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Research Article

Goal directed fluid optimization using Pleth variability index versus corrected flow time in cirrhotic patients undergoing major abdominal surgeries

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KEYWORDS

Fluid optimization;
Corrected flow time;
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Abstract *Purpose:* Several studies have shown that hemodynamic and fluid optimization may result in improved outcome. The aim of this study was to compare between two methods of goal directed fluid optimization using protocols guided by corrected flow time (FTc) of the transesophageal doppler versus Pleth variability index (PVI group) in cirrhotic patients undergoing major abdominal surgeries.

Methods: Sixty cirrhotic patients Child A to B scheduled for major abdominal surgery were randomized into two groups. In both groups 500 mL of Ringer's acetate was infused during induction followed by a 2 mL/kg/h continuous infusion. In FTc group (n = 30) patients with (FTc) less than 350 ms were treated with bolus of fluid challenge according to a preset protocol. In PVI group (n = 30), PVI higher than 13% patients were given 250 mL of fluid bolus.

Results: There was no significant differences in the volume of crystalloids or colloids transfused to both groups with a mean value of 2670 ± 1680 mL and 670 ± 330 mL in the FTc guided fluid group while mean values were 2730 ± 1760 mL and 690 ± 290 mL in the PVI fluid guided group respectively ($P > 0.05$). Also, there was no significant differences between groups regarding the intra or postoperative hemodynamic parameters. There was no significant difference regarding the overall morbidity or the hospital stay between the two groups ($P > 0.05$).

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Conclusions: In conclusion, in cirrhotic patients Child A to B, FTc and PVI were considered to be adequate methods for perioperative fluid optimization, However, combination of every clinical finding, recent and conventional monitoring techniques to all haemodynamic data should be applied whenever possible.

1. Introduction

Perioperative fluid optimization is an established technique in reducing morbidity after major surgery. Hypovolaemia is associated in particular with improper organ perfusion and increased length of hospital stay, while excessive fluid administration produces the clinical picture of pulmonary, peripheral, and gut edema with associated morbidity and mortality [1,2]. Intraoperative determination of fluid requirement traditionally incorporates clinical evaluation, measurement of heart rate, arterial pressure, and central venous pressure (CVP) which are insensitive to detect hypovolaemia [3]. Fluid requirements necessarily vary according to individual physiology and specific circumstances of surgery. Therefore, fixed or formula based filling regimes dependent on patient weight or length of operation are considered to be inappropriate, and may be unable to detect occult hypovolaemia. Previous literatures suggested that perioperative goal-directed therapy (GDT) based on flow-related hemodynamic parameters improves patient outcome [4,5], particularly in high-risk patients [6,7]. Previous intraoperative fluid management studies differs largely according to study design and monitoring techniques used. Most of the studies used were the pulmonary artery catheter (PAC), which is highly invasive and may not be useful in the routine perioperative setting [8–11].

Transesophageal Doppler (TED) is a minimally invasive method with increasing popularity in perioperative fluid therapy [12]. Of the TED variables (Fig. 1), corrected flow time (FTc) has been used and evaluated as a preload index [13], and the use of FTc for intraoperative volume optimization has been reported to reduce the incidence of complications and hospital stay after surgery [14]. On the other hand, respiratory variations in the pulse oximeter plethysmographic waveform amplitude have been shown to be useful in perioperative fluid management in the operating theatres [15]. Depending on this principle, Pleth variability index (PVI) is a novel algorithm allowing for automated and continuous calculation of the respiratory variations in the pulse oximeter waveform amplitude, can also predict fluid responsiveness noninvasively in mechanically ventilated patients [16]. It measures the dynamic change in perfusion index (PI) that occurs during a complete respiratory cycle. Pulse oximetry uses red and infrared light and a constant amount of light (DC) from the pulse oximeter is absorbed by skin, other tissues, and non-pulsatile blood, whereas a variable amount is absorbed by the pulsating arterial inflow. PVI calculation measures changes in PI over a time interval sufficient to include one or more complete respiratory cycles as PVI = $[(PI_{max} - PI_{min})/PI_{max}]$ X100 and is displayed continuously (Fig. 2).

The aim of this study was to verify the impact of goal directed fluid optimization using corrected flow time (FTc) versus Pleth variability index (PVI) in patients undergoing major abdominal surgeries, regarding the intraoperative fluid management, postoperative course and hospital stay.

2. Patient and method

After obtaining written informed consent and Institutional Review Board approval, 60 cirrhotic patients Child A to B were scheduled for open major abdominal surgery (intestinal resection, liver resection, whipple, hepato-biliary procedures) were studied between January 2010 and March 2011. Patients under 18 years, permanent cardiac arrhythmias, ejection fraction below 30% by ultrasound cardiac assessment and patients undergoing emergency surgery were excluded from the study. The study was a single-center, prospective randomized trial carried out in the National Liver Institute which is a tertiary, university affiliated hospital. Patients were randomized preop-

Figure 1 Transesophageal Doppler with FTc less than 350 ms suggests hypovolaemia.

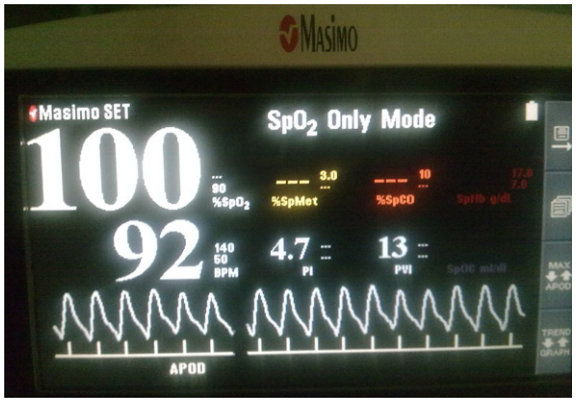

Figure 2 PVI higher than 13%, 250 mL bolus of colloid were given.

eratively either into a corrected flow time fluid guided protocol group ($n = 30$) or Pleth variability index fluid management ($n = 30$) using a closed envelope system. Randomization was performed by a member of the research team. In both groups thoracic epidural catheter was inserted then standard general anesthesia was induced with fentanyl 2 μg/kg, propofol 2 mg/kg and rocuronium 0.9 mg/kg. After intubation of the trachea, the lungs were ventilated to maintain normocapnia (end expiratory partial pressure of carbon dioxide level 32–38 mm Hg) using a constant fresh gas flow of 1 L/min. Maintenance of anesthesia was performed with sevoflurane, fentanyl and rocuronium keeping entropy reading (GE healthcare – Helsinki, Finland) between 40 to 60. Normothermia was achieved with a forced-air warming device (Bair Hugger – Arizant – UK). Standard monitoring for both groups included electrocardiogram, invasive arterial blood pressure via right radial artery catheter, central venous pressure (7 Fr, 20 cm; Arrow International, Reading, PA) was placed through the right internal jugular vein by ultrasound guided method (Sonosite – Nano Max ultrasound system – USA), pulse oximetry, nasopharyngeal core temperature, inspiratory and expiratory gas concentrations.

In both groups 500 mL of Ringer's acetate were infused during induction followed by a 2 mL/kg/h continuous infusion. In the FTc group The transesophageal doppler probe (Cardio QTM, Deltex Medical, Chichester, UK) was inserted orally. The ideal probe tip location is at the level between the fifth and sixth thoracic vertebrae because at that level the aorta is adjacent and parallel to the esophagus. This location is achieved by superficially land marking the distance to the third sternocostal junction anteriorly and is approximately 30–40 cm in the average adult. After insertion, the TED probe is then rotated on its axis to achieve an optimal signal prior to taking measurements. For patients with corrected flow time (FTc) less than 350 ms which denotes hypovolaemia, were give a bolus of Ringer's acetate solution 250 ml over 5 minutes and if no response i.e. FTc still below 350 ms, patient was followed by bolus of colloid challenge in the form of 6% hydroxyethyl starch solution (HES 130/0.4; Voluven; Fresenius Kabi, Stans, Switzerland) 3 mL/kg over 5–10 min and the following protocol was followed: Stroke volume (SV) the same or increased, but if FTc < 350 ms – repeat fluid challenge, while if SV increased by 10%, FTc > 350 ms – repeat fluid challenge till no increase in SV and when FTc > 400 ms – no further fluids till FTc or SV decreased by 10% [17].

In the PVI-group patients, the pulse oximeters (Masimo set version, Masimo Co., Irvin, California, USA) is placed on patient's right finger for monitoring of PVI. If PVI was higher than 13% for more than 5 min, a bolus of Ringer's acetate solution 250 mL over 5 minutes and if no response i.e. PVI still above 13%, it was followed by 250 mL bolus of the same colloid were given and the dose was repeated every 5 min if PVI was still higher than 13% [18]. In both groups, norepinephrine was given as needed to maintain a MAP more than 65 mm Hg and hemoglobin value below 8 g/dL was considered to be a trigger for transfusion of packed red blood cells. All patients were admitted to the intensive care unit (ICU) postoperatively and patients from both groups were managed by the same physicians (ICU and general ward) who were not involved in the intraoperative management, data collection or group allocation of the study. Complications were assessed daily by senior anesthesiologists during the ICU stay and senior surgeons during the rest of the hospital stay and both were blinded to group allocation and study design using standard predefined criteria. All data were collected by a resident blinded to the study design and group allocation. To ascertain comparable preconditions between the groups with respect to preoperative comorbidity and type of surgery, all patients underwent POSSUM (physiological and operative severity score for the enumeration of mortality and morbidity) scoring by using an online software calculator (http://www.vasgbi.com/riskpossum.htm) [19]. Patients were considered to be ready for hospital discharge when they showed stable cardiovascular and respiratory conditions, ability to take oral fluids, sufficient pain control, mobilization (as far as possible), spontaneous micturition, infection parameters within normal range, consciousness comparable with the preoperative state and non-irritated wound conditions. These criteria were classified by specialist surgeons, who were not involved in the study design or group allocation.

2.1. Statistical analysis

Data was statistically analyzed using statistical package for social science (SPSS) program version 17 for windows and Epi info program version. For all the analysis a P-value < 0.05 was considered statistically significant. Data were shown as mean, standard deviation or value and 95% confidence interval (95% CI) and frequency and percent All data were tested with Kolmogorov–Smirnov Z test and were found normally distributed and so presented with mean ± SD. Mann–Whitney test was done for quantitative variables which were not normally distributed and P-value < 0.05 was considered significant. Continuous, normally distributed data were compared using paired and unpaired Student's t-test and a Bonferroni correction for repeated measurements was applied. Binominal data were compared using chi-squared analysis and Fisher's exact test.

3. Results

There were no significant differences in patient characteristics regarding the age, Child classification, co-morbid risk factors, physiological or operative POSSUM score, surgery type or duration, blood loss or postoperative hematology, of the two groups were remarkably similar overall. So, it is therefore very unlikely that patient characteristic variables might influence the results of the study significantly. There was no significant differences between both groups regarding the physiological POSSUM score consequently it is very unlikely that preoperative factors made a significant contribution to the difference in outcome. Also, the operative POSSUM scores were virtually identical indicating an even overall distribution of operative difficulty (Table 1). There was no significant differences in the volume of crystalloids or colloids transfused to both groups (Table 2) with a mean value of 2670 ± 1680 mL and 670 ± 330 mL in the FTc guided fluid group while mean values were 2730 ± 1760 mL and 690 ± 290 mL in the PVI fluid guided group respectively ($P > 0.05$). Postoperatively on ICU admission and on 24 h after, there were no significant differences between groups regarding the hemodynamic parameters and serum lactate (Table 3). There was no significant difference regarding the overall morbidity or the hospital stay (Fig. 3), between the two groups ($P > 0.05$) (Table 4).

Table 1 Demographic data and preoperative criteria in both groups: FTc and PVI groups.

Parameter	FTc group (n = 30)	PVI group (n = 30)
Age (years)	56.8 (7.9)	55.6 (6.6)
Weight (kg)	80.8 (6.1)	79.1 (5.3)
Height (cm)	169 (7.6)	168 (7.9)
Gender (male/female)	10/5	9/6
Child (A/B)	17/13	16/14
Co morbid risk factors		
COPD	6 (20)	5 (16)
Ischemic heart diseases	6 (20)	5 (16)
Hypertension	11 (36)	10 (33)
Renal insufficiency	3 (10)	3 (10)
Diabetes mellitus	13 (43)	14 (46)
Physiological POSSUM score	18 (7)	17.5 (6.5)
Operative POSSUM scores	16 (8)	15.5 (7.5)

FTc: corrected flow time; PVI: Pleth variability index, COPD: Chronic Obstructive Pulmonary Disease; POSSUM: physiological and operative severity score. Data presented by mean (SD) or number (%). $P > 0.05$ in all data.

Table 2 Operative data, hemodynamics and volume of replacement.

	FTc group (n = 30)	PVI group (n = 30)
Surgical procedure		
Whipple	9 [30]	8 [26]
Liver resection	12 [40]	15 [50]
Hepato-biliary	6 [20]	5 [16]
Splenectomy	3 [10]	2 [6]
Approximate blood losses (mL)	740 (530)	810 (660)
Duration of surgery (min)	309 (103)	288 (89)
Physiologic parameters		
Heart rate (beat/min)[#]	79 (19.6)	78 (17.8)
MAP (mm Hg)[#]	87 (12.2)	91 (14.9)
CVP (mm Hg)[#]	9.4 (3.9)	9.2 (4.1)
SpO_2[#]	[99.1]	[99.1]
Lactic acid highest value (mg/dL)	12.6 (2.9)	13.7 (2.8)
Intraoperative oligurea	4 [13]	5 [16]
Intraoperative fluid		
Crystalloid replacement (mL)	2670 (1680)	2730 (1760)
Colloid replacement (mL)	670 (330)	690 (290)
Blood products		
PRBC (mL)	680 (430)	710 (380)
FFP (mL)	740 (270)	690 (240)
Patients receiving norepinephrine	5 [16]	5 [16]

FTc: corrected flow time; PVI: Pleth variability index; bpm: beats per minute; CVP: central venous pressure; FFP: fresh frozen plasma; MAP: mean arterial pressure; PRBC: packed red blood cells; oligurea denotes urine output less than 0.5 for more than two successive hours. [#]Mean of values taken automatically every 5 min. All data presented as mean (standard deviation) or [percentage]. Normal range of lactic acid (4.5–19.8 mg/dL), $P > 0.05$ in all data.

4. Discussion

Fluid management and optimization in cirrhotic patients are always the daily practice in the national liver institute either during anesthesia, surgical interventions or in the postoperative critical care setting. Hemodynamic management is related to the optimization of oxygen delivery to tissues and has been shown to be able to improve postoperative outcome and to decrease the cost of surgery [20,21]. In the operating room, Conventional intraoperative monitoring may not predict accurately fluid requirements [22]. So, the anesthesiologist and his/her patients have to deal with two risks: hypovolemia on one side and hypervolemia on the other side. Both risks potentially can lead to a decrease in oxygen delivery to the tissues and to an increase in postoperative morbidity. On the other hand, CVP is no longer seen to be a satisfactory measure to optimize fluid administration, its use can now be questioned intraoperatively, and there is a reduction in the use of centrally placed venous catheters in high-risk patients undergoing major peripheral vascular and abdominal surgery [23]. However, recent randomized trials and meta-analyses have confirmed that intraoperative fluid

Table 3 Postoperative hemodynamic, physiologic status and volume of replacement in the first 24 of ICU admission.

Parameter	FTc group (n = 30)	PVI group (n = 30)
On admission to ICU		
Mean arterial pressure (mm Hg)	84 (12.6)	83 (13.8)
Heart rate (beat/min)	82 (10.1)	81 (12.2)
CVP (mm Hg)	10 (2.4)	10.2 (1.9)
SpO_2 (%)	[98.3]	[98.3]
Hematocrit (%)	27.1 (3.4)	27.8 (2.9)
Lactic acid highest value (mg/dL)	9.9 (2.6)	10.5 (3.1)
At 24 h after admission to ICU		
Mean arterial pressure (mm Hg)	82 (9.5)	83 (8.1)
Heart rate (/min)	78 (10.8)	79 (11.2)
CVP (mm Hg)	9.4 (2.9)	9.1 (2.7)
Lactic acid highest value (mg/dL)	9.1 (2.9)	9.4 (2.6)
Postoperative oligurea	2 [6]	2 [6]
Postoperative norepinephrine IVI	2 [6]	2 [6]

ICU: intensive care unit; SpO_2: oxygen saturation; CVP: central venous pressure; oligurea denotes urine output less than 0.5 for more than two successive hours; all data presented as mean (standard deviation) or [percentage]. Normal range of lactic acid (4.5–19.8 mg/dL), $P > 0.05$ in all data.

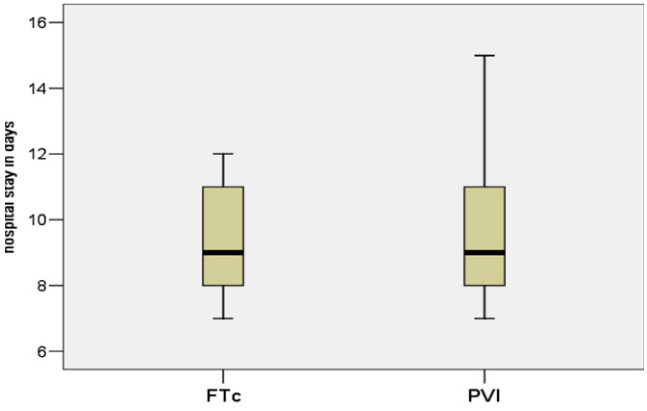

Figure 3 Days of postoperative hospital stay of both groups.

Table 4 Postoperative complications till discharge from the hospital.

Complication	FTc group (n = 30)	PVI group (n = 30)
Abdominal complication		
Nausea and vomiting, hematemesis, bowel obstruction, Intestinal leak, biliary leak, biliary stricture	5 [16]	4 [13]
Cardiovascular		
Myocardial infarction, pulmonary edema, arrhythmia, hypotension	3 [10]	4 [13]
Hepatic decompensation		
Encephalopathy, hypoalbuminemia, hyper bilirubinemia, metabolic acidosis, Progressive ascites (drains), coagulopathy (platelet count $<100{,}000/\mu m$ or prothrombin $<50\%$c)*	4 [13]	5 [13]
Infection		
Sepsis, pneumonia, urinary tract, wound	3 [10]	3[10]
Respiratory		
Pulmonary embolism, ALI/ARDS, postoperative mechanical ventilation	3 [10]	4 [13]
Renal		
Postoperative renal impairment (UOP $<$ 500 mL/day or serum creatinine >1.7 mg/dL or dialysis)#	5 [16]	4 [13]
Postoperative mortality	0	0
Number of patients with complications	14 [46]	13 [43]
Total number of complications	23	24
Complication/patient ratio	1.64	1.84
ICU days	3.96 (0.76)	3.86 (0.72)
Hospital days	9.2 (1.71)	9.6 (2.12)

ICU: intensive care unit; ALI: acute lung injury; ARDS: adult respiratory distress syndrome. *(If platelet at least 150,000/μL preoperatively; if prothrombin at least 70% preoperatively; #if creatinine 1.5 mg/dL or less preoperatively), UOP: urine output. All data presented as mean (standard deviation) or [percentage]. $P > 0.05$ in all data.

optimization using TED [24–27] or PVI [18] improve outcome, but none of the previous literatures compared between these two tools in cirrhotic patients.

This study showed there were no significant differences between both method used for intraoperative fluid management regarding the intraoperative fluid management, postoperative course and hospital stay.

Clinical studies have mostly shown outcome benefits only within postoperative nausea and vomiting, ileus, morbidity, and hospital stay [27–30]. However, only limited pathophysiological data are available to explain this benefit. Lopes et al. [31], in their work revealed that there is reduced morbidity and hospital stay by GDT and this was associated with a reduced interleukin-6 response. Other studies on perioperative changes of the vascular barrier suggest that the endothelial glycocalyx plays a key role [28,32].

The basic advantage of the FTc derived from TED is that it is considered as a minimally invasive tool (although there is still the theoretical risk of esophageal trauma). The disadvantages include difficulty in positioning the probe tip, especially in the elderly patient. FTc is affected not only by left ventricular preload but also by other haemodynamic factors, and it is inversely proportional to the after load [33]. Moreover, hypotensive patients with a low FTc may not respond to a fluid challenge in a pathological condition, which prevents adequate filling of the left ventricle (e.g. pericardial tamponade, massive pulmonary embolus, and tight mitral stenosis) [34]. Consequently, we should put in mind that, low FTc does not always correspond to low left ventricular preload; low FTc can even represent a volume overload state. This means that simple fluid challenge guided by only FTc could further aggravate deterioration in haemodynamic conditions [35]. However, the TED is offering a lot of other data that help in management such scenarios like: cardiac output, peak velocity, systemic vascular resistance and stroke volume.

The recent availability of plethysmographic variability index (PVI) as a continuous monitor that able to analyze the beat-to-beat changes was proved to be very useful in assessing fluid status [36]. Trending of PVI has the ability for monitoring the surgical patients, both intraoperatively and also, postoperatively, for the appropriate hydration states which is considered as a privilege not present in TED, since it may show some tolerance difficulties in fully awake postoperative patients.

In conclusion, FTc and PVI are considered to be adequate methods for perioperative fluid optimization, However, there may be no single parameter that can guide fluid therapy under all situations. Therefore, combination of every clinical finding, recent monitoring techniques and all haemodynamic data should be applied whenever required, even conventional methods like CVP or PAC which if used in conjunction with other fluid monitoring tools as corrected flow time (FTc), Pleth variability index variation (PVI), Stroke volume variation (SVV) and pulse pressure variation (PPV) and other methods might be of a greater value in different clinical and surgical scenarios.

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