ± 19.43	90.74 ± 14.78	0.043
CI (L / min / m^2)	3.28 ± 0.67	3.7 ± 0.79	0.010
CVP (mmHg)	10 [8, 9]	10 [7, 13.25]	0.777
SBP (mmHg)	105 [99, 113.5]	119 [105, 132.25]	0.001
DBP (mmHg)	47.59 ± 9.45	54.44 ± 9.79	0.004
MAP (mmHg)	65.67 [62.17, 69.5]	79 [66, 83.08]	< 0.01
PP (mmHg)	59.51 ± 10.53	64.62 ± 14.12	0.112
$EtCO_2$ (mmHg)	35.22 ± 4.8	38.03 ± 5.07	0.015
After PLR			
HR (b.p.m)	103 [82, 117.5]	89.5 [76.75, 101]	0.028
CI (L / min / m^2)	4.3 ± 0.84	3.69 ± 0.79	0.008
CVP (mmHg)	11 [8.5, 11.5]	11 [9.75, 14]	0.118
SBP (mmHg)	120 [113, 132]	128.5 [120.5, 136.5]	0.052
DBP (mmHg)	51 [45, 60]	56.5 [51.5, 66.75]	0.005
MAP (mmHg)	72.33 [70, 83]	82.67 [75.33, 85.17]	0.005
PP (mmHg)	70.11 ± 11.28	68.91 ± 14.5	0.968
$EtCO_2$ (mmHg)	38.81 ± 4.93	39.03 ± 4.51	0.548
Dynamic index			
SVV%	16 [11, 20.5]	9 [6, 12]	< 0.001

Values are expressed mean ± standard deviation (SD) or as median [25–75% interquartile range, IQR], as appropriate.

ETCO2 : end-tidal carbon dioxide; PLR : passive leg raising test; HR : heart rate; CI: cardiac index; CVP : central venous pressure; SBP : systolic blood pressure; DBP : diastolic blood pressure; MAP : mean arterial pressure; PP : pulse pressure; SVV : stroke volume variability; PPV : pulse pressure variability; △HR% : The variations of HR were presented as percentage change from baseline; △CVP% : The variations of CVP were presented as percentage change from baseline; △SBP% : The variations of SBP were presented as percentage change from baseline; △DBP% : The variations of DBP were presented as percentage change from baseline; △MAP% : The variations of MAP were presented as percentage change from baseline; △PP% : The variations of PP were presented as percentage change from baseline; △EtCO2 : The variations of EtCO2 were from baseline; △EtCO2% : The variations of EtCO2 were presented as percentage change from baseline

	Responders (n = 37)	Non-responders (n = 34)	*p* value
PPV%	15.78 ± 6.87	7.71 ± 4.03	< 0.001
△HR%	0.98 [-1.44, 3.39]	0 [-3.36, 2.88]	0.216
△CVP%	0 [0, 13.39]	8.12 [0, 42.5]	0.143
△SBP%	14.78 [10.1, 21.15]	6.86 [-1.48, 21.07]	0.030
△DBP%	8.51 [4.96, 17.7]	7.29 [-2.32, 25.76]	0.427
△MAP%	10.95 [6.35, 21.34]	5.49 [-1.4, 18.67]	0.076
△PP%	19.6 [8, 26.79]	0 [-5.16, 15.47]	0.001
△$EtCO_2$mmHg	4 [3, 4.5]	1 [0, 2]	< 0.001
△$EtCO_2$%	10.39 ± 3.66	2.97 ± 5.08	< 0.001

Values are expressed mean ± standard deviation (SD) or as median [25–75% interquartile range, IQR], as appropriate.

ETCO2 : end-tidal carbon dioxide; PLR : passive leg raising test; HR : heart rate; CI: cardiac index; CVP : central venous pressure; SBP : systolic blood pressure; DBP : diastolic blood pressure; MAP : mean arterial pressure; PP : pulse pressure; SVV : stroke volume variability; PPV : pulse pressure variability; △HR% : The variations of HR were presented as percentage change from baseline; △CVP% : The variations of CVP were presented as percentage change from baseline; △SBP% : The variations of SBP were presented as percentage change from baseline; △DBP% : The variations of DBP were presented as percentage change from baseline; △MAP% : The variations of MAP were presented as percentage change from baseline; △PP% : The variations of PP were presented as percentage change from baseline; △EtCO2 : The variations of EtCO2 were from baseline; △EtCO2% : The variations of EtCO2 were presented as percentage change from baseline

All responders had higher SBP, DBP, MAP, PP, and $EtCO_2$ than their baseline after PLR (all $p < 0.001$). In the fluid responsiveness group, there was no statistical difference in the changes of HR before and after PLR ($p = 0.869$). In the fluid responsiveness group, there was no statistical difference in the changes of CVP before and after PLR ($p = 0.092$). All fluid non-responders showed higher CVP, SBP, DBP, MAP, PP and $EtCO_2$ than their individual baseline ($p < 0.01$, $p < 0.01$, $p = 0.002$, $p = 0.001$, $p = 0.023$, $p = 0.003$; respectively). In the fluid non-responsiveness group, there was no statistical difference in the changes of HR before and after PLR ($p = 0.369$).

A positive relationship was observed between the change of CI and the change of $EtCO_2$ (Fig. 1, r = 0.538; $p < 0.001$). A positive relationship was also observed between the change of CI and PPV (Fig. 2, r = 0.584; $p < 0.001$).

Prediction of fluid responsiveness

Dynamic hemodynamic indexes were selected to evaluate fluid responsiveness. Table 3 and Fig. 3 show the results of the ROC analysis. The area under the curve (AUC) of SVV, PPV, △$EtCO_2$, △$EtCO_2$% were greater than 0.8. The AUC of PPV-△$EtCO_2$% was greater than either △$EtCO_2$% (0.942 vs. 0.884, $p = 0.046$) or PPV (0.942 vs.

0.852, $p = 0.011$, Table 3). There was no statistical difference between the AUC of PPV and $\triangle EtCO_2\%$ (0.852 vs. 0.884, $p = 0.5843$, Table 3). The combination of PPV and $\triangle EtCO_2\%$ was a better predictor of fluid responsiveness than each variable independently.

Table 3
Factors associated with response to PLR

Variables	Cut-off value%	AUC	*p* value	Sensitivity (%)	Specificity (%)	PV+	PV-	LR+	LR-
SVV	> 13	0.835 (0.728 to 0.913)	< 0.001	72.97 (55.9 to 86.2)	82.35 (65.5 to 93.2)	81.8 (68 to 90.5)	73.7 (61.7 to 82.9)	4.14 (1.9 to 8.8)	0.33 (0.2 to 0.6)
PPV	> 10	0.852 (0.748 to 0.925)	< 0.001	81.08 (64.8 to 92)	79.41 (62.1 to 91.3)	81.1 (68.5 to 89.4)	79.4 (66 to 88.5)	3.94 (2 to 7.8)	0.24 (0.1 to 0.5)
△SBP	> 9.73	0.649 (0.527 to 0.759)	0.030	78.38 (61.8 to 90.2)	61.76 (43.6 to 77.8)	69 (58.5 to 77.9)	72.4 (57.4 to 83.7)	2.05 (1.3 to 3.2)	0.53 (0.2 to 0.7)
△PP	> 4.48	0.722 (0.603 to 0.822)	0.001	83.78 (68 to 93.8)	64.71 (46.5 to 80.3)	72.1 (61.6 to 80.6)	78.6 (62.9 to 88.8)	2.37 (1.5 to 3.8)	0.25 (0.1 to 0.5)
$\triangle EtCO_2$	> 2	0.887 (0.789 to 0.95)	< 0.001	86.49 (71.2 to 95.5)	79.41 (62.1 to 91.3)	82.1 (70 to 90)	84.4 (70.1 to 92.5)	4.2 (2.1 to 8.2)	0.17 (0.07 to 0.4)
$\triangle EtCO_2\%$	> 5.88	0.884 (0.785 to 0.948)	< 0.001	91.89 (78.1 to 98.3)	76.47 (58.8 to 89.3)	81 (69.7 to 88.7)	89.7 (74.2 to 96.3)	3.91 (2.1 to 7.2)	0.11 (0.04 to 0.3)
PPV-$\triangle EtCO_2\%$	> 0.667	0.942 (0.86 to 0.984)	< 0.001	83.78 (68 to 93.8)	94.12 (80.3 to 99.3)			14.24 (3.7to55.1)	0.17 (0.08 to 0.4)

AUC = area under the curve; $\triangle EtCO_2$ = end-tidal carbon dioxide variation with passive leg raising; PV + = positive predictive value; PV- = negative predictive value; LR + = positivelikelihoodratio;LR-=negative like lihoodratio; ETCO2 : end-tidal carbon dioxide; SBP : systolic blood pressure; PP : pulse pressure; SVV : stroke volume variability; PPV : pulse pressure variability; △SBP% : The variations of SBP were presented as percentage change from baseline; △PP% : The variations of PP were presented as percentage change from baseline; △EtCO2 : The variations of EtCO2 were from baseline; △EtCO2% : The variations of EtCO2 were presented as percentage change from baseline

Discussion

The main finding of this study is that $EtCO_2$ variation was correlated with changes in cardiac output induced by a simplified PLR maneuver. PPV, $\triangle EtCO_2$, and △EtCO2% of fluid-responders were significantly greater than

those in the non-responders. The AUC of PPV-$\triangle EtCO_2$% combination was significantly greater than either $\triangle EtCO_2$% or PPV.

CO_2 is the product of tissue cell's metabolism. It simply diffuses to the circulating blood, which is then transported to the lung and diffuses from the lungs into the exhaled gas, which is measured by the $EtCO_2$ monitoring technology[23]. The normal value of $EtCO_2$ is 30 to 43 mmHg, which is 2 to 5 mmHg lower than the CO_2 content of arterial blood. The $EtCO_2$ value is affected by the following three parts: the amount of CO_2 generated by cell metabolism, the ability of the lungs to remove CO_2 from the veins, the cardiac output. The absolute value of $EtCO_2$ cannot be simply used to judge the cardiac output due to the different ventilation and cell metabolic states of patients at different times. Within a few minutes of the PLR test, assuming that the volume of alveolar ventilation and body metabolism are constant, when the output volume drops, the blood flow in the lungs decreases significantly, and $EtCO_2$ decreases accordingly, and *vice versa*. The change of $EtCO_2$ can sensitively reflect the change of CI, and thus can determine the fluid responsiveness. In the PLR test, the fluid responsiveness could be predicted by observing the change of $EtCO_2$.

Numerous studies have proved that dynamic hemodynamic indicators such as SVV and PPV can also be used to determine whether there is fluid responsiveness[24]. Our data showed that both $\triangle EtCO_2$% and PPV positively correlate with CI. This is similar to the results of the study of Toupin and colleagues. They conducted a PLR study on 90 cardiac surgical patients who were receiving mechanical ventilation and found that $\triangle EtCO_2$% was positively correlated with $\triangle CI$[20].

We found that the AUC of SVV, PPV, and $\triangle EtCO_2$% were greater than 0.8, showing that $\triangle EtCO_2$% and PPV could predict fluid responsiveness well with high specificity and sensitivity. The results of several studies show that the cut-off value of $EtCO_2$% during PLR is 5%[18, 19, 25]. Yao *et al*. conducted a PLR study on 41 postcardiac shock patients who were receiving mechanical ventilation. They used PiCCO to monitor cardiac output and mainstream sampling equipment to monitor $EtCO_2$. The result showed that the AUC of $\triangle EtCO_2$% was 0.87, its cut-off value was > 5.8%, its sensitivity was 75.2%, and its specificity was 90%[26]. Toupin *et al*. found that during PLR, the AUC of $\triangle EtCO_2$ was 0.8, its cut-off value was $\geq$ 2 mmHg, its sensitivity was 75%, and its specificity was 70%[20]. These were also confirmed by our data in patients with sepsis.

Our data suggested that the combination of $\triangle EtCO_2$ and PPV can predict fluid responsiveness better than the use of only $\triangle EtCO_2$ or PPV. We combined these two methods to overcome their shortcomings. Because the cut-off value of $\triangle EtCO_2$ was so small (2 mmHg), the application of this threshold value is prone to errors, which means the change may come from measurement error rather than a response to a changed CI. On the other hand, although PPV can be easily obtained by minimally invasive radial artery monitoring without a PiCCO catheter, the accuracy of PPV in predicting is not satisfactory. Therefore, we combined $\triangle EtCO_2$% with PPV to make a new predictor. The reason we chose $\triangle EtCO_2$% plus PPV was that one could monitor PPV without invasive CI monitoring (e.g., PiCCO). Meanwhile, one could obtain $\triangle EtCO_2$% by using a sidestream infrared gas analyzer connected to the patient's monitor, which is also non-invasive. By doing so, one can predict fluid responsiveness accurately, easily, and non-invasively.

$EtCO_2$ monitoring as a substitute to CI during PLR has some limitations. First, the assessment of $EtCO_2$ variations is based on the assumption that breathing and metabolism are stable in a short period while performing the PLR maneuver. If there is a significant change in metabolic rate (such as in fever or shivering), $EtCO_2$ cannot fully reflect the change of CI. However, the maximum hemodynamic effect of PLR is in the first minute, during which the metabolic rate of patients is unlikely to change dramatically. Second, this study was conducted only in patients with septic shock. The applicability of other types of shock (e.g., cardiogenic shock, obstructive shock, etc.) needs further study. Third, studies have shown that the change in $EtCO_2$ can also reflect the change of CI in patients with regular and stable spontaneous breathing. However, such patients were not evaluated in this study. Fourth, there are several ways to monitor $EtCO_2$. It is not known whether the data and the critical value obtained by using the main gas prevalent infrared method are applicable to other methods.

Conclusions

It was effective to predict the fluid responsiveness of patients with septic shock by using $\triangle EtCO_2$ and PPV in the PLR test. The combination of PPV and $\triangle EtCO_2$% was a better predictor of fluid responsiveness than solely the use of each variable.

Abbreviations

CI: cardiac index; CO = cardiac output; CVP = central venous pressure; $\triangle$PetCO2 = change of end-tidal carbon dioxide partial pressure; DBP = diastolic blood pressure; $EtCO_2$ = end-tidal carbon dioxide; HR = heart rate; ICU = intensive care unit; IQR = interquartile range; MAP = mean arterial pressure; NR = non-responders; PiCCO = pulse indicating continuous cardiac output; PLR = passive leg raising; PP = pulse pressure; PPV = pulse pressure variability; R = responders; RASS = richmond agitation-sedation scale; ROC = receiver-operating characteristic; SBP = systolic blood pressure; SD = standard deviation; SV = stroke volume; SVV = stroke volume variability.

Declarations

Ethics approval and consent to participate

This prospective study was approved on January 23rd, 2018, by the Ethics Committee of Fujian Provincial Hospital (Approval # K2018-01-23). The study was registered on December 26th, 2019, at the Chinese Clinical Trial Registry (ChiCTR1900028210). Written informed consent was obtained from each patient's next of kin.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

XFZ, RGY, FHL, and HC participated in study designing; XFZ, TFH, SRG, YRZ and QC participated in data collecting and analysis, XFZ and HC drafted the manuscript. All authors edited the manuscript and approved the final manuscript.

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Figures

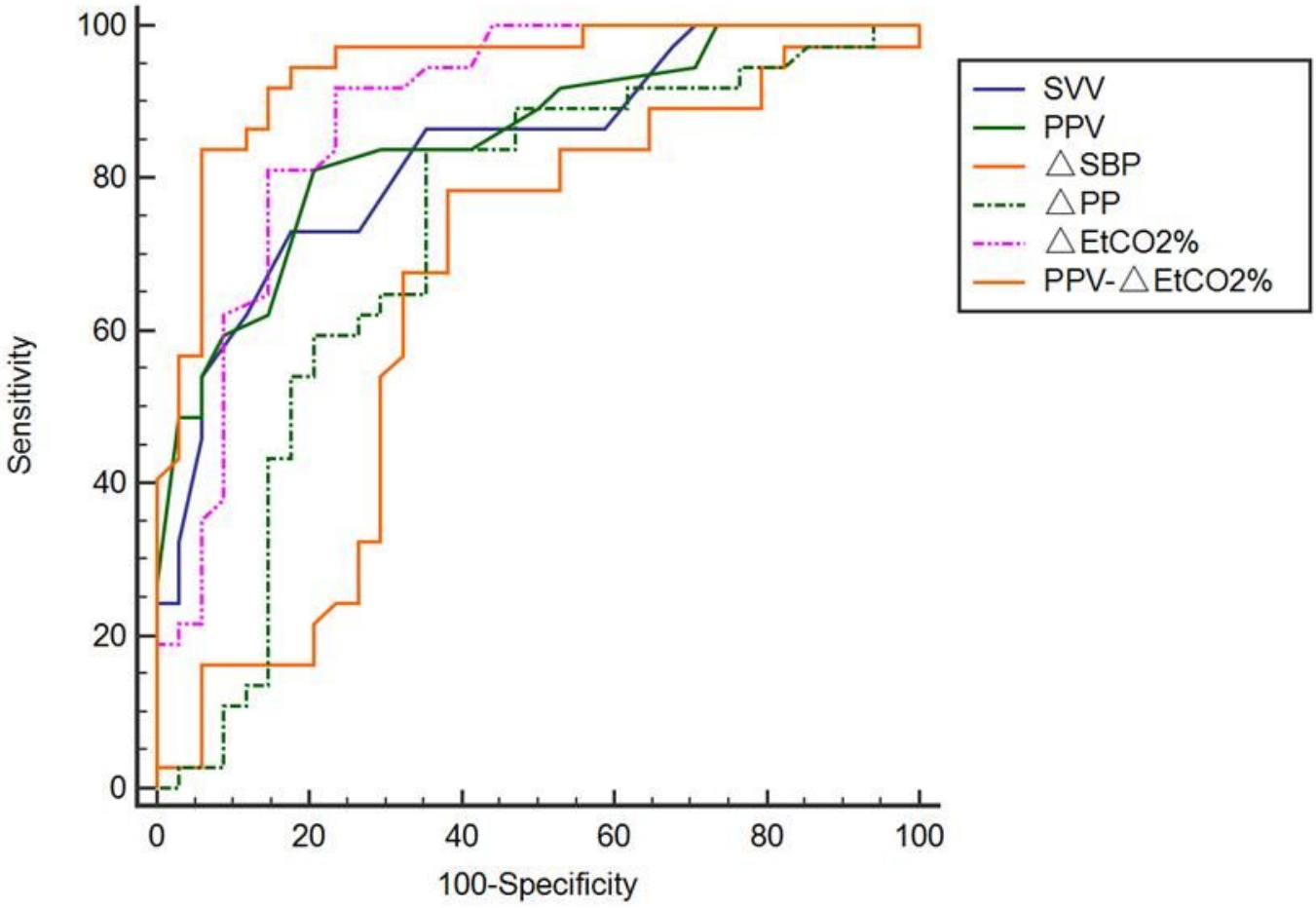

Figure 1

Linear regression analysis of the relationship between PLR-induced changes in CI and EtCO2. CI cardiac index, EtCO2 end-tidal CO2, PLR passive leg raising

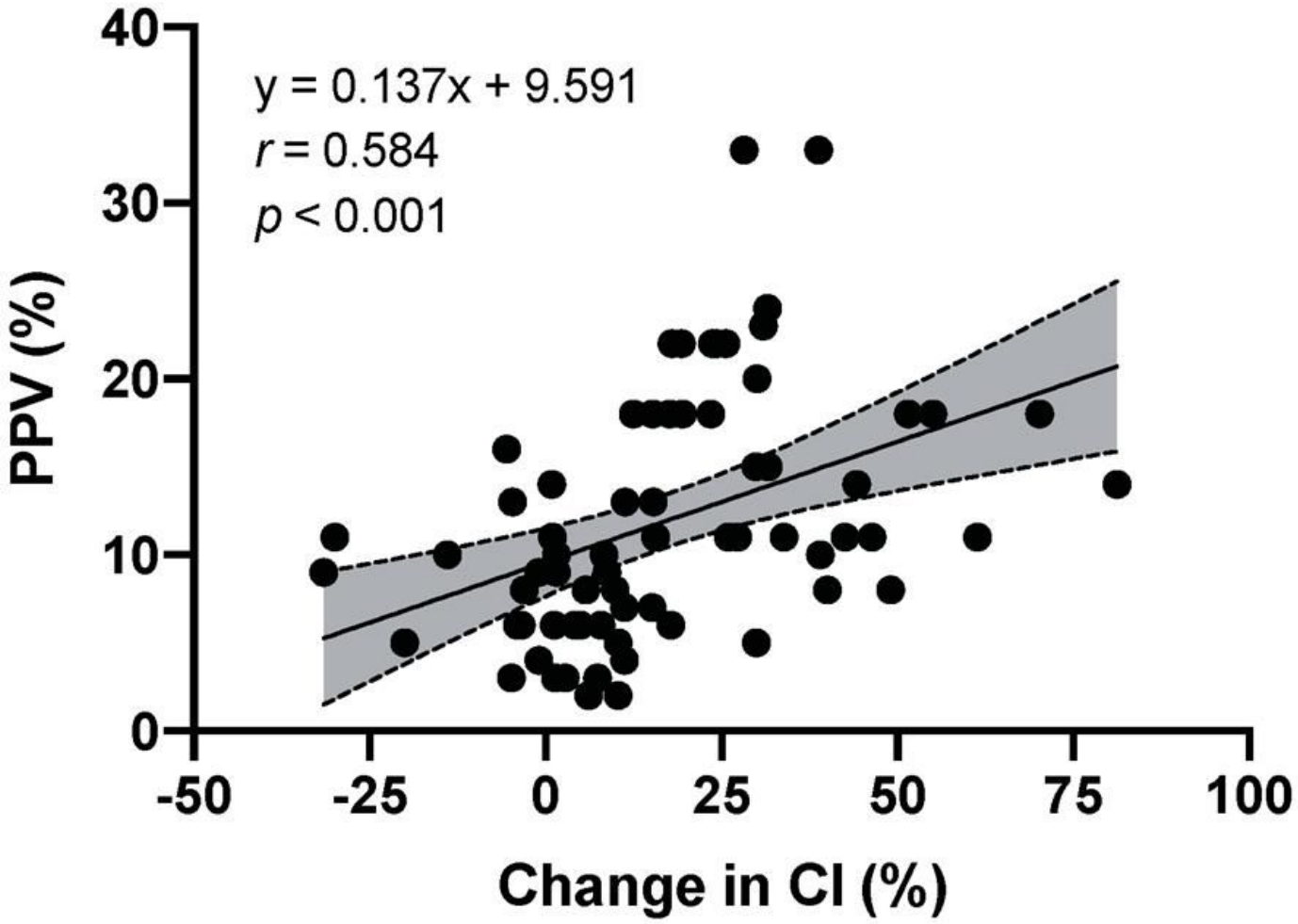

Figure 2

Linear regression analysis of the relationship between PLR-induced changes in CI and PPV CI cardiac index, PPV pulse pressure variability, PLR passive leg raising

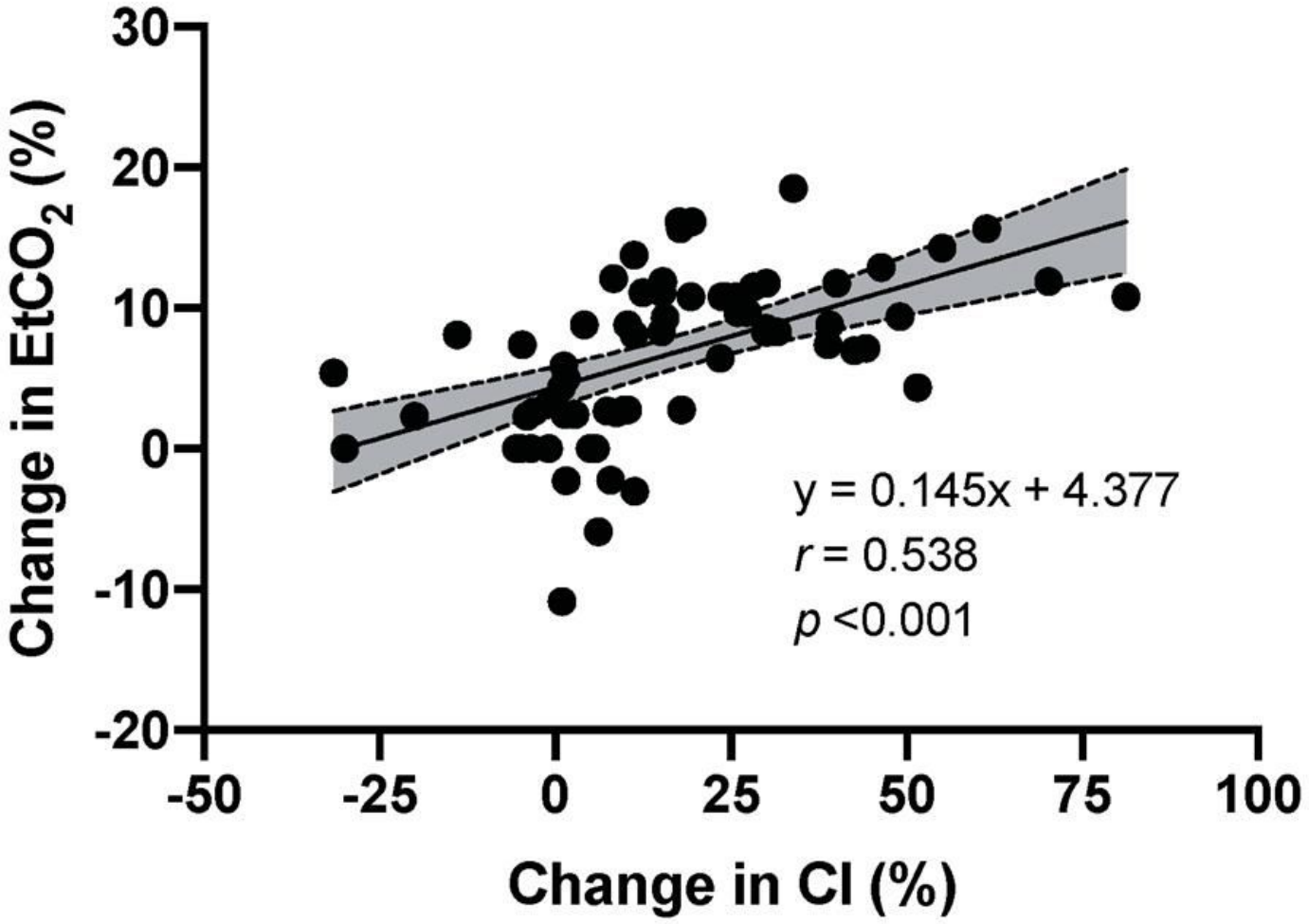

Figure 3

ROC curves showing the ability of the PLR-induced changes in SVV, PPV, △SBP, △PP, △EtCO2 mmHg, △EtCO2% and PPV-△EtCO2%. △EtCO2 end-tidal carbon dioxide variation, △EtCO2% end-tidal carbon dioxide variation ratio, △PP pulse pressure variation, △SBP systolic blood pressure variation, PPV pulse pressure variability, SVV stroke volume variability