The Effect of Intra-Operative Plethysmography Variability Index-guided Fluid Therapy on Serum Lactate Levels; A Randomized Double-blinded Clinical Trial

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ABSTRACT

Background: Goal-directed fluid therapy may improve perioperative fluid management. This study aimed to evaluate the effects of Pleth variability index (PVI)-guided fluid therapy on changes in intraoperative serum lactate levels in comparison with liberal fluid therapy.

Methods: This study was a randomized double-blinded clinical trial that was conducted in the operating room of a university hospital. Inclusion criteria comprised patients aged 18–60 years and classified as American Society of Anesthesiologists physical status class I and II, who were candidates for elective thyroidectomy. In total, 44 patients meeting the inclusion criteria were enrolled in the study and randomly assigned to two groups: the liberal and PVI groups. In both groups, 5 mL/kg bolus of normal saline was infused prior to the anesthesia induction. In the PVI group, 100 mL bolus of normal saline was administered every 5 min if the PVI remained >13% during the operation. In the liberal group, continuous crystalloid infusion (5–6 mL/kg/h) was administered throughout the surgery. Arterial blood samples were taken, and serum lactate levels were measured following anesthesia induction and just before tracheal extubation.

Results: In the PVI group, mean serum lactate decreased at the end of the surgery, with a difference of −0.6 ± 0.13 mmol/L, whereas it increased in the liberal group (0.070 ± 0.3, P<0.05).

Conclusion: In conclusion, we found that using intraoperative PVI-guided fluid therapy could decrease serum lactate levels and total fluid administration compared to the liberal method.

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Fluid therapy is an important aspect of the perioperative period and a major challenge for anesthesiologists. Adequate intravascular volume is clearly one of the keys to preserving cardiac output and organ perfusion, thus preventing tissue hypoxia. There is a lack of strong guidance and evidence regarding the optimal approach to fluid therapy, particularly during the perioperative period [1] and uncertainty in determining and assessing adequate intravascular volume can be frustrating [2]. Traditionally, liberal intra-operative fluid administrations have been used for many years. Some authors have proposed restrictive fluid therapy during surgery. Recently, goal-directed fluid therapy has led to better patients’ outcome [3–4].
Cardiac filling pressures have been used for many years to guide intravascular volume replacement; however, it is now clear that this method does not reliably predict fluid responsiveness [5]. Recent evidence supports individually tailored goal-directed fluid therapy (GDFT) based on hemodynamic parameters in patients undergoing mechanical ventilation [6-7]. Respiratory variations in pulse oximeter plethysmographic (ΔPOP) waveform amplitude assist in predicting fluid responsiveness and are associated with arterial pulse pressure (ΔPP) variations [8].

Pleth variability index (PVI) collects data automatically and continuously and calculates respiratory variations in the photoplethysmogram from data collected via a pulse oximetry sensor. PVI is visually correlated with ΔPOP but uses a different algorithm. PVI is a measure of dynamic changes in the perfusion index (PI) that occur during the respiratory cycle [8-9].

Serum lactate level has been used as an indicator of peripheral organ perfusion. It was shown that intraoperatively, a raised in serum lactate level accompanies poor prognosis [10-11]. The present study was designed to compare PVI-guided intraoperative fluid therapy’s serum lactate level with a liberal approach to fluid therapy. We hypothesized that PVI-guided serum therapy could change serum lactate levels. Changes in intraoperative serum lactate levels were primary outcome measures, and the amount of fluid administered was a secondary outcome measure.

**Methods**

A randomized double-blinded clinical trial comprising 44 patients meeting the inclusion criteria was conducted, following approval of the Ethics Committee of Tehran University of Medical Sciences and after obtaining written informed consent. (Clinical Trial registration number: IRCT20150929024268N3) Inclusion criteria comprised of patients aged 18–60 years with BMI<29, and classified as American Society of Anesthesiologists (ASA) physical status I and II, who were candidates for elective thyroidectomy, with no cardiac arrhythmia or any documented lung diseases. Exclusion criteria comprised patients who either experienced intraoperative dysrhythmias or heart rate (HR) more than 90/min for>10 minutes, had intraoperative bleeding over 300 mL or a PI value less than 1, or whose duration of surgery was>3 hours. Standard monitoring, including ECG, Non-Invasive Blood Pressure, HR, and SpO2, was initiated for all patients on arrival to the operating room. Based on previously prepared computer-based randomization, patients were randomly enrolled in either the PVI group or the liberal group.

**PVI monitoring and perioperative fluid therapy**

A B9 pulse oximeter (Pooyandegan Saadat) was placed on the patient’s index finger for continuous PVI monitoring. Propofol (2 mg/kg) plus fentanyl (2 µg/kg) was used for induction of anesthesia, and atracurium (0.5 mg/kg) was used to facilitate tracheal intubation. Isoflurane was used for anesthesia maintenance following tracheal intubation, after which a 20-gauge catheter was inserted in the radial artery of the non-dominant hand. The ventilator was set to maintain normocapnia (end-tidal carbon dioxide partial pressure 4.7–5.3 kPa).

In the PVI group, 5 mL/kg bolus of normal saline was administered prior to anesthesia induction, and continuous crystalloid infusion using 2 mL/kg/h of normal saline was administered throughout the surgery. If the PVI was>13% for 5 min, a 100 mL bolus of normal saline was administered and repeated every 5 min if the PVI remained>13%. If the PVI dropped to <13%, the continuous normal saline infusion was terminated until the PVI reached 13%.

In the liberal group, 5 mL/kg bolus of normal saline was administered prior to anesthesia induction and continuous crystalloid infusion (5–6 mL/kg/h) was administered throughout the surgery. Arterial blood samples were taken from all patients before anesthesia induction and also at the end of the surgery just before tracheal extubation.

**Statistical analyses**

The distribution of quantitative data was analyzed using the Kolmogorov-Smirnov test following a normal distribution. Age, weight, intraoperative fluid usage, and changes in serum lactate levels were compared in groups using the independent t-test. The ASA physical class and sex were compared using the chi-square test. Two-tailed P<0.05 was considered statistically significant.

**Results**

Overall, 44 patients were eligible to participate in the study (Figure 1); Basic patient characteristics are presented in table 1, in which there was no significant difference between the two groups. No patient required any vasoactive drugs during surgery.

There was no statistically significant difference in the baseline mean serum lactate levels at the beginning of surgery. Intraoperative fluid administration of total crystalloids was significantly less in the PVI group (930.5±110.3 mL) than in the liberal group (1660.5±295.3 mL) (P<0.05). Changes in serum lactate levels at the end of surgery decreased (~0.6±0.08 mmol/L) in the PVI group and increased in the liberal group (0.07±0.3 mmol/L) (P=0.02). Urinary output didn’t differ between the liberal group (120±10.2 mL) and the PVI group (113±9.2 mL) (P=0.34) (see table 2). No surgical or
anesthesia-related complications were reported in any patient.

**Table 1 - Patient demographic characteristics.**

|                      | PVI group | Liberal group | P value |
|----------------------|-----------|---------------|---------|
| Age a (years)        | 29.6      | 31.1          | 0.15    |
| Weight a (kg)        | 72.3      | 75.0          | 0.12    |
| Duration of Surgery a (min) | 168.1    | 172.4         | 0.94    |
| Sex (Female/Male)    | 10/12     | 13/9          | 0.77    |
| ASA (I/II)           | 17/5      | 19/3          | 0.93    |

* Data are presented as mean
*aThere was no significant difference in groups
PVI= Pleth variability index, ASA= American Society of Anaesthesiologists physical status classification

Table 2 - Intra-operative fluid volume, serum lactate level changes and intra-operative urinary output between groups.

|                      | PVI group     | Liberal group |
|----------------------|---------------|---------------|
| Intra-operative fluid (mL) * | 930.5 ± 110.3 | 1660.5 ± 295.3 |
| Changes in serum lactate levels during surgery (mmol/L) * | −0.60 ± 0.07 | 0.07 ± 0.3 |
| Intra-operative urinary output(mL) a | 113 ± 9.2 | 120 ± 10.2 |

* Data are presented as mean ± SD
*a P value < 0.05
*aThere was no significant difference in groups
PVI= Pleth variability index

**Discussion**

In the present study, the effect of PVI-guided intraoperative fluid therapy was compared with traditional liberal fluid administration with respect to changes in serum lactate levels before and after surgery as well as the volume of intraoperative fluid administration. We showed that PVI-guided intraoperative fluid therapy reduced both serum lactate levels and fluid requirements during thyroidectomy.

Perioperative fluid therapy has been of interest to researchers for many years. Distinct approaches to
different endpoints have been proposed to improve patient outcomes after major non-cardiac surgery through better optimization of perioperative fluid therapy [12].

Previously, Forget et al. [13] studied the effect of PVI on serum lactate levels, and although our results partially agree with theirs, interestingly, unlike their study, the lactate levels did not increase in the PVI group in our study, and a decrease in lactate levels in the PVI group was observed, which could be attributed to the differences in the duration and type of surgery performed. Additionally, unlike the study of Forget et al., [13] our study utilized a type of surgery that was associated with the least anticipated hemodynamic changes, as most confounding factors such as tachycardia and arrhythmias may alter the results of PVI readings.

Similar results were observed in another study showing that PVI-based goal-directed perioperative fluid management can reduce the levels of intraoperative fluids, particularly those of crystalloids and blood lactate, in patients under combined general/epidural anesthesia; [14] however, the mentioned study used a different type of surgery, a different definition of liberal fluid therapy, and vasopressor infusions.

Despite these favorable results, PVI and Doppler-based stroke volume optimizations were poorly correlated. [15] It should be noted that a small sample size of patients was an important shortcoming of the above studies.

A positive correlation between PVI and systolic pressure variation as a measure of fluid responsiveness has been demonstrated in critically ill patients; however, more studies are required in the intensive care unit setting, particularly because some studies have concluded that early GDFT does not improve outcomes in critically ill patients with septic shock [16-18].

The applicability of PVI may be limited by potential interference from several factors such as spontaneous breathing activity, arrhythmia, tachycardia, low peripheral perfusion, or use of vasopressors. [19, 20] As stated above, various positive aspects of GDFT have been proposed and studied such as reduction of the levels of intraoperative fluids, reduction of serum lactate and improvement on the outcome of critically ill patients with septic shock.

Although current evidence mostly demonstrates that the pros of GDFT outweigh the cons, there is no strong agreement regarding the most effective goals or the most appropriate monitoring device for guiding perioperative fluid therapy, mainly because many confounding factors must be accounted for during the literature review of GDFT. Important confounding factors include the definitions used for standard fluid therapy and GDFT, which vary in different studies. Other factors that differ in studies include triggers for fluid bolus administration, technologies used, defined goals for GDFT, or GDFT protocols [21].

Other issues that should be considered when implementing GDFT protocols are the availability of the technology and cost-effectiveness of GDFT. Although it has been proposed that GDFT may save medical care costs and gain quality-adjusted life-years compared with those of traditional fluid treatments, [22, 23] the devices used during GDFT are expensive and the routine anesthesia monitoring device is rendered due to its price, particularly in developing countries. As predicted, intravascular fluid shift during thyroidectomy is not usually significant; consequently, the lactate changes during this type of surgery may not be clinically important. Nevertheless, positive changes in lactate levels in liberal fluid therapy and negative changes during PVI-based fluid therapy illustrate the significance of our study. Furthermore, less intraoperative fluid usage in PVI-directed fluid therapy is a valuable finding.

In the present study of ASA class I and II patients, we recommend that the validity of PVI be studied more thoroughly in more critical patients and children as well as in patients requiring surgeries with more anticipated intravascular blood shift.

**Conclusion**

In conclusion, PVI-based intra-operative fluid therapy reduces serum lactate level as well as intraoperative fluid administration.

**References**

[1] Pearse RM, Ackland GL. Perioperative fluid therapy. BMJ. 2012; 344:e2865.

[2] Kudnig ST, Mama K. Perioperative fluid therapy. J Am Vet Med Assoc. 2002; 221(8):1112-21.

[3] Sulzer JK, Sastry AV, Meyer LM, Cochran A, Buhrman WC, Baker EH, et al. The impact of intraoperative goal-directed fluid therapy on complications after pancreaticoduodenectomy. Ann Med Surg (Lond). 2018; 36:23-8.

[4] Weinberg L, Wong D, Karalapillai D, Pearce B, Tan CO, Tay S, et al. The impact of fluid intervention on complications and length of hospital stay after pancreaticoduodenectomy (Whipple’s procedure). BMC anesthesiol. 2014; 14(1):35.

[5] Marik PE, Cavallazzi R. Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. Critical care medicine. 2013; 41(7):1774-81.

[6] Rollins KE, Lobo DN. Intraoperative goal-directed fluid therapy in elective major abdominal surgery: a meta-analysis of randomized controlled trials. Anna surg. 2016; 263(3):465-76.

[7] Waldron NH, Miller TE, Gan TJ. Perioperative goal-directed therapy. J Cardiothorac Vasc Anesth. 2014; 28(6):1635-41.

[8] Cannesson M, Desebbe O, Rosamel P, Delannoy B,
Robin J, Bastien O, et al. Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. Br J Anaesth. 2008; 101(2):200-6.

[9] Cannesson M, Delannoy B, Morand A, Rosamel P, Attot Y, Bastien O, et al. Does the pleth variability index indicate the respiratory-induced variation in the plethysmogram and arterial pressure waveforms? Anesth Analg. 2008;106(4):1189-94.

[10] Munoz R, Laussen PC, Palacio G, Zienko L, Piercey G, Wessel DL. Changes in whole blood lactate levels during cardiopulmonary bypass for surgery for congenital cardiac disease: an early indicator of morbidity and mortality. J Thorac Cardiovasc Surg. 2000; 119(1):155-62.

[11] Kanazawa T, Egi M, Shimizu K, Toda Y, Iwasaki T, Morimatsu H. Intraoperative change of lactate level is associated with postoperative outcomes in pediatric cardiac surgery patients: retrospective observational study. BMC Anesthesiol. 2015; 15(1):29.

[12] Thacker JK, Mountford WK, Ernst FR, Krukas MR, Mythen MMG. Perioperative fluid utilization variability and association with outcomes. Ann surg. 2016; 263(3):502-10.

[13] Forget P, Lois F, De Kock M. Goal-directed fluid management based on the pulse oximeter–derived pleth variability index reduces lactate levels and improves fluid management. Anesth Analg. 2010;111(4):910-4.

[14] Yu Y, Dong J, Xu Z, Shen H, Zheng J. Pleth variability index-directed fluid management in abdominal surgery under combined general and epidural anesthesia. J Clin Monit Comput. 2015; 29(1):47-52.

[15] Bahlmann H, Hahn R, Nilsson L. Agreement between Pleth Variability Index and oesophageal Doppler to predict fluid responsiveness. Acta Anaesthesiol Scand. 2016; 60(2):183-92.

[16] Dharn D, Datta R, Gupta N, editors. Correlation Between Plethysmographic Variability Index and Systolic Pressure Variation as an Indicator for Fluid Responsiveness in Hypotensive Patients on Ventilator in The Intensive Care Unit of a Tertiary Care Hospital. Anesthesia and Analgesia; 2016: Lippincott Williams & Wilkins Two Commerce Sq, 2001 Market St, Philadelphia ….

[17] Investigators A, Group tACT. Goal-directed resuscitation for patients with early septic shock. N Engl J Med. 2014; 371(16):1496-506.

[18] Mouncey PR, Osborn TM, Power GS, Harrison DA, Sadique MZ, Grieve RD, et al. Trial of early, goal-directed resuscitation for septic shock. N Engl J Med. 2015;372(14):1301-11.

[19] Philipp L, Closhen D, Fukui K, Schmidtmann I, Ikeda M, Pestel G. Non-invasive assessment of functional haemodynamic parameters: 3AP4-4. Eur J Anaesthesiol. 2011; 28:36.

[20] Monnet X, Guerin L, Jozwiak M, Bataille A, Julien F, Richard C, et al. Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine. Br J Anaesth. 2012; 110(2):207-13.

[21] Joshi GP, Kehlet H. CON: perioperative goal-directed fluid therapy is an essential element of an enhanced recovery protocol? Anesth Analg. 2016; 122(5):1261-3.

[22] Bartha E, Davidson T, Hommel K-G, Carlsson P, Kalman S. Cost-effectiveness Analysis of Goal-directed Hemodynamic Treatment of Elderly Hip Fracture PatientsBeforeClinical Research Starts. Anesthesiology. Anesthesiology. 2012; 117(3):519-30.

[23] Ebm C, Cecconi M, Sutton L, Rhodes A. A cost-effectiveness analysis of postoperative goal-directed therapy for high-risk surgical patients. Crit Care Med. 2014; 42(5):1194-203.