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Original Article

Goal-directed fluid management based on the auto-calibrated arterial pressure-derived stroke volume variation in patients undergoing supratentorial neoplasms surgery

Jie Wu[1*], Yanhui Ma[1*], Tianlong Wang[1], Geng Xu[2], Long Fan[1], Ying Zhang[1]

Departments of [1]Anesthesiology, [2]Neurosurgical Oncology, Xuanwu Hospital, Capital Medical University, Beijing, China. [*]Equal contributors.

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Abstract: Objective: This study was designed to assess the influences of arterial pressure continuous output (APCO) derived stroke volume variation (SVV)-guided fluid management on postoperative complications and outcome in the patients undergoing supratentorial neoplasms surgery. Methods: Sixty-six patients undergoing elective supratentorial neoplasms surgery were randomly divided into the control group and APCO group. Before the induction of general anesthesia, colloids 3 ml/kg were given in the two groups followed by crystalloid infusing according to physical requirement. The degree of brain edema was assessed one day postoperative. Results: Intraoperative colloids and total infused fluid volume were significantly higher in APCO group than control group. The degree of brain edema at 1 day postoperative was not significantly different between the two groups (3 (2, 4) vs. 3 (2, 4), P=0.96). The lactate concentration at the end of surgery in the patients of APCO group was significantly decreased compared with baseline (P<0.001). The incidence of postoperative complications (4 vs. 11; P=0.047) was decreased in the APCO group. Conclusions: Fluid management guided by SVV during supratentorial neoplasms surgery is associated with a lower incidence of postoperative complications and do not induce additional risk of brain edema.

Keywords: Fluid therapy, length of stay, neurosurgical procedures, physiologic/instrumentation, postoperative complication

Introduction

In the patients undergoing neurosurgery, the use of preoperative diuretics, sympathetic inhibition by general anesthetic and intraoperative blood loss all may cause intravascular volume reduction and consequently compromise vital organ blood perfusion including brain. The appropriate fluid administration is challenge. The current studies are not available to guide a rational fluid management in neurosurgical patients. The fluid overloading was not recommended in patients with neuropathlogical disease due to the risk of brain edema, especially for those patients with blood brain barrier dysfunction. Restrictive fluid strategy can reduce the incidence of perioperative complications and hospital stay in patients undergoing other type major surgeries [1, 2]. Although restricted fluid management is a generally accepted way for neurosurgical patient [3], the consensus is still not clear. Excess fluid restriction may cause hypovolaemia which is considered as a significant risk for organ and tissue hypoperfusion and hence resulting in organ dysfunction [4].

Conventional hemodynamic variables such as central venous pressure (CVP) and pulmonary artery occlusion pressure were used to guide intravascular fluid administration. However, they are not reliable predictors for fluid responsiveness [5, 6]. Dynamic variables provide better predictions for fluid responsiveness. Among these variables, the auto-calibrated arterial pressure derived stroke volume variation (SVV) is a good predictor for fluid responsiveness [7, 8]. SVV obtained from the FloTrac/Vigileo system, which is so-called arterial pressure continuous cardiac output (APCO), is a sensitive predictor for fluid responsiveness in patients with minimal infusion before brain surgery [9].

The aim of this study was to assess whether fluid management guided by SVV would improve the outcome of patients undergoing supratentorial neoplasms surgery compared with by a standard conventional hemodynamic variable such as CVP or blood pressure.

Methods

The study protocol approval was granted by the Ethics Committee of Xuanwu Hospital of Capital Medical University, Beijing, China. After written informed consent were obtained, 66 patients with ASA physical status I or II undergoing supratentorial neoplasms (meningeoma, glioma or metastatic tumor) surgery were recruited. The patients with serious cardiovascular or respiratory disease, severe aortic stenosis or regurgitation, permanent cardiac arrhythmias, severe peripheral vascular disease, or obesity (body mass index ≥35 $kg{\cdot}m^{-2}$), reoperation in 24 h were excluded. Patients were randomly divided into APCO group or control group by sealed envelope.

Standardized monitoring included the ECG, heart rate, noninvasive blood pressure monitoring, peripheral pulse oxygen saturation, end-tidal carbon dioxide measurement ($P_{ET}CO_2$) and nasal temperature by Datex S/5 monitor (Datex/Ohmeda®, GE Healthcare) through the surgery. A catheter was inserted into the right or left radial artery under local anesthesia for the arterial blood pressure monitoring. General anesthesia was induced with midazolam 0.04 mg/kg, fentanyl 3-4 μg/kg, propofol 1.5-2 mg/kg and rocuronium 50 mg. After tracheal intubation, the lungs were ventilated with a tidal volume of 8-10 ml/kg and respiratory rate 10-14/min, I:E was set for 1:1.5 to maintain $P_{ET}CO_2$ between 30 to 35 mmHg with fresh oxygen flow of 3 L/min. Anesthesia was maintained with infusion of propofol (3 to 4 mg/kg/min), remifentanil (0.1 to 0.2 μg/kg/min) and vecuronium (3 to 4 mg/h). The depth of anesthesia was judged and maintained to 40-60 of bispectral index. Patients' nasal temperature was kept on 36-37°C by a circulating water blanket.

In both groups, patients received dynamic monitoring with the FloTrac/Vigileo device (software version 3.02, Edwards Lifesciences, Irvine, CA, USA). A 20G arterial catheter was connected to the Vigileo monitor via the FloTrac pressure transducer. A central venous access was inserted via subclavian vein catheter after anesthesia induction. The correct position of the central venous catheter was verified by simultaneous ECG tracing. The zero mark was set at the level of the patient's midaxillary line corresponding to the fourth ribs in the supine position and at the level of the patient's sternal right marginal of 3-4 intercostals level in lateral position, and zero was corrected with atmospheric pressure.

Fluid management protocol

The colloid per 3 ml/kg (hydroxyethyl starch 6%, 130/0.4, Voluven®, Fresenius Kabi) was infused for more than 5 minutes before induction, followed by continuous infusion of crystalloid (0.9% saline) to meet the physiological requirement per hour (4,2,1 rule, which need 4 ml/kg/h for the first 10 kg, then 2 ml/kg/h for the next 10 kg, then 1 ml/kg/h for the left) in both groups.

In the APCO group, a bolus volume of 50 ml colloid was infused for two minutes if the SVV in the consecutive three times (internal for 1 minute) was more than 12% after the central venous catheter was inserted. The bolus volume was repeated every 5 minutes if SVV was still more than 12%. Vasoactive agent (ephedrine or phenylephrine) was administered in APCO group if the mean arterial pressure (MAP) was less than or equal to 70 mmHg for more than 1 minute. Catecholamine support with dobutamine was initiated only if CI remained below 2.5 $l/min/m^2$. CVP was only recorded in the cases without guiding fluid management.

In the control group, a bolus of colloids with 50 ml were infused if CVP was lower than 8 mmHg along with MAP less than 80% preoperatively for at least 1 minute. The patient was resting quietly for 5 minutes. If the MAP was below 70% of baseline for at least 1 minute, a bolus injection of 50 ml colloids was given. If MAP was less than or equal to 70 mmHg for more than 1 minute, ephedrine or phenylephrine was given simultaneously. SVV and CI were only recorded in the cases without guiding fluid management and dobutamine administration.

The protocol was repeated every 5 minutes. Intraoperative hemoglobin value below 80 g/L

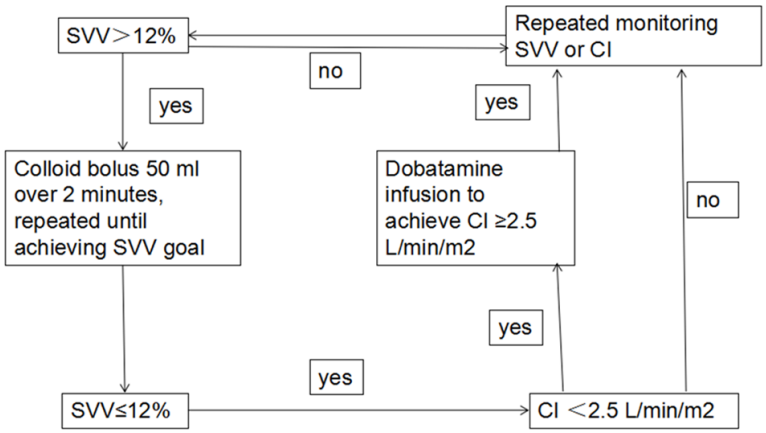

Figure 1. Fluid management protocol in APCO group. SVV, Stroke volume variation; CI, cardiac index.

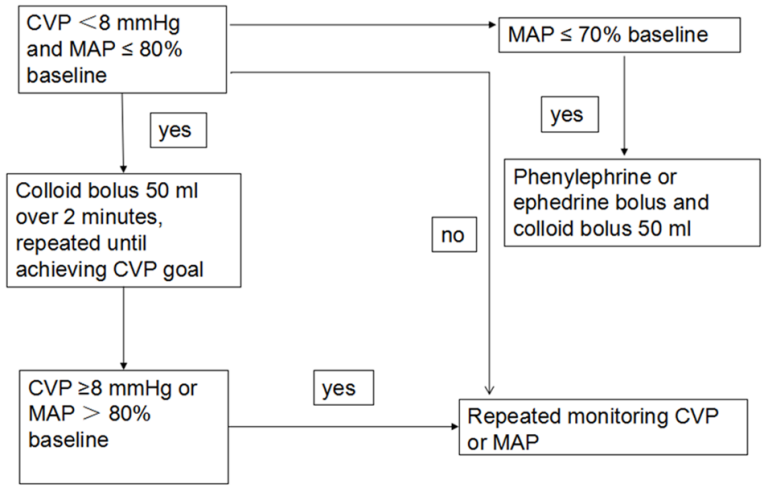

Figure 2. Fluid management protocol in control group. CVP, central venous pressure; MAP, mean arterial pressure.

was considered to be a trigger for transfusion of packed red blood cells. Details of the protocols for both the groups are summarized (**Figures 1** and **2**).

Intraoperative measurements

The infused total fluid volumes of colloids, crystalloids, urine output and blood loss were recorded throughout the surgery. Arterial blood samples were obtained and immediately analyzed by a blood gas analyzer (ABL 800 Radiometer, Copenhagen, Denmark) for the plasma lactate, pH, glucose and base excess (BE).

The arterial blood gas, transaminase, serum creatinine (Cr) and urea concentrations were measured at 10 minutes before induction, the time of dura mater incision, the end of the operation and 24 h postoperation. The usage of vasoactive agents was also recorded. All patients were admitted to intensive care unit (ICU) after the operation.

Postoperative data collection

All patients were managed in the ICU of neurosurgery, who were not aware of the patients' assignment. During the postoperative hospitalization, the incidents of complications such as postoperative infection, noninvasive ventilation support, arrhythmia (the changes of heart rate or rhythm which need intervention), hypotension, hepatic and kidney dysfunction, stroke, intracranial hemorrhage and death were collected and recorded. The length of postoperative hospitalization and ICU stay was recorded for each group. The standard hemodynamics parameters, intravenous fluids and blood products' amounts administered in the first 24 h postoperative were recorded. All patients underwent a CT scan at first day after surgery. The discharged standards were set as stable vital signs, uneventful wound healing and no treated discomforts. All the postoperative patients' data were collected by an anesthesiologist blinded to the group assignment.

Statistical analysis

A pilot study with 20 patients (10 per group) was executed for the power analysis, which showed the incidence of complication decreased by 20% with the SVV-guided fluid management. The calculated sample size for a 0.05 difference (2-sided) with a power of 80% was twenty four patients per group. Thirty-three patients were recruited into each group in case of possible dropouts in this study. SPSS 16.0 was used for statistical analysis. The results

Table 1. The distribution of patient characteristics, intraoperative hemodynamics, profile of surgery and anesthesia, comorbidity in both groups SVV, stroke volume variation; CVP, central venous pressure; CI, cardiac index

Items	APCO group (n=33)	Control group (n=30)	*P* value
ASA class I/II	13/20	9/21	0.597
Age (y)	50±9	50±9	0.919
Gender (male/female)	15/18	14/16	0.923
Weight (kg)	69±12	64±10	0.135
Height (cm)	163±7	164±8	0.601
Duration of anesthesia (min)	259±41	259±63	0.968
Duration of surgery (min)	194±39	192±52	0.883
Types of surgery			
Glioma/meningeoma/metastatic tumor (n)	15/16/2	13/15/2	0.919
Baseline value in hemodynamics			
SVV (%)	9.3±2.9	9.4±3.4	0.901
MAP (mmHg)	95±9	96±10	0.963
HR (beats/min)	68±9	65±8	0.899
CI (ml/min/m^2)	3.4±0.5	3.3±0.6	0.589
Hemodynamic parameters by the end of surgery			
SVV (%)	10.4±1.3	12.9±4.1	0.002
CVP (mmHg)	7.0±1.8	6.9±1.8	0.722
MAP (mmHg)	88±7	83±10	0.052
HR (beats/min)	68±9	66±9	0.282
CI (ml/min/m^2)	3.0±0.6	2.8±0.5	0.104
Chronic disease history			
Hypertension	4 (12.1%)	4 (13.3%)	1.000
Diabetes mellitus	2 (6.1%)	3 (10%)	0.662
Stroke	0 (0%)	1 (3.3%)	0.476
Carotid artery stenosis	0 (0%)	1 (3.3%)	0.476

were expressed as mean ± standard deviation (SD), medians with 25% to 75% interquartile ranges, or number (percentage). Continuous, normally distributed data were analyzed with independent samples and paired Student's t test. Continuous, non-normally distributed data were analyzed with the Wilcoxon test. The change in time-dependent variables was tested using ANOVA on repeated measurement. Binominal data were compared with Pearson or continuity correction chi-squared analysis and Fisher's exact test. A *P* value <0.05 was considered as statistically significant.

Results

Basic characteristics

66 patients scheduled for neurosurgery were included. 63 patients have completed the protocol and their data were analyzed. Two patients in the control group did not achieve the predefined operation. The other one patient in the control group underwent surgery again because of a subdural hematoma.

Demographic characteristics of the patients in both groups are summarized in **Table 1**. There were no significant differences of ASA physical status, age, sex ratio, weight, height, duration of anesthesia, duration of surgery, the patient's history and type of surgery between the two groups. There were no differences of preoperative hemodynamics parameters between the two groups. The SVV at the end of the surgery in APCO group was significantly lower than that in the control group (10.4 *vs*. 12.9%, *P*=0.002).

Comparison of fluid replacement and related-parameters

The infused colloid and total fluid volume in the APCO group were significantly higher than that in the control group (colloid volume: 775 *vs*. 487 ml, *P*<0.001; total fluid volume: 1478 *vs*. 1183 ml; *P*<0.001) (**Table 2**). No differences were found with regard to urinary output and blood loss between the two groups. The injected bolus times of norepinephrine or epinephrine were similar between two groups. The vomiting score of 1 (1 to 1) (median (interquartile range) in the control group versus 1 (0.75 to 2; *P*=0.048) in the APCO group was found. There were no significant differences of nausea scoring, postoperatively hospitalized days (10.4 *vs*. 12.2 d; *P*=0.100) and ICU stay (15.1 *vs*. 18.0 h; *P*=0.126) between the two groups. The degree of brain edema at 1 day postoperative was also not significantly different between the two groups. (3 (2, 4) vs. 3(2, 4), *P*=0.96) (**Figure 3**).

Table 2. Intraoperative and postoperative fluid replacement and related-parameters comparison with patients in both groups

Variables	APCO group (n=33)	Control group (n=30)	*P* value
Intraoperatively infused volume (ml)			
Crystalloids (normal saline)	471±100	459±147	0.700
Colloids	775±236	487±243	<0.001
Blood (ml)	0 [0, 400]	0 [0, 400]	1.000
Total	1478±312	1183±294	<0.001
Urine output	774±351	804±394	0.752
Estimated blood losses	435±92	420±135	0.617
Transfused in operation room	4 (12.1%)	4 (13.3%)	1.000
Postoperative fluids replacement (24 h)			
Crystalloids	2667±623	2508±665	0.334
Colloids	500 [0, 1000]	500 [0, 1000]	1.000
Blood	0 [0, 400]	0 [0, 800]	1.000
Urine output	2495±727	2321±818	0.377
Preoperative diuretics	3/30	4/26	0.894
Intraoperative vasoactive drugs	0 [0, 1]	1 [1, 2]	0.502
Nausea scoring	1 [1, 2]	1 [1, 2]	0.063
Vomiting scoring	1 [1, 1]	1 [0.75, 2]	0.048
The degree of brain edema	3 [2, 4]	3 [2, 4]	0.960
ICU stay (h)	15.1±8.1	18.0±5.5	0.100
Postoperative hospitalization (days)	10.4±3.9	12.2±5.1	0.126

Nausea scoring: 0 = excellent, no nausea; 1 = no nausea at rest but movement; 2 = intermittently nausea at rest but accentuated at movement; 3 = nausea at rest. Vomiting scoring: 1 = no vomiting; 2 = minimal vomiting, 1 to 2 times/day; 3 = serious vomiting, 3 to 5 times/day; 4 = sever vomiting, in excess of 5 times/day.

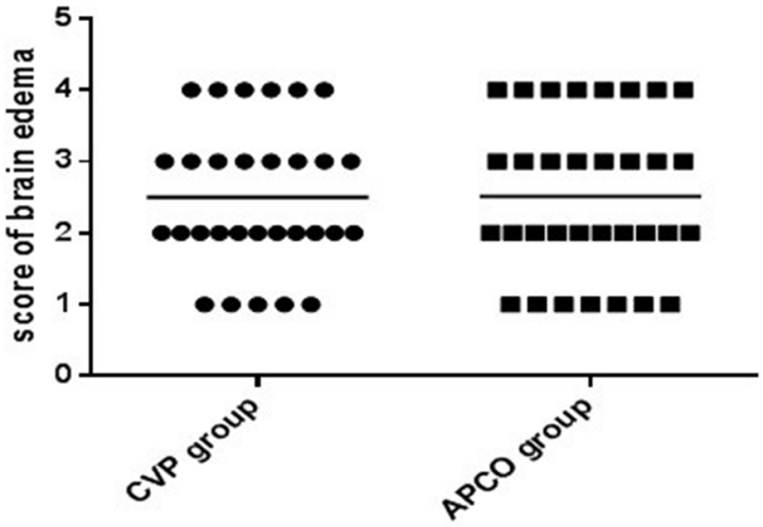

Figure 3. The scatter diagram of score of brain edema at 1 day postoperative. The score of brain edema: 1 = no brain edema; 2 = brain edema without ventricular compression; 3 = brain edema with ventricular compression, and without mid line shift; 4 = brain edema with ventricular compression and mid line shift.

Biochemical measurements

The lactate concentration at the end of surgery in the patients of APCO group was significantly decreased compared with baseline ($P<0.001$). Such difference in control group was not found. Lactate concentration by the end of the operation in APCO group was much lower than that in the control group (0.91 *vs*. 1.31 mmol/l; $P<0.001$). There were no significant differences of BE, pH, transaminase, Cr and urea value between the two groups (**Table 3**).

Comparison of postoperative complications

There were significantly less total postoperative complications in APCO group compared with control group (4 *vs*. 11; $P=0.047$) (**Table 4**).

Discussion

Optimization of perioperative fluid management includes fixed crystalloid administration to compensate extravascular losses and avoid fluid excess, individualized goal-directed colloids administration to maintain a maximal stroke volume (SV) [10]. Our data indicated that intraoperative fluid management optimization with Vigileo/FloTrac-related SVV monitor was beneficial for maintaining hemodynamic stability during operation, reducing blood lactate concentration at the end of

Table 3. Biochemical measurements (mean ± SD)

Index	Group	n	Baseline	Incision of dura mater	The end of surgery	First postoperative 24 hrs
Lactate (mmol/L)	APCO	33	1.26±0.48	1.00±0.41	0.91±0.25*	1.26±0.50
	Control	30	1.33±0.63	1.18±0.50	1.31±0.46	1.43±0.61
BE (mmol/L)	APCO	33	1.21±1.73	-0.064±1.70	-0.22±1.76	0.02±1.81
	Control	30	0.77±1.52	-0.68±1.55	-0.51±1.61	-0.46±1.61
ALT (IU/L)	APCO	33	20±14	17±14	17±13	16±11
	Control	30	20±15	18±14	16±14	16±13
AST (IU/L)	APCO	33	20±9	17±7	18±7	24±11
	Control	30	20±8	18±8	19±10	22±9
Cr (μmol/L)	APCO	33	50±11	50±11	51±11	50±13
	Control	30	53±10	52±11	53±10	53±10
Urea (mmol/L)	APCO	33	4.76±1.69	4.60±1.70	4.37±1.49	3.41±1.26
	Control	30	4.31±0.96	4.26±0.98	4.12±0.94	3.58±1.14
pH	APCO	33	7.43±0.03	7.42±0.03	7.43±0.04	7.38±0.04
	Control	30	7.43±0.02	7.42±0.04	7.42±0.05	7.38±0.03
GLU (mmol/L)	APCO	33	5.7±0.6	5.4±0.6*	5.5±0.7	7.8±1.9
	Control	30	6.0±1.0	5.9±1.1	5.9±1.0	8.2±1.8

BE, base excess; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GLU, glucose. *P<0.001 APCO group vs. control group.

Table 4. The comparison of postoperative complications and numbers of patient with complications between two groups

Postoperative complications		APCO group	Control group	P value
Lung infection	Chest X-ray, WBC>10×10^9/L or <4×10^9/L			
	Clinical diagnose	0	1	0.476
Wound infection/dehiscence	The changes of heart rate or rhythm which need intervention	0	1	0.476
Arrhythmias	SBP≤90 mmHg or MAP≤30% baseline	0	2	0.223
	Mask or nasal >24 hrs, re-intubation			
	UO <500 ml/d or required dialysis			
Hypotension	Transaminase≥80 IU/L and TBIL≥2 mg/dl; Transami-Nase≥200 IU/L or TBIL≥3 mg/dl	2	4	0.581
NIV support	CCT	2	3	0.745
Renal dysfunction		0	0	
Hepatic dysfunction		0	0	
Stroke		0	0	
Total number		4	11	0.047
Number (percentage) of patients with complications		3 (9.1%)	8 (26.7%)	0.133

NIV, Non-invasive ventilator; UO, urine output; TBIL, total bilirubin; CCT, cranial computed tomography.

operation, reducing postoperative complications, postoperative hospitalization and ICU stay in patients undergoing neurosurgery.

Although previous study has demonstrated that the Pulse index Continuous Cardiac Output (PiCCO) system may be better off to evaluate fluid responsiveness in neurosurgical patients, the device has not been widely applied in clinical practice [11]. The FloTrac/Vigileo device is a minimally invasive device and easy to set up [12, 13], which needs only arterial pressure monitoring access. SV derived from arterial waveform and demographic data could be rapidly calculated without external calibration. Therefore, we decide to use the SVV derived from FloTrac/Vigileo as the target of fluid responsiveness in this study. De Backer et al. [14] reported that the third-generation FloTrac/Vigileo (version 3.0 or higher) device was more

accurate than previous versions. The new software (version 3.02) provided substantial improvements over the previous versions and refinements, which increased this technology's reliability [15]. Thus, the third-generation device was used in our study for obtaining reliable data.

Previous researches have showed that the SVV can predict fluid responsiveness in patients during surgery. Derichard et al. [16] has reported that the optimal threshold value for SVV was 12%. However, the optimal cut-off value for $SVV_{FloTrac}$ is still uncertain. Hofer et al. [8] has shown that the cut-off value of SVV with FloTrac/Vigileo was 9.6% in the patients undergoing elective cardiac surgery. A recent research has proposed that the SVV value more than 11.5% can be used to predict positive responsiveness to volume loading in the patients with brain surgery [9]. Taking together, higher SVV value is associated with severer hypovolemic status [17]. Therefore, we set used the cut-off value of SVV more than 12% as the goal of SVV-guided fluid management in this study.

Forget et al. [18] has reported that the average amount of SVV-guided fluid infusion was much higher. In other goal-directed therapy (GDT) researches, this finding was attributed to the colloids replacement [19-21]. Benes et al. [22] has found that there were much more colloids administered in the GDT group. In the present study, infused colloids volume in the APCO group was also higher than control group. The difference may be explained by the different goal-directed fluid management strategy. (Benes et al. SVV<10% vs. ours: SVV≤12%). There was a positive correlation between fluid balance and ICP [23]. Although fluid was higher than control group, there was no statistically significant difference in degrees of brain edema at the fist day postoperative.

Adequate intravascular volume is crucial to maintain tissue perfusion. Lactate is a sensitive variable of organ perfusion. Lactate level can be improved by the optimization of the fluid status and cardiac preload [5, 21]. GDT fluid management by dynamic variables can decrease intraoperative and postoperative lactate levels [18]. Excessive fluid restriction may increase intraoperative lactate level [24]. Chytra et al [25] showed that GDT fluid management with lower lactate level was associated with a reduction of infectious complications.

In accordance with our results, Benes et al. [22] has also reported that SVV-guided fluid management could reduce postoperative complications. Mayer et al. [26] has also demonstrated that SVV-guided fluid optimal management with FloTrac/Vigileo device was associated with a lower incidence of complications. Lopes et al. [21] has found that pulse pressure variation kept below 10% by colloid could significantly reduce the complications. The incidence of postoperative complication and the number of patients with complication in our study were lower than other trials [26]. Possible explanation for this difference is the higher numbers of chronic diseases and older patients in other trails. Although there were no significant differences of postoperative hospitalization and ICU stay between the two groups, a declining trend could be found in the APCO group.

There were several limitations in present study. Firstly, the accuracy of FloTrac system is influenced by phenylephrine and ephedrine administration and transient hemodynamic change [27, 28]. The changes of parameters and hemodynamic lasting for more than one minutes were considered to be meaningful in order to minimize the flaws by vasoactive agent and other factors. Secondly, Westphal et al. [29] showed that pharmacologic vasodilation (relative hypovolemia) can induce dynamic variables amplification similar to hypovolemia. The inhalant or intravenous anesthetic agents which have vasodilatory properties could induce changes of dynamic variables. In addition, the rate of physiological requirement of crystalloid infusion and the loading volume of 50 ml in each time may lead to the effect of artificial restrictive fluid infusion, though it is not serious impact on patients.

Conclusion

In conclusion, the incidence of postoperative complications and lactate levels were decreased in the patients with fluid management guided by SVV. Patients in APCO group are given more colloids. SVV-guided fluid man-

agement may reduce the risk of excessively restrictive fluid infusion without additional risk of brain edema.

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Disclosure of conflict of interest

None.

Address correspondence to: Tianlong Wang, Department of Anesthesiology, Xuanwu Hospital, Capital Medical University, No. 45 Changchun Street, Xicheng District, Beijing 100053, China. Tel: 0086-10-83198899; Fax: 0086-10-83198899; E-mail: tianlongwang@cntv.cn

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