JOURNAL OF INONU LIVER TRANSPLANTATION INSTITUTE

DOI: 10.14744/jilti.2025.00719
J Inonu Liver Transpl Inst 2025;3(3):83–88

Original Research

Evaluation of Correlation Between Pleth Variability Index and Blood Lactate Level in Living Liver Donors

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Abstract

Objectives: This study primary objective to compare simultaneous Pleth Variability Index (PVI) and blood lactate measurements taken during different surgical phases to determine whether PVI is a reliable parameter for fluid monitoring in this patient group. Our secondary objective is to monitor changes in PVI in fluid-restricted liver donors.

Methods: The study was conducted in ASA I–II living liver donors aged 18–55 undergoing right hepatectomy; patients with cardiovascular disease or drug allergies were excluded. PVI and PI were recorded noninvasively using the Masimo SET® device. Measurements were taken at surgical start (T1), 1 hour (T2), end of surgery (T3), postoperative 3 hours (T4) and 24 hours (T5): AST, ALT, BUN, creatinine and blood lactate; and at T1–T4: SpO2, heart rate, arterial pressures, CVP, urine output, blood loss, administered fluid volumes, PVI and PI. Anesthesia and surgery durations, graft weight, and transfused blood/products were recorded.

Results: Our study involved 51 living donors (31 males and 20 females) with a mean age of 28.78 ± 9.64 years. In the intra-group evaluation of PVI, no significant differences were observed across all time periods, but significant correlations in lactate levels were found at multiple time points ($p<0.05$). A notable correlation between PVI and lactate levels was identified during the T3 period. Additionally, significant changes in sodium and creatinine were observed in T3 and T4 ($p<0.05$), along with an increase in bleeding and a decrease in urine output during the first hour of surgery (T2) ($p<0.05$).

Conclusion: We found a correlation between lactate levels at the end of surgery and PVI values in liver transplant donors. Despite adequate hepatic blood flow, hepatocyte damage during surgery may impact lactate metabolism. Therefore, further studies are needed to explore the relationship between PVI and lactate levels in various surgical procedures.

Keywords: Liver translantation, living liver donor, pleth variability index, lactate

Please cite this article as "Kaya F, Sanli M, Gulhas N. Evaluation of Correlation Between Pleth Variability Index and Blood Lactate Level in Living Liver Donors. J Inonu Liver Transpl Inst 2025;3(3):83–88".

During donor hepatectomy, goal-directed fluid therapy is implemented to reduce bleeding and limit the use of blood products. Close monitoring of fluid status is essential to ensure adequate tissue perfusion. In traditional fluid management regimens, fluid monitoring has been conducted using static parameters of cardiac preload, such as central venous pressure (CVP) measurements from central venous catheters or pulmonary artery wedge pressure (PAWP). However, nowadays, dynamic fluid monitoring can be performed non-invasively using

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Submitted Date: 13.11.2025 **Revised Date:** 09.12.2025 **Accepted Date:** 17.12.2025 **Available Online Date:** 14.01.2026
Journal of Inonu Liver Transplantation Institute - Available online at www.jilti.org

the Masimo Radical-7 monitor to measure the Pleth Variability Index (PVI).[1] In fluid-restrictive regimens, invasive methods, such as monitoring blood lactate levels, can be used to closely track tissue oxygenation in a static and invasive manner.

With the advancement of monitoring methods today, many invasive techniques have been replaced by non-invasive measurement techniques. The Masimo Radical-7, through a finger probe, can non-invasively measure parameters such as blood hemoglobin levels, tissue fluid, and oxygenation levels, which can provide advantages in major surgeries like liver transplantation. Laboratory measurements of lactate from patient blood are a reliable method to assess tissue oxygenation and ensure adequate volume replacement. However, in live liver donors, the rapid increase in blood lactate levels following liver resection and manipulation makes it an inaccurate indicator of tissue perfusion adequacy. Additionally, this method is invasive and time-consuming.[2]

The accuracy and reliability of fluid monitoring using the PVI and its correlation with lactate levels have been tested. In major abdominal surgeries utilizing PVI for fluid monitoring, low lactate levels have been achieved, emphasizing its potential reliability.[3] The aim of this study is to compare the PVI and blood lactate values simultaneously obtained during different surgical phases in living liver transplantation donors and to investigate the reliability of PVI in this patient group.

Methods

This study was conducted after obtaining approval from the Malatya Clinical Research Ethics Committee (2015/121) and patient consent, involving living donors for liver transplantation undergoing right hepatectomy, classified as ASA I-II and aged between 18-55 years. Patients were selected by random assignment. Patients that were rejected for participation, had a history of cardiovascular disease, or had allergies to medications to be used during the operation were excluded from the study. The primary objective of these products is to determine whether there is a relationship between PVI and lactate levels. Our secondary objective is to monitor changes in PVI in fluid-restricted liver donors. This study was conducted prospectively and randomly in living liver donors.

Without the application of premedication, patients were brought into the operating room where electrocardiography (ECG), peripheral oxygen saturation (SpO_2), and non-invasive blood pressure monitoring were performed. All patients had a peripheral venous access established through the back of the hand using a 20-gauge intravenous catheter. After preoxygenation with 100% O2, induction was achieved with 1 mg/kg of 2% lidocaine, 1 µg/kg of fentanyl, 5 mg/kg of thiopental, and 0.1 mg/kg of vecuronium. After achieving adequate muscle relaxation, patients were intubated, and isoflurane (Forane Liquid Abbott 100 mL) was administered in concentrations ranging from 0.5% to 1.5% using a 50/50 mixture of oxygen and air. A second peripheral venous access was established using a 16-gauge intracath. Invasive arterial blood pressure monitoring was accomplished by catheterizing the radial artery on the non-dominant side. A three-way 7.5 French central venous catheter was placed in the right internal jugular vein for the purpose of monitoring CVP. A pulse oximeter probe (Masimo SET® Rainbow, Masimo Corp., Irvine, CA) was preferably placed on the ring finger of the left hand, with the surrounding area covered to prevent interference from ambient light. By connecting to a Masimo monitor equipped with PVI software, the perfusion index (PI) and PVI variables were automatically measured. Additionally, remifentanil (0.25 µg/kg/min) and cisatracurium (0.5 µg/kg/h) were added as infusions for maintenance.

During the liver dissection phase, IV crystalloids were administered in a restricted manner. When the CVP exceeded 10 mmHg and urine output was less than 0.5 ml/kg/hr, 5-10 mg of furosemide was given.

Blood tests were conducted and recorded at the beginning of the surgery (T1), after the first hour (T2), at the end of the surgery (T3), three hours postoperatively (T4), and 24 hours postoperatively (T5) for AST, ALT, BUN, creatinine, and blood lactate levels. Additionally, parameters such as SpO_2, heart rate, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), CVP, urine output, blood loss, amounts of crystalloids and colloids administered, PVI, and PI were measured and recorded during the T1, T2, T3, and T4 periods.

Anesthesia and surgery durations, the weight of the graft obtained, and the administered blood and blood products, including noradrenaline, ephedrine, mannitol, and furosemide, were documented.

For postoperative analgesia, 0.05 mg/kg of IV morphine was administered following the removal of the liver graft. At the end of the operation, patients were extubated after the neuromuscular blockade effect was antagonized with neostigmine and atropine. In the postoperative recovery unit, a patient-controlled analgesia device was programmed with an infusion: no bolus of 15 mg and a lockout interval of 10 minutes. Patients with an Aldrete recovery score of 10 were transferred to the surgical intensive care unit.

Power Analysis

To achieve this aim, a theoretical sample size calculation was conducted using G*Power (version 3.1.9.3). This calculation, based on an assumed effect size of 0.50, an alpha error of 0.05, and a study power of 0.80, indicated that a minimum of 51 patients would be required for to determine the correlation between PVİ and lactate.

Statistical Analysis

The statistical analysis of the data was performed using the SPSS 16.0 (SPSS version 16.0 (SPSS Inc., Chicago, IL). software package. Data related to quantitative variables were presented as mean (± standard deviation, SD), while data related to qualitative variables were reported as frequency (n) and percentage (%). The normality of the quantitative variable data was assessed using the Shapiro-Wilk normality test ($p > 0.05$). The change of variables over time was analyzed using the Wilcoxon test, and the relationships between variables were evaluated using the Spearman Rank Correlation analysis. Fisher's Exact Chi-Square test and Pearson Chi-Square test were employed for the statistical evaluation of qualitative variables. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 51 cases, consisting of 31 male and 20 female living donors who underwent kidney transplantation, were included in the study. The distribution of the demographic characteristics of the donors is presented in Table 1. In the intra-group evaluation of PVI, there was no significant difference in correlation across all time periods.

In the intra-group evaluation of blood lactate levels, the correlations between T1 and T2, T4, and T5 values, as well as between T2 and T3, T4 values, and between T4 and T3, T5 values were found to be statistically significant ($p<0.05$).

In the inter-group evaluation of blood lactate levels, a statistically significant correlation was observed between PVI and lactate level during the T3 period (Fig. 1). The ALT, AST, and lactate values of the donors are provided in Table 2.

Table 1. Distribution of donors' demographic characteristics (mean±SD or number)

Gender (Female/Male)	20/31
ASA (I/II)	15/36
Age	28.78±9.64
Height (cm)	170.50±9.04
Weight (kg)	69.60±11.76
Body mass index	23.93±3.39
Duration of anesthesia (min)	439.31±98.09
Surgical duration (min)	370±96.48

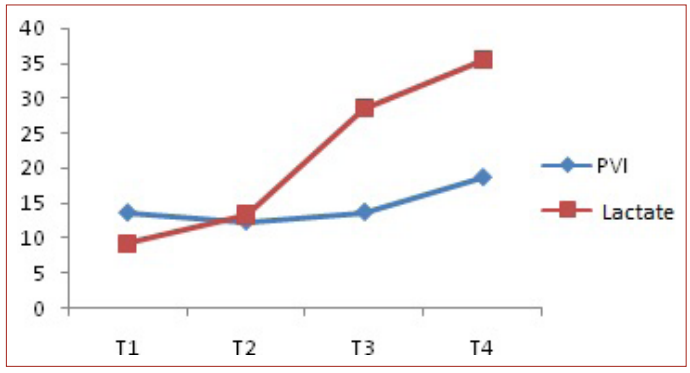

Figure 1. Start of surgery (T1), 1st hour of surgery (T2), End of surgery (T3), 3rd hour postoperatively (T4) change in PVI and lactate values over time.

Na, BUN, Creatinine values of donors are given in Table 3. The bleeding amounts of the donors and the amounts of crystalloid and colloid given are given in Table 4.

Hemodynamic data of the cases are given in Table 5. The liver graft weight of the donors, ICU and hospital stay conditions are indicated in Table 6.

Discussion

In our study aimed at comparing the correlation between PVI and lactate levels in kidney transplant donors, a correlation was found between the PVI measured at the end of the surgery (T3) and the lactate values. However, no correlation was detected between the PVI and lactate values measured at the beginning of the surgery (T1), at the first hour of the surgery (T2), and at the third hour postoperatively (T4).

Since intravenous lactate-containing solutions (such as Ringer's Lactate) can alter blood lactate levels during the operation,[2] they were not used in our study. Lactate levels provide an indirect yet sensitive measurement of organ perfusion. Lactate is clearly associated with energy deficiencies and tissue hypoxia due to intravascular volume adequacy and the redistribution of blood flow. Perioperative blood lactate levels can affect postoperative complications and the average length of hospital stay.[4] Hyperlactatemia is associated with morbidity and mortality risks in patients with liver failure.[2] Due to changes in hepatic blood flow and lactate metabolic capacity after surgery, lactate concentration tends to increase following donor hepatectomy. Increases in hepatic blood flow and lactate concentration may help predict the prognosis of patients undergoing liver resection due to hepatoma. However, the relationship between the liver profile post-liver resection and hyperlactatemia is less well understood.[2]

Shin et al.[2] assessing graft function in their study comparing changes in lactate and prothrombin time between cadaveric and living donor liver transplants during the early

Table 2. Donors' ALT, AST, Lactate values (mean±SD)

	T1	T2	T3	T4	T5
ALT	16.29±9.27	43.70±27.12	127.35±170.58	161.31±197.83	229.92±228.94
	p<0.001*	p<0.001*	p<0.001*	p<0.001*	
AST	20.96±8.00	45.86±23.48	130.09±145.67	169.92±189.59	201.82±171.33
	p<0.001*	p<0.001*	p<0.001*	p<0.001*	
Lactate	9.23±4.01	13.28±6.38	28.51±10.18	35.42±14.44	12.28±5.59
	p<0.001*	p<0.001*	p<0.001*	p<0.001*	

*p<0.05 Change relative to T1. (T1) Start of surgery, (T2) 1st hour of surgery, (T3) End of surgery, (T4) 3rd hour postoperatively, (T5) 24th hour postoperatively.

Table 3. Donors' Na, BUN, Creatinine values (mean±SD)

	T1	T2	T3	T4	T5
Na	138.62±2.35	138.27±2.39	140.39±2.27	138.68±2.44	135.92±2.55
	p=0.202	p<0.001*	p=0.963	p<0.001*	
BUN	13.11±3.89	13.03±3.77	13.23±3.66	12.60±3.75	11.84±3.89
	p=0.955	p=0.480	p=0.073	p<0.001*	
Creatinine	0.67±0.09	0.68±0.09	0.71±0.13	0.75±0.14	0.63±0.10
	p=0.092	p<0.001*	p<0.001*	p<0.001*	

*p<0.05 Change relative to T1. (T1) Start of surgery, (T2) 1st hour of surgery, (T3) End of surgery, (T4) 3rd hour postoperatively, (T5) 24th hour postoperatively.

Table 4. Donors' urine and bleeding volumes, crystalloid and colloid volumes administered (mean±SD)

	T1	T2	T3	T4
Urine	150.19±181.99	126.27±152.61	477.84±364.79	243.13±160.64
	p=0.522	p<0.001*	p<0.001*	
Bleeding	0.98±7.00	63.23±33.64	260.88±91.49	18.43±20.06
	p<0.001*	p<0.001*	p<0.001*	
Crystalloid	273.52±227.23	195.29±256.84	1137.05±660.63	462.78±173.79
	p=0.121	p<0.001*	p<0.001*	
Colloid	0±0	9.80±70.01	378.43±274.09	1.96±14.00
	p=0.317	p<0.001*	p=0.317	

*p<0.05 Change relative to T1. (T1) Start of surgery, (T2) 1st hour of surgery, (T3) End of surgery, (T4) 3rd hour postoperatively.

reperfusion period, reported that lactate and INR values normalized more rapidly in cadaveric recipients within one hour post-reperfusion. They attributed this to the larger size of the grafts in cadaveric cases. In contrast, our study focused on liver donors.

M. Feissel et al.[5] found that the PVI obtained automatically by the pulse oximeter is a reliable indicator of fluid responsiveness. It has been published that it can noninvasively predict fluid responsiveness in mechanically ventilated patients undergoing non-cardiac surgery under general anesthesia,[6] in mechanically ventilated patients undergoing major surgery,[1] in mechanically ventilated patients in the ICU,[7] in patients after cardiopulmonary bypass,[8] and in mechanically ventilated patients in early-phase septic shock.[9] Additionally, Tsuchiya et al.[10] reported that PVI could predict decreases in mean arterial pressure during anesthesia induction with propofol, suggesting that this measurement could be useful in identifying the occurrence of severe hypotension in high-risk patients during anesthesia induction.

Wenqing Lu et al.[11] reported that in patients undergoing mechanical ventilation under general anesthesia, extracellular fluid volume is beneficial when using noninvasive continuous hemodynamic monitoring with PVI. In line with these studies, our findings showed that PVI values were correlated with the CVP values of the patients.

Forget et al.[3] demonstrated that when fluid management was guided by PVI in patients undergoing major abdomi-

Table 5. Donors' SpO_2 and Heart Rate SAP, DAP, MAP, CVP, PVI, PI values (mean±SD)

	T1	T2	T3	T4
SpO_2	99.07±1.33	99.35±1.09	99.62±0.91	97.94±1.89
	p=0.094	p<0.001*	p<0.001*	
Heart rate	84.52±20.13	80.92±14.17	97.88±12.44	98.41±15.88
	p=0.249	p<0.001*	p<0.001*	
SAP	109.52±18.36	109.96±16.09	111.09±16.38	142.00±20.96
	p=0.656	p=0.459	p<0.001*	
DAP	71.01±14.06	67.43±9.30	67.52±14.80	86.03±12.50
	p=0.170	p=0.123	p<0.001*	
MAP	85.47±16.19	83.58±12.09	83.21±14.90	103.92±13.90
	p=0.623	p=0.367	p<0.001*	
CVP	10.19±3.38	10.27±3.31	10.27±3.81	7.62±2.68
	p=1.00	p=0.754	p<0.001*	
PVI	13.59±8.43	12.29±5.61	13.68±6.75	18.74±9.42
	p=0.746	p=0.577	p<0.001*	
PI	4.74±3.22	2.83±2.57	1.27±1.67	3.46±2.31
	p<0.001*	p<0.001*	p<0.001*	

*p<0.05 Change relative to T1. (T1) Start of surgery, (T2) 1st hour of surgery, (T3) End of surgery, (T4) 3rd hour postoperatively.

Table 6. Donor liver graft weight, length of stay in the ICU and hospital (mean±SD)

KC graft weight (g)	736.56±149.30
Stay in ICU (days)	3.58±2.88
Hospital stay (days)	8.17±4.31

nal surgery, the volume of intraoperative fluid infusion significantly decreased, and both intraoperative and postoperative lactate levels showed a marked reduction during and 48 hours after surgery.

In our study, the lack of correlation between PVI and lactate levels at certain periods of the operation may depend on the type of surgery performed. This is because over 99% of lactate is cleared through the first-pass metabolism in a healthy liver,[12] and hepatocyte damage during liver resection may disrupt this metabolism. Therefore, even with adequate intravascular volume, lactate levels may still rise in patients.

AST and ALT, being hepatic cytoplasmic enzymes, are released into circulation due to cell membrane damage during parenchymal resection, leading to elevations in liver enzyme levels afterward. However, the extent to which this increase persists following human liver resection has not been clearly documented. In our study, we observed a rise in ALT and AST levels at the first hour of surgery (T2), at the end of the procedure (T3), and at three hours postoperatively (T4) compared to baseline at the start of surgery (T1).

Limitations

Our study had several limitations. First, it was conducted at a single center. In liver donors on fluid-restricted regimens, PVI and lactate changes may not be sufficient for target organ oxygenation. We believe that analyzing target tissue mediators would yield better results.

Conclusion

We found that the lactate levels at the end of the surgery in liver transplant donors were consistent with PVI values. Although hepatic blood flow may be adequate, we believe that hepatocyte damage occurring during liver surgeries could influence lactate metabolism. We also think that further studies are needed to investigate the correlation between PVI and lactate levels in other types of surgeries.

Disclosures

Ethics Committee Approval: This study was conducted after obtaining approval from the Malatya Clinical Research Ethics Committee (2015/121) and patient consent, involving living donors for liver transplantation undergoing right hepatectomy, classified as ASA I-II and aged between 18-55 years.

Peer-review: Externally peer-reviewed.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data that support the findings of this study are not openly available for reasons of sensitivity but are available from the corresponding author upon.

Authorship Contributions: Concept – M.S.; Design – M.S., N.G.; Supervision – M.S., F.K., N.G.; Materials – M.S., F.K.; Data collection or processing – M.S., F.K., N.G.; Analysis and/or interpretation – M.S., F.K.; Literature search – M.S., N.G.; Writing – M.S., F.K., N.G.; Critical review – M.S., N.G.

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