Section Editor: **Dwayne Westenskow**

Goal-Directed Fluid Management Based on the Pulse Oximeter–Derived Pleth Variability Index Reduces Lactate Levels and Improves Fluid Management

Patrice Forget, MD,* Fernande Lois, MD,* and Marc de Kock, MD, PhD*

BACKGROUND: Dynamic variables predict fluid responsiveness and may improve fluid management during surgery. We investigated whether displaying the variability in the pulse oximeter plethysmogram (pleth variability index; PVI) would guide intraoperative fluid management and improve circulation as assessed by lactate levels.

METHODS: Eighty-two patients scheduled for major abdominal surgery were randomized into 2 groups to compare intraoperative PVI-directed fluid management (PVI group) versus standard care (control group). After the induction of general anesthesia, the PVI group received a 500-mL crystalloid bolus and a crystalloid infusion of 2 mL · kg^{-1} · h^{-1}. Colloids of 250 mL were administered if the PVI was >13%. Vasoactive drug support was given to maintain the mean arterial blood pressure above 65 mm Hg. In the control group, an infusion of 500 mL of crystalloids was followed by fluid management on the basis of fluid challenges and their effects on mean arterial blood and central venous pressure. Perioperative lactate levels, hemodynamic data, and postoperative complications were recorded prospectively.

RESULTS: Intraoperative crystalloids and total volume infused were significantly lower in the goal-directed PVI group. Lactate levels were significantly lower in the PVI group during surgery and 48 hours after surgery ($P < 0.05$).

CONCLUSIONS: PVI-based goal-directed fluid management reduced the volume of intraoperative fluid infused and reduced intraoperative and postoperative lactate levels. (Anesth Analg 2010; 111:910–4)

Hypovolemia occurs frequently in the operating room. Its diagnosis remains difficult, but assessment of the adequacy of intravascular volume is of prime importance to maintain cardiac output and thus avoid tissue hypoxia. In 1 meta-analysis the authors observed that perioperative hemodynamic optimization reduced mortality.[1]

For many years, cardiac filling pressures were used to guide intravascular volume therapy. This, however, is not a reliable predictor of fluid responsiveness.[2] Dynamic variables (indices evaluating the response to a cyclic preload variation) provide a better prediction of fluid responsiveness.[3] Among these, the arterial pulse pressure variation induced by mechanical ventilation has been demonstrated as one of the best tools to guide volume therapy.[3] Lopes et al. showed an improvement in postoperative outcome after high-risk surgery when the pulse pressure variation was used to guide intraoperative fluid therapy.[4] Natalini et al. and Cannesson et al. demonstrated that respiratory variations in the amplitude of the pulse oximeter plethysmographic waveform and in the pulse pressure both predict fluid responsiveness.[5–8] Zimmerman et al. showed that pleth variability index (PVI) predicts fluid responsiveness as accurately as does stroke volume variation.[9] Nevertheless, it remains unknown whether the optimization of the plethysmogram variability that occurs intraoperatively improves fluid management and circulation. To investigate this, we used a pulse oximeter to continuously monitor the PVI.[7] We measured the impact of PVI-based goal-directed fluid management on perioperative lactate levels.

METHODS

After approval of the Ethics Committee of St.-Luc Hospital (Brussels, Belgium) (www.clinicaltrials.gov, no. NCT00816153), and after obtaining written informed consent, a pilot study including 20 patients (10 per group) was conducted for the power analysis. Results showed an improvement of 20% of the primary outcome (whole blood lactate levels) with the use of the PVI. A sample size of 37 patients per group was calculated for a 0.05 difference (2-sided) with a power of 80%.

Between May and September 2008, we obtained written informed consent from 86 patients who met the inclusion criteria: older than 18 years and the absence of cardiac arrhythmias, ultrasonographic cardiac ejection fraction <30%, lung pathology prohibiting mechanical ventilation with tidal volumes larger than 6 mL · kg^{-1}, and kidney dialysis. They were scheduled for esophagectomy, gastric resection/suture, hepatectomy, pancreatectomy, or intestinal and colorectal surgeries. Patients were randomized to either the PVI group or the control group.

Heart rate, arterial blood pressure, oxygen saturation, inhaled gas concentrations, and temperature were measured

From the *Department of Anesthesiology, Université catholique de Louvain, St.-Luc Hospital, Brussels, Belgium.

Accepted for publication May 27, 2010.

Address correspondence and reprint requests to Patrice Forget, Department of Anesthesiology, St.-Luc Hospital, av. Hippocrate 10–1821, 1200 Brussels, Belgium. Address e-mail to forgetpatrice@yahoo.fr.

DOI: 10.1213/ANE.0b013e3181eb624f

continuously by a Datex S/5 monitor (Datex Ohmeda®, GE Healthcare). A Masimo Set version V7.1.1.5 pulse oximeter (Masimo Co., Irvine, California) was placed on the patient's finger for the continuous monitoring of PVI. A 20-G radial arterial catheter and a central venous access catheter were inserted at the end of the induction phase. A thoracic epidural catheter was placed before the induction of the general anesthesia. Anesthesia was induced with propofol 2 to 4 mg · kg^{-1} and atracurium or rocuronium 0.4 to 0.6 mg · kg^{-1} and maintained with sevoflurane or desflurane. The lungs were ventilated with 6 to 8 mL · kg^{-1} of tidal volume, I:E = 1:2. The frequency was set to maintain normocapnia (P_{ACO_2} target = 40 ± 3 mm Hg).

In the PVI group, 500 mL of crystalloids (NaCl 0.9% or P-Lyte®, Baxter) was infused during induction, followed by a 2 mL · kg^{-1} · h^{-1} continuous infusion. If PVI was higher than 13% for >5 minutes, we gave a 250-mL bolus of colloid (hydroxyethyl starch 6%, Voluven®, Fresenius Kabi). The dose was repeated every 5 minutes if PVI was still higher than 13%. Norepinephrine was given as needed to maintain a mean arterial blood pressure >65 mm Hg.

In the control group, 500 mL of crystalloids was infused during induction, followed by a continuous infusion of crystalloids (4 to 8 mL · kg^{-1} · h^{-1}). A bolus of colloids was given if acute blood loss of >50 mL occurred, if the mean arterial blood pressure decreased below 65 mm Hg, or if the central venous pressure decreased below 6 mm Hg. A repeat bolus was given after waiting 5 minutes if any one of the criteria was met. If the mean arterial blood pressure decreased below 65 mm Hg and remained unresponsive to fluids, norepinephrine was given to maintain the mean arterial blood pressure above 65 mm Hg.

Arterial blood samples were taken at the time of skin incision, each hour during surgery and 6, 12, 18, 24, 36, and 48 hours after the end of surgery. The lactate concentration was measured using an ABL 620 analyzer (Radiometer, Copenhagen, Denmark). Serum creatinine concentrations were measured 24 and 48 hours after surgery. The anesthesiologist identified and recorded instances of intraoperative hypotension (systolic blood pressure 20% below the value measured the day before surgery, while the patient was resting quietly for at least 15 minutes) and oliguria (urine output <0.5 mL · kg^{-1} for >2 hours).

During the first 30 days after surgery, a blinded postoperative care team member identified, collected, and recorded instances of postoperative infection, pulmonary embolism, acute myocardial infarction, acute lung injury/acute respiratory distress syndrome, pulmonary edema, arrhythmia, stroke, cardiac arrest, coagulopathy (platelets <100,000 μL^{-1}, international normalized ratio >2), hepatic dysfunction, nausea or vomiting necessitating treatment, upper digestive hemorrhage, leakage of anastomosis, and mortality.

Statistical Analysis

Data were analyzed by comparing the patients in the PVI group with those in the control group using a modified intention-to-treat analysis (4 patients were excluded after the randomization for intraoperative arrhythmia or cancellation of the surgery, 2 per group; Fig. 1). The remaining 82 patients completed the protocol and were analyzed. No patient met abandon criteria.

Student's *t* test was used to compare normally distributed continuous variables and χ^2 for categorical variables. Homogeneity of variances was verified by the Levene's test. A *P* value <0.05 was considered statistically significant. Data are expressed as mean (±SD), mean [95% confidence interval], or number (percentage). STATISTICA (data analysis software system) version 7 (Statsoft, Inc., 2004) was used for all analyses.

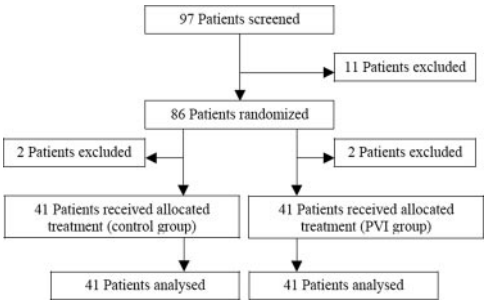

Figure 1. Trial profile. PVI group: pleth variability index–guided fluid management.

Table 1. Preoperative Characteristics, Incidence of Chronic Diseases, Type and Duration of Surgery and Anesthesia, Use of Epidural Analgesia in the Pleth Variability Index (PVI) Group (PVI-Guided Fluid Management) and Control Group

	PVI group (*N* = 41)	Control group (*N* = 41)
Age (years)	59 ± 14	61 ± 12
Weight (kg)	71 ± 15	68 ± 16
Height (cm)	169 ± 9	170 ± 9
Sex (female/male)	16/25 (39/61)	16/25 (39/61)
ASA score		
2	22 (54)	22 (54)
3	19 (46)	19 (46)
Chronic diseases		
Cirrhosis	3 (7)	0 (0)
Chronic obstructive pulmonary disease	2 (5)	2 (5)
Hypertension	18 (44)	13 (32)
Peripheral vascular disease	7 (17)	7 (17)
Coronary artery disease	5 (12)	2 (5)
Other cardiomyopathy	2 (5)	4 (10)
Diabetes mellitus	4 (10)	2 (5)
Preoperative biological values		
Hemoglobin (g · dL^{-1})	12.5 ± 2	12.7 ± 2
Serum creatinine (mg · dL^{-1})	0.96 ± 0.2	0.97 ± 0.3
Type of surgery		
Upper gastrointestinal	7 (17)	5 (12)
Hepato-biliary	11 (27)	15 (37)
Lower gastrointestinal	24 (59)	22 (54)
Laparoscopic approach	5 (12)	5 (12)
Duration of surgery (minutes)	295 ± 125	301 ± 154
Duration of anesthesia (minutes)	346 ± 125	356 ± 158
Epidural analgesia	33 (81)	29 (71)

One patient per group had two types of surgery. Data are presented as mean ± SD or number (%). $P > 0.05$ for all the data.

RESULTS

Table 1 lists the patients' history and surgery. There were no preoperative differences between the goal-directed fluid

Table 2. Fluids Administered, Blood Loss, Hemodynamic Status, Physiologic Status, and Renal Function During and After Surgery in the Pleth Variability Index (PVI) Group (PVI-Guided Fluid Management) and in the Control Group

	PVI group (*N* = 41)	Control group (*N* = 41)	*P* value
Intraoperative fluids (mL)			
Crystalloids	1363 [1185–1540]	1815 [1568–2064]	**0.004**
Colloids	890 [709–1072]	1003 [779–1227]	0.43
Blood products	141 [53–230]	99 [20–179]	0.48
Total of intraoperative fluids	2394 [2097–2692]	2918 [2478–3358]	**0.049**
Blood losses	349 [230–468]	440 [242–637]	0.43
Postoperative fluids (24 hours)			
Crystalloids	3107 [2760–3454]	3516 [3009–4024]	0.17
Colloids	268 [126–409]	358 [175–540]	0.43
Blood products	8 [−8–25]	44 [−45–133]	0.41
Lactate levels (mMol · L^{-1})			
Maximum intraoperative	1.2 [1–1.4]	1.6 [1.2–2]	**0.04**
At 24 hours	1.4 [1.3–1.5]	1.8 [1.5–2.1]	**0.02**
At 48 hours	1.2 [1–1.3]	1.4 [1.2–1.5]	**0.03**
Lactate levels >1.7 mMol · L^{-1}			
Intraoperatively	7 (17)	4 (10)	0.33
At 24 hours	2 (5)	28 (68)	**<0.0001**
At 48 hours	0	8 (20)	**0.003**
Lactate levels >5 mMol · L^{-1}			
Intraoperatively	0	1 (2)	0.31
At 24 hours	0	1 (2)	0.31
At 48 hours	0	1 (2)	0.31
Intraoperative hypotension	22 (54)	28 (68)	0.17
Continuous infusion of norepinephrine			
Intraoperative	9 (22)	9 (22)	1.0
At 24 hours	3 (7)	1 (2)	0.31
Renal function diuresis			
Intraoperative oliguria	13 (32)	17 (42)	0.34
Postoperative oliguria (24 hours)	3 (8)	3 (8)	0.97
Serum creatinine (mg · dL^{-1})			
At 24 hours	1.01 [0.9–1.1]	1.12 [0.9–1.3]	0.32
At 48 hours	0.91 [0.8–1]	1.09 [0.9–1.3]	0.11
Initiation of dialysis	1 (2)	0 (0)	0.32

Lactate levels: normal value 0.9–1.7 mMol · L^{-1}. Oliguria was defined as a urinary output <0.5 mL · kg^{-1} for more than 2 hours. Data are presented as mean [95% confidence interval] or number (%).

$P < 0.05$ was considered as statistically significant (boldface numerical entries).

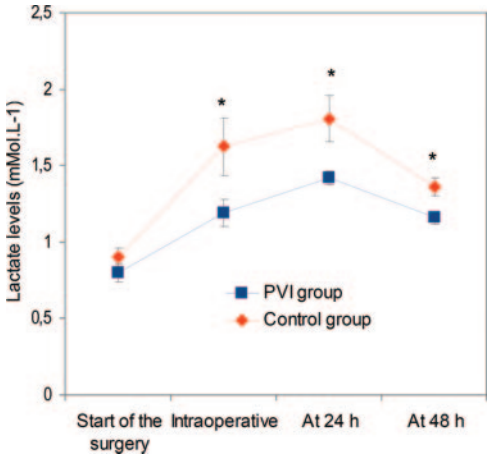

Figure 2. Lactate levels during and after surgery in the pleth variability index (PVI)–guided group (PVI-guided fluid management) and in the control group. Intraoperative: maximum intraoperative value. Data are presented as mean ± SEM. *$P < 0.05$.

management group and the control group. Table 2 shows that during surgery, patients in the PVI-directed fluid management group were given less total fluid and less crystalloid intraoperatively than was the control group. There were no differences postoperatively. Figure 2 shows that lactate levels were lower in the PVI group during and after surgery. There were no statistically significant differences in the incidence of hypotension, cardiovascular rescue, or renal dysfunction. Two patients in the PVI group died from septic shock 20 days and 33 days after surgery because of a failed anastomosis (Table 3).

DISCUSSION

We found that PVI-guided fluid management resulted in less crystalloid administered perioperatively and reduced lactate levels during and after major abdominal surgery. Lactate levels provide an indirect but sensitive measure of organ perfusion. Lactate is clearly correlated with the adequacy of intravascular volume, tissue hypoxia, and energy failure due to bloodflow redistribution.[10] Lactate levels can be improved by the optimization of the fluid status and cardiac preload.[2,4]

Our results confirm the conclusion of Lopes et al. The use of the noninvasive PVI, or the invasively obtained pulse pressure variation, improves perioperative fluid management.[4] In Lopes et al.'s study, the average amount of fluids was larger in the group guided by pulse pressure variation, in contrast with our results. The difference in results may be explained by the presence of hypovolemia in some patients and hypervolemia in others. These results therefore argue the superiority of

Table 3. Postoperative Complications and Intensive Care Unit/Hospital Stay in the Pleth Variability Index (PVI) Group (PVI-Guided Fluid Management) and in the Control Group

	PVI group (N = 41)	Control group (N = 41)	P Value
Postoperative complications			
Infection of surgery site	8 (20)	8 (20)	1.0
Other infections (pulmonary, line-related, other abdominal)	6 (15)	7 (17)	0.77
Cardiovascular complications (acute myocardial infarction, acute lung injury/acute respiratory distress syndrome, pulmonary edema, arrhythmia)	4 (10)	8 (20)	0.26
Coagulopathy	5 (12)	6 (15)	0.75
Nausea and/or vomiting	0 (0)	4 (16)	0.08
Upper digestive hemorrhage	4 (10)	3 (7)	0.78
Leakage of anastomosis	5 (12)	5 (12)	1.0
Morbidity (event per patient)	1.2 ± 1.8	1.5 ± 2.2	0.46
Mortality	2 (5)	0 (0)	0.16
Length of stay			
Postoperative mechanical ventilation	1 (2)	3 (7)	0.31
Intensive care unit (days)	2.2 ± 5.7	1.8 ± 7.2	0.71
Hospital (days)	15.1 ± 14.3	16.0 ± 17.8	0.78

Data are presented as mean ± SD or number (%).

goal-directed fluid management over simplistic restrictive or liberal approaches for fluid management, avoiding hypovolemia and hypervolemia.[11,12]

Unlike Lopes et al., we did not find an improvement in terms of the number of complications. The much higher incidence of hypovolemia reported by Lopes et al. may account for this difference. The clinical significance of lower lactate levels in our relatively small study may be questioned. Additionally, fluid management in the control group was different by design, favoring greater fluid crystalloid administration (2 mL · kg^{-1} · h^{-1} in the PVI group vs. 4 to 8 mL · kg^{-1} · h^{-1} in the control group), and it was possibly influenced by the fact that the control group had a greater blood loss (440 [242 to 637] mL vs. 349 [230 to 468] mL) (although this was not statistically significant). When mean arterial blood pressure decreased to <65 mm Hg, the PVI group received norepinephrine, whereas the control group received norepinephirne and a bolus of crystalloid. In our study a "learning contamination bias" may have blunted the differences between the groups. This bias occurs when a team member gains experience with pulse pressure variation and begins, intuitively, to use respiratory variations of the arterial pressure curve to treat patients in the control group. However, small variations are difficult to see without using a device that makes the calculations from the curve.

The PVI was calculated by the new Masimo Set pulse oximeter (Masimo Co., Irvine, California) from the respiratory variations in the perfusion index (PI). The PI is the percentage amplitude difference between the pulsatile infrared signal and the nonpulsatile infrared signal. The PVI is calculated by measuring changes in the PI during the respiratory cycle: $PVI = [(PI_{max} - PI_{min})/PI_{max}] \times 100$. Cannesson et al. have demonstrated that the PVI predicts fluid responsiveness in the operating room. They showed that the cutoff value to distinguish responders from nonresponders to intravascular volume expansion (in terms of an increase of cardiac index) was a PVI >14%.[7] We confirmed their results in a preliminary study (data not shown) and consequently chose 14% as the threshold for fluid loading.

Whereas the PVI may be useful in most patients, our exclusion criteria limit the application of our results in some patients. To maintain homogeneity between the 2 study groups, we did not include patients with severe cardiac insufficiency (ejection fraction <30%) or chronic dialysis. Moreover, the dynamic variables must not be calculated in the presence of arrhythmia. One patient per group was excluded because of an intraoperative arrhythmia. Additionally, these results cannot be extrapolated to other devices that calculate the respiratory variation of the plethysmographic curve. The algorithm used to process the signal may explain the poor accuracy observed by others.[13] Moreover, we did not measure the possible impact of the use of epidural analgesia and thoracotomy in some patients.

In conclusion, the use of PVI-guided fluid management was associated with lower lactate levels during major abdominal surgery. Patients in the PVI-guided group were given less crystalloid. Reduced lactate levels in PVI-guided patients suggests that PVI-guided fluid management may lead to fluid administration that is tailored to each individual patient's needs.

ACKNOWLEDGMENTS

Masimo Corporation graciously provided devices during the study protocol.

REFERENCES

1. Poeze M, Greve JWM, Ramsay G. Meta-analysis of hemodynamic optimisation: relationship to methodological quality. Crit Care 2005;9:R771–9
2. Cavallaro F, Sandroni C, Antonelli M. Functional hemodynamic monitoring and dynamic indices of fluid responsiveness. Minerva Anestesiol 2008;74:123–35
3. Michard F, Teboul JL. Predicting fluid reponsiveness in ICU patients. A critical analysis of the evidence. Chest 2002; 121(6):2000–8

4. Lopes MR, Oliveira MA, Pereira VO, Lemos IP, Auler JO Jr, Michard F. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. Crit Care 2007;11(5):R100
5. Desebbe O, Cannesson M. Using ventilation-induced plethysmographic variations to optimize patient fluid status. Curr Opin Anaesthesiol 2008;21:772–8
6. Natalini M, Rosano A, Taranto M, Faggian B, Vittorielli E, Bernardini A. Arterial versus plethysmographic dynamic indices to test responsiveness for testing fluid administration in hypotensive patients: a clinical trial. Anesth Analg 2006;103(6):1478–84
7. Cannesson M, Desebbe O, Rosamel P, Delannoy B, Robin J, Bastien O, Lehot JJ. 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
8. Cannesson M, Attof Y, Rosamel P, Desebbe O, Joseph P, Metton O, Bastien O, Lehot JJ. Respiratory variations in pulse oximetry plethysmographic waveform amplitude to predict fluid responsiveness in the operating room. Anesthesiology 2007;106(6):1105–11
9. Zimmermann M, Feibicke T, Keyl C, Prasser C, Moritz S, Graf BM, Wiesenack C. Accuracy of stroke volume variation compared with pleth variability index to predict fluid responsiveness in mechanically ventilated patients undergoing major surgery. Eur J Anaesthesiol 2009; [Epub ahead of print]
10. Valenza F, Aletti G, Fossali T, Chevallard G, Sacconi F, Irace M, Gattinoni L. Lactate as a marker of energy failure in critically ill patients: hypothesis. Crit Care 2005;9(6):588–93
11. Bundgaard-Nielsen M, Holte K, Secher NH, Kehlet H. Monitoring of peri-operative fluid administration by individualized goal-directed therapy. Acta Anaesthesiol Scand 2007;51(3):331–40
12. Bundgaard-Nielsen M, Ruhnau B, Secher NH, Kehlet H. Flow-related techniques for preoperative goal-directed fluid optimisation. Br J Anaesth 2007;98(1):38–44
13. Landsverk SA, Hoiseth LO, Kvandal P, Hisdal J, Skare O, Kirkeboen KA. Poor agreement between respiratory variations in pulse oximetry photoplethysmographic waveform amplitude and pulse pressure in intensive care unit. Anesthesiology 2008;109(5):849–55