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Potential value of pleth variability index in intraoperative fluid management of geriatric patients

Geriatrik hastaların intraoperatif sıvı yönetiminde pleth değişkenlik indeksinin potansiyel değeri

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Abstract
Aim: This study was designed to determine the effects of pleth variability index (PVI) guided monitoring on the optimal intravascular volume replacement during hip and knee arthroplasty in geriatric patients, and whether using PVI could reduce blood transfusion and vasopressor requirements.
Methods: One-hundred geriatric patients who underwent elective hip and knee arthroplasty were included, assigned to either PVI group (volume replacement was PVI guided) or to a control group (volume replacement was based on traditional methods). Sealed envelope technique was used for randomization. Perioperative hemodynamic parameters, infusion rate of crystalloids, colloids, blood/blood products, ephedrine hydrochloride requirements and perioperative urine outputs were recorded.
Results: Crystalloid infusion rate was higher (9.5 vs. 6.8 ml/kg/h, p<0.001) and ephedrine requirement was lower (2.0% vs. 38.0%, p<0.001) in group PVI. Postoperatively, the percentage of patients with high BUN, creatinine, and lactate levels were higher among controls (p<0.001). PVI group had significantly lower mean heart rate intraoperatively.
Conclusions: Our findings suggest that intraoperative fluid replacement guided by PVI monitoring provides hemodynamic stability, preserves normal levels of BUN, creatinine, and lactate, and reduces unnecessary use of vasopressor agents in elderly surgical patients.

Keywords: Geriatric, pleth variability index, anesthesia, intraoperative fluid management, renal function.

Öz
Amaç: Bu çalışma, geriyatrik hastalarda kalça ve diz artroplastisi sırasında pleth değişkenlik indeks (PVI) monitörizasyonunun optimal intravasküler volüm replasmanı üzerindeki etkilerini ve PVI kullanımının kan transfüzyonu ve vazopressör gereksinimlerini azaltıp azaltmayacağını belirlemek için tasarlanmıştır.
Yöntemler: Elektif kalça ve diz artroplastisi uygulanan 100 geriyatrik hasta, PVI grubuna (volüm replasmanı PVI rehberliğinde yapıldı) veya kontrol grubuna (geleneksel yöntemlere dayalı volüm replasmanı yapıldı) dahil edildi. Randomizasyon kapalı zarf usulu yöntemine göre yapıldı. Perioperatif hemodinamik parametreler, kristaloidlerin, kolloidlerin, kan ve kan ürünlerinin infüzyon miktarı, efedrin hidroklorür gereksinimleri ve perioperatif idrar çıkışları kaydedildi.
Bulgular: Kristalloid transfüzyonu grup PVI'da daha yüksekti (9,5'e karşı 6,8 ml/kg/saat, p<0,001) ve efedrin gereksinimi daha düşüktü (%2,0'ye karşı %38,0, p<0,001). Ameliyat sonrası BUN, kreatinin ve laktat düzeyleri yüksek olan hastaların yüzdesi kontroller arasında daha yüksekti (p<0,001). PVI grubu, intraoperatif anlamlı olarak daha düşük ortalama kalp hızına sahipti.
Sonuç: Bulgularımız, PVI monitorizasyonu ile intraoperatif sıvı replasmanının hemodinamik stabilite sağladığını, normal BUN, kreatinin ve laktat seviyelerini koruduğunu ve geriyatrik cerrahi hastalarda gereksiz vazopressör ajan kullanımını azalttığını göstermektedir.

Anahtar Kelimeler: Geriyatrik, pleth değişkenlik indeksi, anestezi, intraoperatif sıvı yönetimi, renal fonksiyonlar.
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Introduction

Aging is closely related with the progressive structural and functional deteriorations of the body systems, predisposing elderly patients to increased risk for perioperative organ decompensation [1]. Nevertheless, organ function assessment is not always easy in this age group. Inadequate compensatory responses to fluid load or dehydration as a result of the structural and functional deteriorations, are the biologic prices of the older body systems [2,3]. Therefore, this age group deserves optimal intraoperative fluid management [4].

A number of different intraoperative fluid management protocols are being utilized for achieving optimal fluid status in this setting. One of the main approaches includes goal-directed fluid therapy (GDT). The perioperative use of GDT allows the anesthesiologists to closely monitor the patient and assists in achieving the optimal risk/benefit balance, minimizing end organ deteriorations [5]. Dynamic hemodynamic indices based on respiratory variations are used to guide intraoperative GDT [6,7]. It is already accepted that these parameters are superior to static parameters in the assessment of volume responsiveness [8].

Pleth variability index (PVI) is one of the non-invasive dynamic indices allowing continuous monitoring tool [9]. This index is derived from respiratory variations in the perfusion index (PI), providing an automatically measured numerical value [10-13]. PVI monitoring is able to predict intraoperative volume status and fluid responsiveness [14-16]. PVI can also reduce postoperative complication rate as well as the length of hospital stay and mechanical ventilation, after the intermediate-risk surgical procedures [17].

The primary aim of this study was to determine the effects of pleth-guided monitoring on the optimal intravascular volume replacement during hip and knee arthroplasty in geriatric patients, helping to reduce blood transfusion and vasopressor requirements. Secondarily, perioperative blood urine nitrogen (BUN), serum creatinine and lactate levels, as well as urine output were investigated.

Material and methods

Patients

This prospective study included 100 geriatric patients with ASA physical status II-III, aged 64 years or older, who underwent elective hip or knee joint replacement surgery. The study protocol was approved by the ethics committee of Marmara University (date, 09.2019; no, 356). All patients gave written informed consent prior to study entry. The study was conducted in accordance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki Declaration and its later amendments. The study was registered to Australian and New Zealand Clinical Trial Registry (ANZCTR) (www.anzctr.org.au) (number, ACTRN12620000419965).

Patients with severe cardiac arrhythmias and peripheral artery disease, low ejection fraction (under 30%), pulmonary or neurologic pathology, hepatic or renal dysfunctions were excluded from the study. Patients who were decided to require invasive monitoring tools such as cardiac output or intraarterial monitors were not included in the study.

Sealed envelope technique was used for randomization. Patients were assigned to either PVI group (group PVI) in which volume replacement was guided by the aid of the PVI device monitoring or to a control group (group C) in which intraoperative fluid management was done by the standard approach of the institution based on traditional methods such as measurements of blood pressure (BP), heart rate (HR) and electrocardiogram (ECG) (Fig 1) (Fig 2).

Figure 1. Pleth variability index monitor.

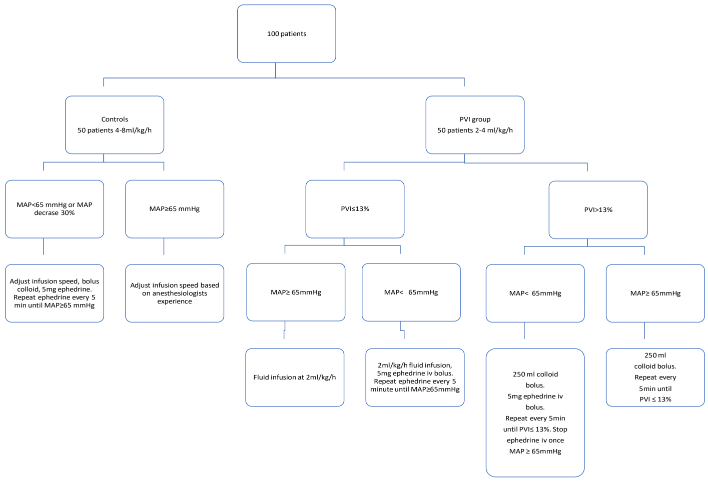

Figure 2. Intraoperative fluid management algorithm for the controls and the study group.

Study outcomes

The primary outcome was the maintenance of hemodynamic stability reducing blood transfusion and vasopressor requirements in geriatric patients in whom fluid administration was guided by the plethysmographic monitoring. Optimization of the intraoperative hemodynamic parameters, perioperative maintenance of normal levels of BUN, serum creatinine and lactate, as well as urine output were determined as the secondary outcomes.

Anesthesia management

Preoperative fasting period was strictly 8 hours in all patients. Anesthesia induction was achieved with 2 mg/kg propofol and 1μgr/kg remifentanil. Two minutes after the administration of 0.6 mg/kg rocuronium bromide the trachea was intubated, and volume-controlled ventilation was delivered. Four to 6% desflurane and 67% N2O in oxygen were used for the maintenance of anesthesia. Standard monitoring including heart rate (HR), electrocardiogram (ECG) in DII derivation, noninvasive systolic (SBP), diastolic (DBP) and mean (MAP) blood pressures, peripheral oxygen saturation (SpO2), end tidal carbon dioxide concentration, core body temperature, together with anesthetic agent analyzer to maintain a minimum alveolar concentration of 1, hourly urine output. Finger PVI (Radical 7, Masimo Pulse CO-Oximetry) monitoring was achieved in both groups, however anesthesia team was blinded to the study as well as the PVI readings in the control group. Insertion of the central venous catheter was at the discretion of the responsible anesthesiologist and the values were not taken into the account of the study. Ventilator patterns were set as follows: volume-controlled ventilation with a tidal volume of 8 ml/kg of the ideal body weight, respiratory rate and inspiratory to expiratory ratio adjusted to restore end tidal carbon dioxide between 35-45 mmHg. SpO2 was targeted within the ranges of 96 to 100%.

Intraoperative fluid management

Individualized hemodynamic management aimed to achieve a plethysmographic variability index under 13%, and the standard management strategy aimed to maintain a mean arterial pressure above 65 mmHg during general anesthesia. MAP values under 65 mmHg or under 30% of the patient's preoperative values was defined as hypotension.

Group C

In this group, volume status of the patients was fundamentally appreciated clinically, based on hemodynamic parameters such as HR, MAP together with hourly urine output. Intraoperative fluid administration was performed with lactated ringer solution at a rate of 4-8 ml/kg/h to maintain hydration. In cases of hypotension, crystalloid solution (typically 250 mL) was administered in order to determine responses to fluid bolus. The patient is assumed to be fluid responsive if the desired level of MAP was achieved. If not, the rate of the crystalloid infusion was increased, colloid solution infusion was initiated, and ephedrine hydrochloride was applied by the recommended algorithm shown in Fig 2.

Group PVI

Fluid replacement was maintained with lactated ringer solution at 2-4 ml/kg/h, PVI measurements were used for additional requirements, targeting values lower than 13%. If PVI was higher than 13% for more than five minutes, 250 ml bolus colloid (Gelofusine®) was administered. If PVI was still higher than 13%, colloid bolus infusion was repeated until PVI was lower than 13%.

In both groups, an intravenous bolus of 5 mg ephedrine hydrochloride was given as needed to keep the mean blood pressure above 65 mmHg.

Measurements

The preoperative creatinine, BUN and lactate levels were defined as the levels obtained closest to the surgery. Postoperative values were the highest levels obtained within the 24 h after the surgery.

Hemodynamic parameters and all data in both groups were recorded by another anesthesiologist who was also blinded to the study, at 15-min intervals. In addition, pre and postoperative blood levels, perioperative use of crystalloids, colloids, blood/blood products, bleeding amounts, ephedrine hydrochloride requirements and perioperative urine outputs were recorded and compared statistically.

Statistical Analysis

For data analysis, SPSS (Statistical Package for Social Sciences) version 21 software was used. The difference in crystalloid infusion rates in a previous study was used as the reference for sample size calculation [15]. Accordingly, to detect a difference of 452 ml in the amount of crystalloid infusion, with alpha = 0.05 and 0.80 power, at least a total of 68 patients had to be included (n = 34 in each group). Normality was tested using graphical methods and hypothesis tests. Between-group comparisons of continuous variables were done using student t test for independent samples or Mann-Whitney U test, depending on data distribution. Within-group comparisons of continuous variables were done using student t test for paired samples or Wilcoxon signed-rank test, where appropriate. Pearson chi-square test or Fisher's exact test was used for between-group comparison of categorical variables. Two-way ANOVA test for repeated measurements was used to examine the differences between groups in terms of change in intraoperative variables over time. Comparison of groups at different time points was done with Mann-Whitney U test. Two-sided p values <0.05 were considered indication of statistical significance.

Results

Patients

Demographic characteristics and perioperative parameters were shown in Table 1. Patients in group PVI were older than the controls in a statistically significant manner (p=0.011), but we assumed that its clinical value was negligible. Sex distribution and weight between groups were similar.

Perioperative parameters

Intraoperatively, the rate of crystalloid infusion was higher (9.5 versus 6.8 ml/kg/h, p<0.001) and ephedrine hydrochloride requirement was lower (2.0% versus 38.0%, p<0.001) in group PVI, compared to group C (Table 1). In the preoperative period; BUN, creatinine, and lactate levels were higher in group PVI than group C, staying in normal clinical values. In the postoperative period, although all of the three parameters decreased significantly in group PVI; they increased significantly in group C, when compared to the preoperative values (p<0.001) (Table 2). Postoperatively, the percentage of the highest BUN, creatinine, and lactate levels were more common in group C (p<0.001, p<0.001, and p=0.002, respectively) (Table 1).

There was no difference between groups regarding intraoperative bleeding amount, colloid infusions requirement, erythrocyte suspension requirement, and intra and postoperative hourly urine output.

Figure 3 shows intraoperative changes in HR, MAP, PVI, and PI. The two groups differed in terms of changes in HR (p<0.001) and PVI (p<0.001), but not in terms of MAP (p=0.157) and PI (p=0.138). Group PVI had significantly lower HR and PVI values (p<0.05) except the preoperative values when compared to group C.

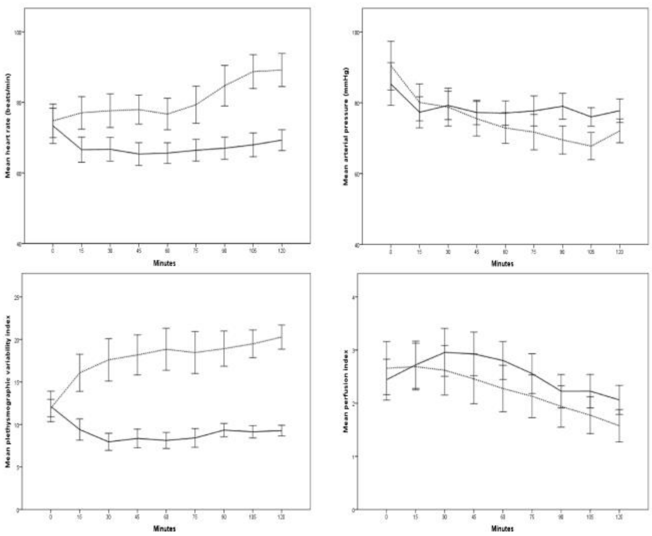

Figure 3. Changes in mean heart rate, arterial pressure, plethysmographic variability index, and perfusion index over time during the operation. Error bars indicate 95% confidence intervals. Straight lines and dotted lines indicate PIV group and controls, respectively.

Table 1. Demographic data.

	All patients (n=100)	PVI group (n=50)	Controls (n=50)	P
Demographics				
Age, years	71.9±6.7	70.3±6.3	73.5±6.8	0.011
Sex, M/F	48/52	25/25	23/27	0.689
Weight, kg	75.3±15.8	78.3±17.4	72.3±13.5	0.099
Intraoperative parameters				
Bleeding, ml	365.7±412.1	337.2±400.1	394.2±425.9	0.184
Crystalloid infusion rate, ml/kg/h	8.2±3.4	9.5±3.9	6.8±2.0	<0.001
Colloid requirement, n (%)	39 (39.0%)	23 (46.0%)	16 (32.0%)	0.151
Ephedrine requirement, n (%)	20 (20.0%)	1 (2.0%)	19 (38.0%)	<0.001
Erythrocyte suspension requirement, (Units)	0.3±0.8	0.2±0.7	0.4±0.9	0.109
Intraoperative urine output, ml/kg/h	1.7±1.1	1.6±1.1	1.8±1.1	0.292
Postoperative parameters				
Postoperative urine output, ml/kg/h	0.6±0.3	0.8±0.3	0.3±0.1	0.292
High BUN, (>23 mg/dL)	22 (22.0%)	3 (6.0%)	19 (38.0%)	<0.001
High creatinine (>1.2 mg/dL)	27 (27.0%)	1 (2.0%)	26 (52.0%)	<0.001
High lactate (>2 mmol/L)	12 (12.0%)	1 (2.0%)	11 (22.0%)	0.002

PVI, plethysmographic variability index; M, male; F, female; BUN, blood urine nitrogen. Unless otherwise stated, data presents as mean ± standard deviation.

Table 2. Changes in BUN, creatinine, and lactate levels compared to baseline.

Parameter	Timing	PVI group (n=50)	Controls (n=50)	p*
BUN, mg/dL	Preoperative	18.8±5.4	14.0±4.4	<0.001
	Postoperative	15.8±4.8	22.0±6.0	<0.001
	Difference	-3.0±4.3	8.0±5.3	<0.001
	p†	<0.001	<0.001	
Creatinine, mg/dl	Preoperative	0.9±0.2	0.7±0.2	<0.001
	Postoperative	0.8±0.3	1.2±0.3	<0.001
	Difference	-0.1±0.1	0.5±0.3	<0.001
	p†	0.004	<0.001	
Lactate, mmol/L	Preoperative	1.2±0.7	0.9±0.3	0.049
	Postoperative	1.0±0.4	1.8±0.6	<0.001
	Difference	-0.2±0.5	0.9±0.6	<0.001
	p†	0.002	<0.001	

Data presented as mean±standard deviation. * for between-group difference. † for within-group difference, postoperative versus preoperative.

Discussion

The principal finding of this study is that PVI monitoring offers a great advantage over other methods based on static parameters, in the perioperative fluid management of the elderly patients undergoing hip and knee joint replacement. The advantages include optimal volume administration with better hemodynamic stability, reduction in the use of vasopressor agents and preservation of BUN, blood creatinine and lactate levels in normal ranges.

PVI is one of the noninvasive methods in the management of fluid administration during surgery, and studies investigating its advantages are usually focused on the postoperative complications and hospital length of stay, presenting contradictory results [17]. To the best of our knowledge, no previous study has investigated the effectiveness of PVI monitoring on the intraoperative fluid management of the geriatric surgical patients. Noninvasiveness and continuity are two main attractive features of PVI monitoring offering great advantages for the vulnerable geriatric patient. Indeed, we found that PVI guided intraoperative fluid management was associated with administration of higher volumes of crystalloid solutions (9.5 versus 6.8 ml/kg/h, respectively), together with significant reductions in the administration of bolus doses of vasopressors (ephedrine hydrochloride in our study), compared to the conventional fluid therapy. This finding emphasizes the recognition of the fine line between the risk of excessive volume load or vasopressor administration in geriatric surgical patients. During hypotensive episodes of the geriatric surgical patients, the fear of administering excessive volume results in the use of excessive and unnecessary vasopressor agent, without evaluating the volume status of the patient.

In fact, many patients receive vasopressors either as intermittent boluses or infusions to counteract intraoperative hypotension not responding to fluid administration. This approach is related to the GDT algorithm in which the use of vasopressors is reasonable only when the preload is adequate [18]. It is evident that when the patient is volume under resuscitated, the end organ perfusion gets worse. This negative effect is correlated with the drug exposure time, and in our study, it is not reasonable to blame ephedrine hydrochloride for the adverse clinical conditions of the patients. Vasopressors exert their effects by elevating cardiac contractility, vascular tonus, and heart rate. The incidence of vasopressor use during surgery was investigated in other studies [8]. Although these studies were not restricted to the geriatric patients, they concluded that fluid administration guided by PVI monitoring reduced the requirement of vasopressors as a result of the recognition of intravascular volume status. The underlying physical status of the elderly is not always stabile. Therefore, the major question is that whether vasopressor administration during surgery is safe or not in volume depleted elderly patients. In fact, geriatric patients experiencing intraoperative hypotension, vasopressor use was shown to be related with postoperative hypertension, together with delirium [19]. Vasopressor use has been reported to be associated with reduced cerebral oxygen saturation that may lead to postoperative cognitive impairment [20,21]. Therefore, the patient's MAP should be high enough to prevent hypotension; but it should be kept in mind that extremely high MAP levels may lead to arrythmias, increased cardiac demand and impaired tissue perfusion. Therefore, vasopressors should only be administered after the optimization of the volume status of the geriatric patients, emphasizing the importance of PVI guided monitoring during hypotensive episodes.

Geriatric patients may already be hypovolemic intraoperatively due to prolonged perioperative fasting times and reluctance in administering fluids, potentially leading to perioperative poor organ perfusion [22]. Hypotension lasting more than 15 minutes is known to be associated with myocardial and renal injury [23]. In elderly, changes in heart rate do not always reflect changes in volume status, probably due to the blunted compensatory responses to hypovolemia. Furthermore, intraoperative tachycardia may not be manifested in response to hypovolemia due to the widespread use of beta blockers in geriatric patients [24]. In our study, beta blocker use was similar between groups, but heart rate values were significantly higher in the control group together with normotension probably due to the administration of ephedrine. High PVI values in these patients have reflected reduced intravascular volume. Intraoperative tachycardia was known to be associated with postoperative adverse outcomes in geriatric population [24]. We assumed that the clinical triad in the control group consisted of hypovolemia, unnecessary use of vasopressors and tachycardia. The disadvantage of this triad carried the risk of the reduction of adequate perfusion to the vital organs such as heart, brain, and kidneys.

In this study, standard fluid management strategy was associated with elevated postoperative BUN, blood creatinine, and lactate levels, while fluid administration based on PVI monitoring did not cause any abnormal blood levels. Similarly, in other studies performed on non-geriatric patients it was demonstrated that fluid management under PVI guidance may reduce postoperative blood lactate levels [11,25,26]. Although they were primarily focused on the effects on the duration of hospitalization, the results of Fischer et al study offered opposite results: lactate levels were similar between PVI-guided and routine fluid management groups. Fluid loading was more frequently performed in the PVI group than in the control group, vasopressor use was similar [17]. Blood lactate level is an indirect marker of the intravascular volume status, tissue hypoxia, or organ dysfunction [27]. In our study, patients in the PVI group had high crystalloid infusion rate and low ephedrine requirements explaining preservation of normal blood lactate levels.

Preoperatively, all patients had normal BUN and blood creatinine levels. Postoperative BUN and blood creatinine levels decreased significantly in patients monitored with PVI. Contrarily, they increased in patients in whom fluid management was guided with static parameters. All patients had normal hourly urine output either in the intra and postoperative periods. Although BUN and creatinine were the known indicators of kidney function, the occurrence of postoperative renal complications may be best diagnosed by measuring glomerular filtration rate, creatinine clearance or some kidney specific markers such as Neutrophil Gelatinase-Associated Lipocalin (NGAL. Being limited to BUN and blood creatinine for the assessment of renal function was one of the major limitations of the study. Creatinine levels may be low in elderly patients due to the diminished muscle mass. Patients in the standard fluid management group had normal perioperative hourly urine output but increased BUN levels, indicating fluid deficit rather than acute kidney injury.

We did not focus on the neurologic outcomes, but none of the patients developed postoperative agitation, delirium or clinically remarkable cognitive dysfunction. The lack of intraoperative cerebral oxygen saturation monitoring and postoperative cognitive function testing stood as another limitation in the study. It was therefore not possible to say that intraoperative volume status or vasopressor use was associated with negative neurologic outcomes.

Our findings showed that PVI-guided fluid management strategy seems to offer an effective, practical, and rational approach to prevent perioperative complications associated with the administration of fluids in elderly patients undergoing hip and knee joint replacement.

In conclusion, we suggested that intraoperative fluid replacement guided by PVI monitoring provided hemodynamic stability, preserved normal levels of BUN, creatinine and lactate blood concentrations reducing unnecessary use of vasopressor agents in elderly surgical patients. We believe that these findings deserve further prospective evaluations to emphasize the effectivity and necessity of the PVI monitoring as part of GDT.

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