



# Pulse Oximeter–Derived Pleth Variability Index is a Reliable Indicator of Cardiac Preload in Patients Undergoing Liver Transplantation

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## ABSTRACT

**Background.** Accurate estimation of cardiac preload during liver transplantation is essential. The right ventricular end-diastolic volume index (RVEDVI) is recognized as a good preload indicator in patients undergoing liver transplantation. Recently, dynamic variation parameters including pleth variability index (PVI) have been used as predictors of fluid responsiveness. However, the correlation between PVI and preload status has not been well studied. We evaluated the relationship between PVI and RVEDVI during liver transplantation.

**Methods.** Eighteen patients undergoing liver transplantation were enrolled in this study. Data of hemodynamic parameters including PVI derived by Masimo Rainbow SET Pulse CO-Oximeter, central venous pressure (CVP), pulmonary arterial occlusion pressure (PAOP), and RVEDVI were obtained at 10 defined time points throughout liver transplantation. The correlation between RVEDVI and CVP, PAOP, and PVI was analyzed using Spearman rank test. We also investigated the ability of PVI to accurately differentiate RVEDVI <123 or >142 mL/m<sup>2</sup> using receiver operating characteristic (ROC) analysis.

**Results.** There was fair to good correlation between PVI and RVEDVI (correlation coefficient = -0.492,  $P < .001$ ). The correlation coefficient between CVP, PAOP, and RVEDVI was 0.345 and 0.463, respectively. A 13.5% cutoff value of PVI estimated the RVEDVI <123 mL/m<sup>2</sup> (area under the curve [AUC] = 0.762). A 12.5% cutoff value of PVI estimated the RVEDVI >142 mL/m<sup>2</sup> (AUC = 0.745).

**Conclusions.** PVI presented as a reliable estimate of preload status and may be a useful predictor of fluid responsiveness in patients undergoing liver transplantation.

**B**ECAUSE major fluid shifts frequently occur during orthotopic liver transplantation (OLT), anesthesiologists face the challenge of maintaining adequate systemic perfusion while preventing pulmonary edema perioperatively. Accurate estimation of cardiac preload and optimal fluid management thus becomes essential in patients undergoing liver transplantation. Conventionally, cardiac filling pressures, such as pulmonary artery occlusion pressure (PAOP) and central venous pressure (CVP), have been used to measure ventricular preload in guiding fluid management. Recent studies have demonstrated that static pressures, such as PAOP and CVP, may not be reliable estimates of cardiac preload status and possibly poor predictors of hemodynamic

response to fluid challenge [1,2]. On the contrary, right ventricular end-diastolic volume index (RVEDVI), obtained by the thermodilution method using a pulmonary artery catheter (PAC), reflects a more accurate preload estimation than either PAOP or CVP during OLT [3].

Dynamic parameters measured in mechanically ventilated patients based on cardiopulmonary interactions, such as pulse pressure variation [4] and stroke volume variation

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(SVV) [5,6], have been consistently demonstrated to be more reliable than static pressure in predicting fluid responsiveness and reflecting preload status [7,8]. Pleth variability index (PVI) is also a dynamic variation parameter that automatically and continuously calculates the respiratory variations in the plethysmographic waveform acquired by the pulse oximeter [9]. Several studies have shown that PVI may predict fluid responsiveness in patients undergoing noncardiac surgeries as well as those under mechanical ventilation in the intensive care unit [10–12]. However, there are still limited studies investigating the direct relationship of PVI and cardiac preload status.

The aims of our study were to evaluate the relationship between PVI derived from pulse oximetry and RVEDVI derived from PAC and to assess PVI against CVP and PAOP as estimates of ventricular preload status in patients undergoing liver transplantation. We also determined the cutoff value of PVI in the estimation of RVEDVI during liver transplantation.

## METHODS

This prospective clinical study was approved by the institutional review board of Chang Gung Memorial Hospital. From August 2014 to December 2014, 18 patients undergoing OLT were enrolled in the study, and written informed consents were obtained from all the participants. Exclusion criteria included preoperative dysrhythmias, significant valvular disease, and intracardiac shunt.

General anesthesia was initiated by induction using intravenous fentanyl 1–2  $\mu\text{g}/\text{kg}$ , propofol 1.5–2  $\text{mg}/\text{kg}$ , and cisatracurium 0.2  $\text{mg}/\text{kg}$  followed by tracheal intubation and mechanical ventilation with a tidal volume set at 6–8  $\text{mL}/\text{kg}$ , a respiratory rate at 8–14/min, and a positive end-expiratory pressure at 5  $\text{cm H}_2\text{O}$ . The ventilator was adjusted to maintain end-tidal  $\text{CO}_2$  within the range of 30–35  $\text{mm Hg}$ . General anesthesia was maintained with isoflurane. Muscle relaxation was achieved by cisatracurium administration (0.05  $\text{mg}/\text{kg}$ ) given every 30 minutes throughout the operation.

An 8.0 Fr. PAC (Swan-Ganz CCombo CCO/SvO<sub>2</sub>/CEDV, Edward Lifesciences, Irvine, CA, USA) was inserted into the right internal jugular vein. The PAC was considered properly positioned with pulmonary artery wedge pressure tracing. The PAC was connected to a Vigilance monitor (Edwards Lifesciences) and cardiac output, CVP, PAOP, and RVEDVI were continuously measured. Moreover, continuous assessment of PVI was achieved using a Masimo Rainbow SET Pulse Co-Oximeter probe (Masimo Corporation, Irvine, Calif, United States) applied to the index finger of the participants.

All of the patients received standard surgical procedures performed by the same surgical team. The piggyback procedure was used, but no patient received venovenous bypass. To reperfuse the transplanted graft, the portal venous flow was first restored, followed by hepatic artery anastomosis. All of the recipients were sent to the intensive care unit for postoperative care.

Hemodynamic parameters including PVI, CVP, PAOP, and RVEDVI were collected at 10 defined time points throughout the liver transplantation. The selected time points were (1) 30 minutes after the induction of anesthesia, (2) 15 minutes after skin incision, (3) 1 hour after the surgery commencement, (4) 2 hours after the surgery commencement, (5) 30 minutes before the anhepatic phase, (6) 30 minutes after the anhepatic phase, (7) 30 minutes after portal venous reperfusion, (8) 30 minutes after hepatic artery anastomosis,

(9) 30 minutes after biliary anastomosis, and (10) at the end of the surgery.

## Statistical Analysis

Statistical analysis was performed with SPSS, version 17.0 (SPSS Inc, Chicago, Ill, United States). Linear regressions between RVEDVI and CVP, PAOP, and PVI were analyzed using Spearman rank order correlation coefficient. The area under the curve (AUC) values of receiver operating characteristic (ROC) curves that predict RVEDVI  $<123 \text{ mL}/\text{m}^2$  (indication of fluid challenge) [13] and  $>142 \text{ mL}/\text{m}^2$  (threshold of negative fluid responsiveness) [14] were calculated. The cutoff value of PVI to estimate the RVEDVI was also determined.  $P < .05$  was considered statistically significant.

## RESULTS

Eighteen patients (age,  $50.3 \pm 10.3$  years; body mass index,  $26.5 \pm 4.6 \text{ kg}/\text{m}^2$ ) undergoing OLT were recruited in this study: 13 males and 5 females. A total of 180 paired measurements at 10 defined time points were analyzed. PVI was found to correlate with RVEDVI with a correlation coefficient of  $-0.492$  ( $P < .001$ ), whereas the correlation coefficient between CVP, PAOP, and RVEDVI was 0.345 and 0.463, respectively. A 13.5% cutoff value for the PVI estimated the RVEDVI  $<123 \text{ mL}/\text{m}^2$  with a sensitivity of 82.3% and a specificity of 60.7%, and the AUC of the PVI was 0.762 (95% confidence interval 0.689–0.836; Fig 1A). A 12.5% cutoff value for the PVI estimated the RVEDVI  $>142 \text{ mL}/\text{m}^2$  with a sensitivity of 80.7% and a specificity of 55.7%, and the AUC of the PVI was then 0.745 (95% confidence interval 0.672–0.817; Fig 1B). The results of ROC analysis to distinguish different RVEDVI thresholds for PVI, CVP, and PAOP are summarized in Table 1.

## DISCUSSION

In this study, it was demonstrated that PVI may serve as a reliable estimate of cardiac preload status in patients undergoing OLT, explicitly, higher PVI values correlated with lower RVEDVI values. It was also shown that the relationship between RVEDVI and PVI (correlation coefficient =  $-0.492$ ;  $P < .001$ ) was much stronger than that with CVP or PAOP. PVI provided more accurate estimates of different RVEDVI than CVP or PAOP.

During OLT, significant hemodynamic instability may occur, therefore, it is essential to monitor cardiac preload status. With reliable preload index, the cause of hypotension may be identified earlier and patients' fluid status optimized in a timely fashion. The RVEDVI is so far regarded as the best indicator of ventricular preload in patients undergoing OLT [3,15], and is widely applied during OLT. Although RVEDVI derived by PAC has been considered the gold standard during OLT, PAC is not without risks, including pulmonary artery rupture, iatrogenic injuries, and cardiac dysrhythmia [16]. The literature has compared several static and dynamic hemodynamic variables with RVEDVI. One such is CVP, which has traditionally been used as right

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