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ORIGINAL ARTICLE

Evaluation of pleth variability index as a predictor of fluid responsiveness during orthotopic liver transplantation

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Abstract Fluid management is challenging and still remains controversial in orthotopic liver transplantation (OLT). The pleth variability index (PVI) has been shown to be a reliable predictor of fluid responsiveness of perioperative and critically ill patients; however, it has not been evaluated in OLT. This study was designed to examine whether the PVI can reliably predict fluid responsiveness in OLT and to compare PVI with other hemodynamic indexes that are measured using the $PiCCO_2$ monitoring system. Twenty-five patients were enrolled in this study. Each patient was monitored using the noninvasive Masimo and $PiCCO_2$ monitoring system. PVI was obtained with a Masimo pulse oximeter. Cardiac index was obtained using a transpulmonary thermodilution technique (CI_{TPTD}). Stroke volume variation (SVV), pulse pressure variation, and systemic vascular resistance index were measured using the $PiCCO_2$ system. Fluid loading (10 mL/kg colloid) was performed at two different phases during the operation, and fluid responsiveness was defined as an increase in $CI_{TPTD} \geq 15\%$. During the dissection phase and the anhepatic phase, respectively, 14 patients (56%) and 18 patients (75%) were classified as responders. There were no differences between the baseline values of the PVI of responders and nonresponders. Area under the curve for PVI was 0.56 (sensitivity 35%, specificity 90%, $p = 0.58$) at dissection phase, and was 0.55 (sensitivity 55%, specificity 66%, $p = 0.58$) at

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anhepatic phase. Of the parameters, a higher area under the curve value was found for SVV. We conclude that PVI was unable to predict fluid responsiveness with sufficient accuracy in patients undergoing OLT, but the SVV parameter was reliable.

Introduction

Hyperdynamic circulation due to high cardiac output (CO), low systemic vascular resistance, and relative hypovolemia occur in cirrhotic patients undergoing orthotopic liver transplantation (OLT) [1,2]. The patients encounter major cardiovascular changes during OLT as a consequence of surgical bleeding, vena cava cross clamping, and reperfusion. The fluid management of these patients is very challenging and still remains controversial; however, it is important to avoid fluid overloading and to supply sufficient perfusion to the graft [3].

The concept of fluid responsiveness has been increasingly used to optimize fluid management. Static variables of the cardiac preload, such as central venous pressure (CVP) and pulmonary artery occlusion pressure, are reported as unreliable for evaluating fluid responsiveness [4–7]. It has been suggested that the dynamic indicators measured depend on the respiratory variation of stroke volume estimated using pulse contour analysis of patients receiving mechanical ventilation and the pulse pressure variations obtained from the arterial pulse pressure are superior to the static indicators [7,8]. However, these techniques are either invasive with potential complications or are not constant [7]. Recently, several investigators have focused on noninvasive indicators such as the plethysmographic variability index and the variation of the plethysmographic waveform of pulse oximetry, which have strong relationships with respiratory variations in arterial pulse pressure [9,10].

The Masimo pulse oximeter incorporates an algorithm to continuously measure the changes in pulse volume (PVI) and uses a pulse oximetry probe that is very similar to an ordinary one. The PVI measures the dynamic changes of the perfusion index (PI) over respiratory cycles and is calculated as follows:

$$PVI = [(PI\ maximum - PI\ minimum)/PI\ maximum] \times 100\% \quad (1)$$

[7,11].

The PVI is presented as a safe and useful parameter for evaluating fluid responsiveness of perioperative patients who underwent major abdominal surgery and for critically ill patients [11–15]. However, the accuracy of the PVI is unclear for OLT operations that have hyperdynamic circulation and major cardiovascular changes.

The aims of this study were to evaluate the efficiency of the PVI to predict fluid responsiveness at different surgical phases of OLT and to compare the PVI with other indicators of fluid responsiveness that were measured using the $PiCCO_2$ monitoring system.

Methods

After approval of the study protocol by the Inonu University Medical Faculty Ethics Committee, Malatya, Turkey (Number: 2011/204), signed written informed consent was obtained from the patients' or the relatives of the patient. Twenty-five patients, older than 18 years and undergoing OLT, were included in the study. Patients were excluded from the study if they presented with cardiac arrhythmias, low left ventricular function (ejection fraction $< 40\%$), renal dysfunction, valvular heart disease, pulmonary hypertension, or fulminant hepatic failure. The demographic data, the Child (Child–Turcotte–Pugh) scores and the Model for End Stage Liver Disease scores of the patients were recorded.

Anesthetic method

Unpremedicated patients were brought into the operating room and were monitored using three-lead electrocardiography, pulse oximetry, noninvasive blood pressure, and bispectral index. Anesthetic induction was performed with 3–5 mg/kg thiopental, 1–2 μg/kg fentanyl, and 0.15 mg/kg cisatracurium besylate. Anesthesia was maintained with an infusion of 0.1–0.2 μg/kg/min remifentanil, 0.1 mg/kg/h cisatracurium besylate, and with 0.4–1% isoflurane in 40% oxygen/air. The bispectral index level was protected between 40 and 60 throughout the surgery. The ventilator settings were standardized with volume-controlled mode (tidal volume of 8 mL/kg, zero end-expiratory pressure, and respiratory rate was adjusted to maintain end-tidal carbon dioxide levels within 30–40 mmHg) following the intubation.

To prevent hypothermia, warming blankets were used, and intravenously administered fluids were warmed (Hot Line SIMS Medical System Inc., Rockland, MA, USA; Fluido Pressure Chamber, TSCI, Amersfoort, The Netherlands). Patients were given Isolyte S® (Eczacıbaşı-baxter, Istanbul, Turkey) and 6% hydroxyethyl starch for intravascular volume replacement, and 20% human albumin was administered in cases of hypoalbuminemia (albumin < 2.5 g/dL). Fresh frozen plasma was given depending on the prothrombin time (to maintain the international normalized ratio between 1.5 and 2.0) and thrombocyte suspension was given if the thrombocyte count was lower than 50,000/mm^3. An erythrocyte suspension was transfused based on the hemoglobin concentration (transfused if hemoglobin $<$ 7 g/dL). Mannitol and/or furosemide were used when needed to sustain a mean rate of urination of > 1 mL/kg/h. Norepinephrine, dopamine, or epinephrine infusions were administered when the mean arterial pressure was lower

than 60 mmHg, and all of the agents and liquids that were used were recorded. The OLT was performed with a total clamping method without veno-venous bypass.

Hemodynamic monitoring and experimental procedure

The Masimo pulse cooximeter probe (MasimoSET® Rainbow R2-25r and R225a, Masimo Corp., Irvine, CA, USA) was placed on the index finger of the patients and was covered with a shield to eliminate light interference, as recommended by the manufacturer. The PVI and PI variations were automatically measured using the Masimo monitor (Masimo Radical-7, Masimo Corp., Irvine, CA, USA) with PVI software.

Invasive hemodynamic monitoring was initiated after the induction of anesthesia. A 4F-thermodilution catheter was inserted into the left femoral artery, and a triple-lumen central venous catheter (7F, 20 cm) was inserted into the right internal jugular vein or the subclavian vein using the Seldinger technique. Both catheters were connected to the $PiCCO_2$ monitoring system (Pulsion Medical Systems, Munich, Germany).

Fluid loading was performed twice using 10 mL/kg 6% hydroxyethyl starch (130/0.4; Voluven, Fresenius Kabi, Stans, Switzerland) via the central venous catheter at a rate of 1 mL/kg/min after ascite aspiration during the dissection phase and after vena-cava clamping during the anhepatic phase. The initiation of fluid loading was performed according to the discretion of the physician. This was based on the clinical signs of systemic hypoperfusion, which included any reduction of more than 10–20% from the baseline of mean arterial pressure (MAP) or cardiac index as continuously measured using the pulse contour analysis of the $PiCCO_2$ system. Before fluid loading and 10 minutes after fluid loading, the cardiac index (CI_{TPTD}) was determined with the intermittent transpulmonary thermodilution technique using a triplicate injection of cold saline. Cold saline ($\leq 8^{\circ}C$, 15 mL) was injected into the central venous line by the same researcher, and the CI_{TPTD} was obtained by calculating the mean value of the three consecutive measurements. Patients were divided into two groups as responders or nonresponders. If an increase of $CI_{TPTD} \geq 15\%$ from the baseline was observed, the patients were considered to be responders. Conversely, if the CI_{TPTD} increased $< 15\%$, the patient was considered to be a nonresponder to the fluid loading. In addition to these parameters, heart rate, MAP, CVP, stroke volume variation (SVV), pulse pressure variation (PPV), and systemic vascular resistance index (SVRI) were recorded.

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL, USA) and MedCalc statistical software (MedCalc version 10.1.6.0, Ostend, Belgium). Continuous variables were reported as the mean $\pm$ standard deviation, while categorical variables were reported as numbers. Normality for continuous variables of the groups was determined with the Shapiro–Wilk test. A paired *t* test and Wilcoxon test were used for variables within the responders group and the nonresponders group. The Mann–Whitney *U* test was used for the comparison of the variables between the groups. The correlation between continuous variables was examined with Pearson Correlation and Spearman rank correlation tests. Receiver operating characteristic (ROC) curves were generated for PVI, SVV, PPV, and CVP by varying the discriminating threshold of each, and the areas under the ROC curves were calculated and compared using MedCalc statistical software [12]. From an earlier study [5], power analysis showed that 24 patients were necessary to detect a difference of 0.15 between PVI and SVV areas under the ROC curves (SVV 0.95, 5% type I error rate, 80% power, two tailed *t* test). A value of $p < 0.05$ was considered to statistically significant.

Results

The data of all 25 patients (9 women and 16 men) were included in the final analysis. Demographic data, Child scores, Model for End Stage Liver Disease scores, and operation times are presented at Table 1. The mean pulmonary arterial pressure was 27.17 $\pm$ 4.20 mmHg, and the mean left ventricular ejection fraction was 60.65 $\pm$ 1.72%. The etiologies of hepatic failure were hepatitis B (10 patients), hepatitis C (3 patients), hepatitis B + C (2 patients), cryptogenic (6 patients), alcohol (3 patients), and Wilson's disease (1 patient).

A total of 50 fluid loadings were performed. There were 14 responders and 11 nonresponders to the first fluid loading during the dissection phase. One measurement was excluded because CI_{TPTD} was not measured; consequently, the responder/nonresponder ratio was 18/6 for the anhepatic phase. PI levels were $< 1\%$ during 16 of the 100 measurements (before and after fluid loading at both phases). During the study period, PPV was not obtained in nine patients.

The first fluid loading during the dissection phase was associated with significant increases in heart rate, MAP, CVP, and CI_{TPTD}, and with significant decreases in SVV and PPV. While a decrease was observed in PVI, there were no statistically significant differences (Table 2). The baseline PVI was not significantly different between responders and nonresponders. The only baseline parameter that was significantly higher in responders was SVV ($p = 0.01$; Table 3).

The second fluid loading during the anhepatic phase was associated with a significant increase in MAP, CI_{TPTD}, and a significant decrease in PVI, SVV, and PPV (Table 2). Similar to the dissection phase, the baseline level of the PVI was not significantly different between the groups, and only the baseline level of the SVV was significantly higher in responders compared with nonresponders ($p = 0.009$; Table 3).

The ROC analyses of all parameters that were used to evaluate the predictive ability of a 15% increase of CI_{TPTD} upon fluid loading are presented in Table 4. The PVI had no predictive value at the dissection or anhepatic phases. The area under the curve (AUC) was 0.56 for a PVI ≤ 7 (sensitivity 35% and specificity 90%, $p = 0.58$) and 0.55 for a PVI > 16 (sensitivity 55% and specificity 66%, $p = 0.72$) at the dissection and anhepatic phases, respectively (Figures 1 and 2). ROC analysis demonstrated a significant predictive

Table 1 Demographic data.

	$n = 25$	Dissection phase		Anhepatic phase	
		Responders $n = 14$	Nonresponders $n = 11$	Responders $n = 18$	Nonresponders $n = 6$
Age (y)	49.32 ± 11.74	52 ± 8.65	45.9 ± 14.52	49 ± 12.19	50 ± 12.44
Weight (kg)	71 ± 15.47	73.92 ± 18.19	69.45 ± 11.49	73.44 ± 17.08	67.83 ± 11.32
Height (cm)	165 ± 8.27	164.21 ± 9.03	166.18 ± 7.46	165.16 ± 8.27	163.16 ± 8.47
Body mass index (kg/m^2)	26.32 ± 5.29	27.19 ± 5.75	25.21 ± 4.66	26.75 ± 5.55	25.6 ± 5.08
Body surface area (m^2)	1.81 ± 0.21	1.83 ± 0.24	1.79 ± 0.16	1.83 ± 0.23	1.76 ± 0.16
Child scores (A/B/C)	6/7/12	3/4/7	3/3/5	4/6/8	2/1/3
	2.18 ± 0.83	2.28 ± 0.82	2.18 ± 0.87	2.22 ± 0.8	2.16 ± 0.98
MELD scores	17.49 ± 7.88	17.11 ± 8.16	17.97 ± 7.86	16.3 ± 7.2	18.52 ± 8.26
MELD > 20	10	6	4	6	3
Total operation time (min)	509.68 ± 88.56				
Dissection	263 ± 84.52				
Anhepatic	87.40 ± 37.44				
Neohepatic	159.24 ± 50.56				

Data are presented as mean ± standard deviation or *n*. There were no significant differences between responders and responders.
Child = Child–Turcotte–Pugh; MELD = Model of End Stage Liver Disease.

Table 2 Hemodynamic variables recorded at each phase.

	Dissection phase			Anhepatic phase		
	T1	T2	*p*	T3	T4	*p*
HR (min$^{-1)}$	79.60 ± 13.46	85.04 ± 11.82	0.005	90.40 ± 16.05	88.68 ± 16.03	0.34
MAP (mmHg)	74.84 ± 17.53	84.16 ± 14.15	0.02	62.32 ± 13.39	67.00 ± 12.33	0.01
CVP (mmHg)	10.48 ± 5.18	12.76 ± 3.82	0.01	6.12 ± 3.05	6.68 ± 3.22	0.27
PVI (%)	14.08 ± 8.99	11.64 ± 7.30	0.17	18.28 ± 6.74	16.20 ± 6.72	0.02
PI (%)	4.20 ± 2.63	3.58 ± 2.12	0.13	2.38 ± 1.31	2.05 ± 1.30	0.13
CI_{TPTD} (L/min/m$^{2)}$	3.87 ± 0.83	4.70 ± 0.97	<0.0001	2.29 ± 1.25	2.95 ± 1.45	<0.0001
SVV (%)	11.52 ± 5.08	8.27 ± 5,14	0.001	22.48 ± 9.08	19.96 ± 7.20	0.01
PPV (%)	9.80 ± 3.68	6.20 ± 3.82	0.02	26.37 ± 10.43	18.43 ± 9.84	0.001
SVRI (dyne.sec.cm^5.m^2)	1382.4 ± 507.1	1243.5 ± 292	0.11	2160.2 ± 609.8	1929.2 ± 845	0.03

Data are presented as mean ± standard deviation.
CI_{TPTD} = cardiac index determined with the intermittent transpulmonary thermodilution; CVP = central venous pressure; HR = heart rate; MAP = mean arterial pressure; PI = perfusion index; PVI = pleth variability index; PPV = pulse pressure variation; SVRI = systemic vascular resistance index; SVV = stroke volume variation; T1 = baseline value at dissection phase; T2 = 10 minutes after fluid loading at dissection phase; T3 = baseline value at anhepatic phase; T4 = 10 minutes after fluid loading at anhepatic phase.

ability for only SVV. The AUC was 0.77 for a SVV > 9 (sensitivity 92% and specificity 54%, $p = 0.004$) and a 0.85 for SVV > 21 (sensitivity 72% and specificity 83%, $p = 0.0001$) at the dissection phase and anhepatic phases, respectively (Figures 3 and 4).

Considering the correlation between the baseline parameters (PVI, SVV, PPV, and CVP) and subsequent changes of the CI after fluid loading, the PVI, PPV, and CVP showed no significant correlation with ΔCI, in contrast to SVV (at dissection phase r = 0.60, $p = 0.001$; at anhepatic phase r = 0.44, $p = 0.02$; Table 5). Considering all the pairs of measurements, the coefficient of determination between PVI and SVV was 0.63 ($p = 0.001$), and the coefficient of determination between PVI and PPV was 0.77 ($p < 0.0001$) at the anhepatic phase. There were no correlations between the fluid-induced changes of PVI and other parameters.

During the operation, one patient was administered a dopamine infusion. Five patients at the dissection phase and seven patients at the anhepatic phase were administered a norepinephrine infusion. Twenty-one patients were administered an erythrocyte suspension of a mean volume of 2.12 ± 1.45 (0–5) units, and seven patients were administered fresh frozen plasma of a mean volume of 0.66 ± 1.27 (0–5) units; none of the patients needed a thrombocyte suspension. Fifteen patients were administered human albumin of a mean volume of 92 ± 86.21 mL.

Discussion

This study showed that PVI was insufficient to predict the fluid responsiveness of both surgical phases of OLT. The PVI was correlated with SVV and PPV at only the anhepatic

Table 3 Comparison of the baseline hemodynamic variables between responders and nonresponders at the dissection phase and anhepatic phases.

		Responders	Nonresponders	*p*
Dissection phase	HR ($min^{-1)}$	80.42 ± 13.03	78.54 ± 14.57	0.85
	MAP (mmHg)	73.71 ± 20.25	76.27 ± 14.15	0.50
	CVP (mmHg)	11.92 ± 5.81	8.63 ± 3.72	0.13
	PVI (%)	14.65 ± 11.35	13.36 ± 5.08	0.60
	PI (%)	5.09 ± 2.85	3.06 ± 1.85	0.03
	CI_{TPTD} ($L/min/m^{2)}$	3.70 ± 0.71	4.10 ± 0.96	0.16
	SVV (%)	13.57 ± 5.18	8.90 ± 3.70	0.01
	PPV (%)	10.60 ± 3.43	7.66 ± 3.82	0.11
	SVRI ($dyne.sec.cm^5.m^2$)	1390.07 ± 629.64	1372.72 ± 318.97	0.50
Anhepatic phase	HR ($min^{-1)}$	92.33 ± 11.94	87.50 ± 25.83	0.62
	MAP (mmHg)	59.61 ± 12.82	70 ± 14.24	0.10
	CVP (mmHg)	5.66 ± 3.02	7.16 ± 3.31	0.53
	PVI (%)	18.66 ± 6.55	17.16 ± 8.40	0.72
	PI (%)	2.28 ± 1.30	2.67 ± 1.42	0.62
	CI_{TPTD} ($L/min/m^{2)}$	2.04 ± 0.61	3.05 ± 2.23	0.34
	SVV (%)	25.66 ± 7.14	13.66 ± 9.41	0.009
	PPV (%)	27.00 ± 9.19	23.66 ± 17.21	1.00
	SVRI ($dyne.sec.cm^5.m^2$)	2212.33 ± 609.91	2028.33 ± 696.75	0.92

Data are presented as mean ± standard deviation.
CI_{TPTD} = cardiac index determined with the intermittent transpulmonary thermodilution; CVP = central venous pressure; HR = heart rate; MAP = mean arterial pressure; PI = perfusion index; PPV = pulse pressure variation; PVI = pleth variability index; SVRI = systemic vascular resistance index; SVV = stroke volume variation.

Table 4 Receiver operating characteristic curves and cut-off points of variables at the dissection phase and anhepatic phase.

		AUC	95% Confidence interval	Cut-off points	Sensitivity (%)	Specificity (%)	*p*
Dissection phase	PVI (%)	0.56	0.35–0.76	≤7	35	90	0.58
	SVV (%)	0.77	0.56–0.91	>9	92	54	0.004
	PPV (%)	0.74	0.48–0.92	>8	80	66	0.09
	CVP (mmHg)	0.67	0.46–0.84	>8	78	54	0.10
Anhepatic phase	PVI (%)	0.55	0.34–0.75	>16	55	66	0.72
	SVV (%)	0.85	0.64–0.96	>21	72	83	0.0001
	PPV (%)	0.51	0.25–0.76	>4	100	33	0.96
	CVP (mmHg)	0.59	0.37–0.78	≤3	27	100	0.49

AUC = area under receiver operating characteristic curve; CVP = central venous pressure; PPV = pulse pressure variation; PVI = pleth variability index; SVV = stroke volume variation.

phase, but there were no correlations between the fluid-induced changes of PVI and other parameters. Among the parameters, only SVV variable was determined to be reliable. The SVV before fluid loading was higher in the responders. Moreover, changes in CI_{TPTD} secondary to fluid loading were correlated with only SVV before fluid loading.

In a meta-analysis, PVI was identified as a reliable predictor of fluid responsiveness of perioperative and critically ill patients, especially in adults who received mechanical ventilation [11]. Cannesson et al. [12] asserted that a PVI value > 14 predicted fluid responsiveness with 81% sensitivity and 100% specificity (AUC = 0.92) in 25 patients who underwent coronary bypass surgery. In another study of patients who underwent major surgery, a PVI value > 9.5 was identified as an effective parameter to predict fluid responsiveness with 93% sensitivity and 100% specificity (AUC = 0.97) [14].

Our results do not agree with the findings of those previous studies. A possible reason for the discrepancy is that the evaluations of both of the previous studies were performed at stable conditions, just after anesthetic induction and before surgery. However, fluid administrations were given during two different surgical periods, including the dissection and anhepatic phases, in our study. Evaluations at the dissection phase were made after the abdomen was opened and/or ascites were aspirated, instead of at anesthetic induction. The second evaluation was made after total clamping when the preload was significantly reduced and more hemodynamic instability was observed.

Similar to our study, Hood and Wilson [13] evaluated the efficiency of PVI at two different phases of operation, including the preoperative period and intraoperative period, in patients who underwent colorectal surgery. While PVI had a sensitivity of 86% and a specificity of 100%

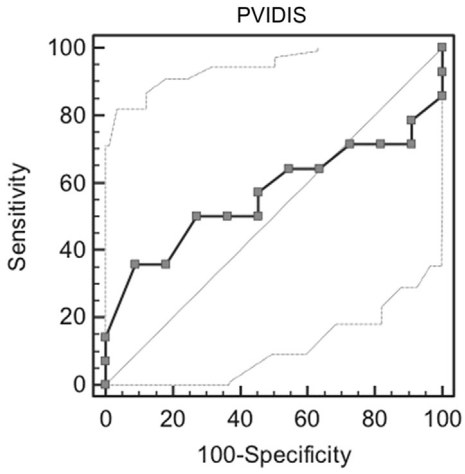

Figure 1. Receiver operating characteristic curves of baseline pleth variability index (PVI) as predictor of cardiac index determined with intermittent transpulmonary thermodilution increases ≥ 15% after fluid loading during dissection phase (DIS) in patients undergoing orthotopic liver transplantation.

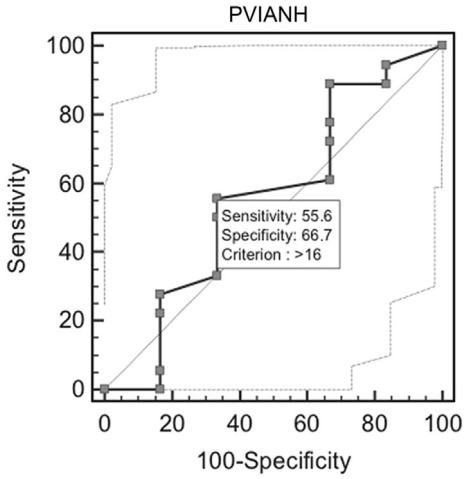

Figure 2. Receiver operating characteristic curves of baseline pleth variability index (PVI) as predictor of cardiac index determined with intermittent transpulmonary thermodilution increases ≥15% after fluid loading during the anhepatic phase (ANH) in patients undergoing orthotopic liver transplantation.

(AUC = 0.96) after the induction, the sensitivity and specificity were reduced to 65% and 67%, respectively (AUC = 0.71), in the dynamic intraoperative conditions. Hood and Wilson [13] performed the study in low-risk patients (American Society of Anesthesiologists physical status Classification I—II), while the patients were in high-risk groups (American Society of Anesthesiologists III—IV) in our study.

Loupec et al. [15] investigated PVI in mechanically ventilated patients with circulatory insufficiency in an intensive care unit. However, they stated that all patients were studied under stable conditions; therefore, the results could not be extended to all critically ill patients, especially patients with cardiogenic shock, patients receiving a

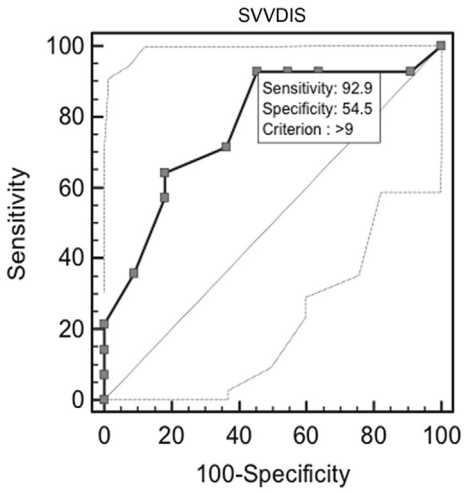

Figure 3. Receiver operating characteristic curves of baseline stroke volume variation (SVV) as predictor of cardiac index determined with intermittent transpulmonary thermodilution increases ≥15% after fluid loading during the dissection phase (DIS) in patients undergoing orthotopic liver transplantation.

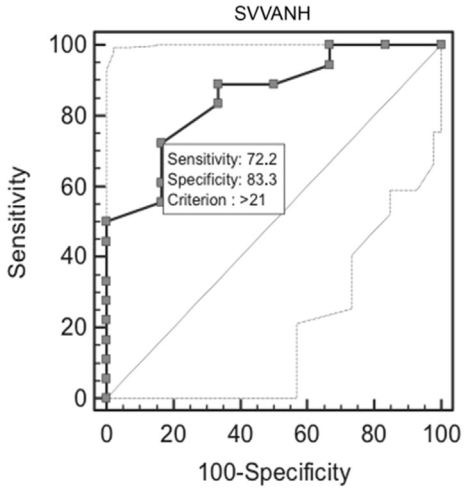

Figure 4. Receiver operating characteristic curves of baseline stroke volume variation (SVV) as predictor of cardiac index determined with intermittent transpulmonary thermodilution increases ≥15% after fluid loading during the anhepatic phase (ANH) in patients undergoing orthotopic liver transplantation.

Table 5 Correlation between the baseline parameters [pleth variability index (PVI), stroke volume variation (SVV), pulse pressure variation (PPV), central venous pressure (CVP)] and subsequent changes in the cardiac index after fluid loading.

	r	*p*
PVI (%)	0.34	0.09
SVV (%)	0.60	0.001
PPV (%)	0.43	0.09
CVP (mmHg)	−0.13	0.52

catecholamine other than norepinephrine, or patients in life-threatening conditions. Thus, the combination of unstable intraoperative conditions and high-risk patients could have caused the results of our study.

Another reason for our low predictability of PVI values could be the alterations of PI that could be related to many different causes. For the calculation of perfusion index, the infrared pulsatile signal is indexed against the nonpulsatile signal and expressed as a percentage, reflecting the amplitude of the pulse oximeter waveform [14]. The manufacturer emphasized that PI value should be bigger than 1 during the PVI measurement [13]. In some studies, it was reported that both PI and PVI can be affected by factors such as vascular disease, hypothermia, low CO, and the use of a vasoconstrictor agent [7,9,10,16]. Broch et al. [9] identified PVI as insufficient to predict fluid responsiveness in their study and asserted that PVI can evaluate fluid responsiveness only if PI is $>$ 4% (i.e., patients with a high perfusion). They performed the analyses according to different PI levels. In our study, PVI values were usually obtained in the presence of low perfusion, which was particularly pronounced at the anhepatic phase; 15% of the evaluations had a PI $<$ 1%, and 62% of the evaluations had a PI $<$ 4%. In our opinion, increased vascular compliance due to hyperdynamic circulation and low vascular resistance in some cirrhotic patients might have caused the low PI. Moreover, an intense sympathetic response to the hemodynamic instability at the anhepatic phase might have led to a pronounced effect (and might be another reason for our low predictability of PVI).

Five patients at the dissection phase and seven patients at the anhepatic phase were administered a norepinephrine infusion. In the study that compared intensive care patients with or without norepinephrine administration, it was shown that patients without norepinephrine administration had higher AUC values than patients with norepinephrine administration [7]. In another study, Monnet et al. [10] stated that PVI could not be obtained in a significant number of intensive care patients who were administered a norepinephrine infusion and that PVI was less reliable than SVV and PPV values obtained using the $PiCCO_2$ system. As a result, they affirmed that it was not a useful variable for patients who were administered norepinephrine.

In our study, CI values were obtained using the $PiCCO_2$ system that was less invasive than premature atrial contraction (PAC). Della Rocca et al. [3] showed that CI values obtained using PAC and the $PiCCO_2$ system were similar in their study of 60 liver transplantation patients [3]. Costa et al. [1] also performed a study to compare PAC and $PiCCO_2$ following OLT, and they emphasized that parameters obtained using $PiCCO_2$ were much better indicators than CVP and pulmonary artery occlusion pressure. The $PiCCO_2$ system is a monitor that can continuously calculate CO with pulse-counter analysis, after the first transpulmonary (transaortic) thermodilution-mediated CO calculation and calibration. However, it has been reported that CO calculation using the pulse counter method might be affected by significant changes of vascular tonus [17]. Therefore, all CI variables were measured after calibration using the transpulmonary thermodilution method in our study.

Our study showed that femoral SVV is the best variable to predict fluid responsiveness at both surgical phases. Moreover, the predictability of SVV was increased at the anhepatic phase. These data are in accord with the findings of several other studies [5,9,10,18—20]. Additionally, PPV has been reported to be a good predictor of fluid responsiveness in several studies [9,10,18,20]. We could not demonstrate this finding in our study; therefore, we cannot conclude that all dynamic indices can predict fluid responsiveness during OLT. However, as a limitation of our study, PPV values were determined in only 16 patients due to data loss. Gouvêa et al. [21] also evaluated the PPV of 15 OLT patients and found that PPV failed to predict fluid responsiveness. In contrast to our study, they evaluated the radial PPV. Consequently, further studies are warranted to elucidate the role of PPV in OLT.

As a second limitation, fluid loading was not performed during the reperfusion phase. The reperfusion of the transplanted liver usually causes severe hemodynamic instability known as the reperfusion syndrome. Instead of a low preload status, cooled blood mixed with potassium protons, and inflammatory mediators cause profound hypotension during this phase. Therefore, to minimize those confounding effects and to avoid overloading of the transplanted liver, fluid loading was not performed during this phase.

We conclude that PVI derived from the Masimo monitor was not a reliable predictor of fluid responsiveness in OLTs that had variable peripheral perfusion and frequent use of vasoconstrictors. Further studies are needed to examine the correlation between PVI and peripheral perfusion and to clarify the effects of catecholamine administration in OLT. Additionally, more studies are needed to determine whether all other dynamic indices can predict fluid responsiveness, although SVV was found to be reliable.

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