

# The Effect of Goal-directed Fluid Management based on Stroke Volume Variation on ICU Length of Stay in Elderly Patients Undergoing Elective Craniotomy: A Randomized Controlled Trial

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## ABSTRACT

**Background:** Inappropriate fluid management during neurosurgery can increase postoperative complications. In this study, we aimed to investigate the effect of goal-directed fluid therapy using stroke volume variation (SVV) in elderly patients undergoing elective craniotomy.

**Materials and methods:** We randomized 100 elderly patients scheduled for elective craniotomy into two groups: goal-directed therapy (GDT,  $n = 50$ ) group and conventional group ( $n = 50$ ). Fluid management protocol using SVV was applied in the GDT group. Decisions about fluid and hemodynamic management in the conventional group were made by the anesthesiologist. Perioperative variables including fluid balance, lactate level, and intensive care unit (ICU) length of stay were assessed.

**Results:** There was no significant difference in ICU length of stay between the two groups: 14 (12, 16.75) hours in GDT group vs 15 (13, 18) hours in control group ( $p = 0.116$ ). Patients in the GDT group received a significantly less amount of crystalloid compared with the control group: 1311.5 (823, 2018) mL vs 2080 (1420, 2690) mL ( $p < 0.001$ ). Our study demonstrated a better fluid balance in the GDT group as 342.5 (23, 607) mL compared with the conventional group 771 (462, 1269) mL ( $p < 0.001$ ).

**Conclusion:** Intraoperative goal-directed fluid management based on SVV in elderly patients undergoing elective craniotomy did not reduce the ICU length of stay or postoperative complications. It did result in an improved fluid balance with no evidence of inadequate organ perfusion.

**Clinical trial registration number:** TCTR20190812003.

**Keywords:** Craniotomy, Elderly, Fluid therapy, Goal-directed therapy, Length of ICU stay, Stroke volume variation.

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## HIGHLIGHTS

Geriatric populations are vulnerable to complications from inappropriate fluid management. Although, the intraoperative goal-directed fluid management based on stroke volume variation (SVV) did not reduce the ICU length of stay or postoperative complications in elderly patients undergoing craniotomy. However, it resulted in better fluid balance with no evidence of inadequate organ perfusion.

## INTRODUCTION

Hypovolemia is a common problem in neurosurgical patients. Various factors, such as preoperative fasting, inadequate fluid intake, use of diuretics to treat intracranial hypertension, and intraoperative blood loss can contribute to intravascular volume depletion which can lead to systemic hypotension, inadequate cerebral perfusion, and poor neurologic outcomes.<sup>1-3</sup> Hypervolemia can also cause harmful consequences in neurosurgical patients such as increased postoperative cardiopulmonary complications, increased hospital length of stay, and brain edema, especially among patients with impaired blood brain barrier.<sup>3-5</sup>

The general principle of fluid management in neurosurgical patients is the maintenance of normovolemia to sustain cerebral perfusion pressure. Fluid administration should be properly managed with hypovolemic patients. Conventional static hemodynamic variables, such as heart rate, blood pressure,

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**Conflict of interest:** None

central venous pressure, or pulmonary artery occlusive pressure are monitored to predict fluid responsiveness in hypotensive patients. However, these static parameters have inadequate sensitivity resulting in erroneous interpretation of volume status and inappropriate fluid administration.<sup>6-8</sup> Many tools and variables have been developed to better detect fluid-responsive patients. Previous studies have found that dynamic variables can provide fast and real-time information on fluid status and have improved

sensitivity for detecting fluid responsiveness compared with static variables.<sup>9,10</sup> These dynamic variables can also prevent improper fluid administration in patients whose cardiac output cannot be augmented by fluid therapy. The European Society of Intensive Care Medicine recommends that fluid therapy in patients experiencing shock should be conserved for fluid-responsive patients and the use of dynamic variables over static variables is also recommended to detect fluid responsiveness.<sup>11</sup>

Stroke volume variation is one of the dynamic variables that can identify fluid-responsive patients.<sup>12,13</sup> This parameter results from the change in stroke volume during respiratory cycles. SVV will increase in hypovolemic patients and data from previous studies indicate that an SVV of more than 12% is associated with intravascular volume depletion. Stroke volume variation can be obtained from an uncalibrated pulse contour analysis device called the FloTrac system. With respect to reliability, hemodynamic variables obtained from the FloTrac system were compared with the variables obtained from the intermittent thermodilution using a pulmonary artery catheter in patients undergoing cardiac surgery. The Bland-Altman analysis of the cardiac output assessed by the FloTrac system showed a comparable mean bias and limits of agreement when using intermittent pulmonary artery thermodilution as a reference method.<sup>14,15</sup> The result from a previous systematic review also showed similar results.<sup>16</sup>

Previous literature revealed that perioperative goal-directed therapy (GDT) using central venous pressure and central venous oxygen saturation reduced postoperative mechanical ventilation duration, frequency of inotropes changes, and acute kidney injury in cardiac surgery.<sup>17</sup> Central venous catheterization is not a routine monitoring in neurosurgery, SVV has also been used as a part of goal-directed fluid management in these patients. Mishra et al. reported that goal-directed fluid management resulted in lesser amount of fluid administration but did not show statistically significant reduction in intensive care unit (ICU) and hospital length of stay compared with the conventional fluid management in supratentorial tumor resection.<sup>18</sup> However, some studies demonstrated the benefit of the goal-directed fluid management such as lesser postoperative complications,<sup>19</sup> shorter ICU length of stay, and lower ICU costs compared with patients in the conventional group.<sup>20</sup>

Geriatric populations are vulnerable to complications from inappropriate fluid management. Although one previous study found that goal-directed fluid management in elderly patients undergoing gastrointestinal surgery could reduce the length of ICU stay,<sup>21</sup> there has been no study focusing on elderly patients undergoing elective craniotomy.

The purpose of this study was to evaluate the effect of goal-directed fluid management based on SVV in elderly patients undergoing elective craniotomy on ICU length of stay.

## MATERIALS AND METHODS

This study was a randomized controlled trial conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand, between August 2019 and March 2022. Enrollment criteria included age  $\geq 60$  years, American Society of Anesthesiologist (ASA) physical status 2–3, and scheduled for elective craniotomy with a surgical duration of more than 2 hours. We excluded patients with permanent cardiac arrhythmias, severe cardiac diseases (left ventricular ejection fraction of less than 30%), significant aortic regurgitation or stenosis, patients with body mass index of more than 35 kg/m<sup>2</sup>,

and patients needing vasopressor therapy before surgery. This study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB No. 249/62) and registered with Thai Clinical Trials Registry (TCTR20190812003). All subjects gave written informed consent.

## Study Protocol

### Preoperative Period

The patients were allocated into two groups using block of four randomization: GDT group and conventional group. Allocation was performed by the research assistant who was not involved in the study. The allocation results were concealed in an opaque envelope and were opened before surgery. The surgeon and research assistant who recorded the preoperative and postoperative data were blinded to the group allocation. Baseline characteristics, including age, sex, weight, height, underlying comorbidity, ASA physical status, diagnosis, operation, tumor size, and Hunt and Hess grading were recorded. A P-POSSUM score was also calculated and recorded to determine the operative risk for each subject.<sup>22</sup> The Edmonton frail scale was also recorded.<sup>23</sup> (The detailed description regarding P-POSSUM score and Edmonton frail scale are available in the supplemental digital content 1 and 2).

### Intraoperative Period

Standard ASA monitoring including electrocardiogram, noninvasive blood pressure, pulse oximetry, and end tidal carbon dioxide monitoring were applied to all patients. Invasive blood pressure monitoring via radial arterial cannulation using 20 G catheter was inserted after anesthesia induction. For the GDT group, the FloTrac sensors (Edwards Lifesciences, Irvine, CA, USA) were connected to the arterial line. Propofol 1.5–2.5 mg/kg and fentanyl 0.5–1  $\mu$ g/kg were used for induction. The tracheal intubation was facilitated using cisatracurium 0.15–0.2 mg/kg. Desflurane in air were used for the maintenance of anesthesia and the minimal alveolar concentration was kept between 1 and 1.4 MAC. Intravenous infusion of propofol was allowed when indicated. Cisatracurium was given to keep train of four count at less than 1. Fentanyl 2–5  $\mu$ g/kg was titrated for analgesia throughout the surgery. Mannitol 0.5–1 gm/kg was given when indicated.

### Study Interventions

Regarding the fluid management protocol, all patients received acetate Ringer's solution 2 mL/kg (ideal body weight) from 6.00 a.m. on the day of surgery continuing until the end of surgery. The fluid and hemodynamic management for patients in the GDT group was guided by our fluid protocol based on SVV. The patients in this group received acetate Ringer's solution 100 mL bolus when SVV was more than 12% and cardiac index was less than 2.5 L/min/m<sup>2</sup>. The fluid bolus was done every 5 minutes until the SVV was 12% or less. In cases of hypotension (mean arterial pressure of less than 65 mm Hg), vasopressor therapy was recommended if SVV was more than 12% and the cardiac index was more than 2.5 L/min/m<sup>2</sup>. Inotrope was recommended for the treatment of hypotension if SVV was less than 12% and the cardiac index was less than 2.5 L/min/m<sup>2</sup>. The fluid protocol is shown in supplemental digital content 3. In the conventional group, the decision about fluid and hemodynamic management was left to the discretion of the attending anesthesiologist. For both groups, a blood transfusion was recommended when hematocrit was less than 30% or blood loss exceeded allowable blood loss.

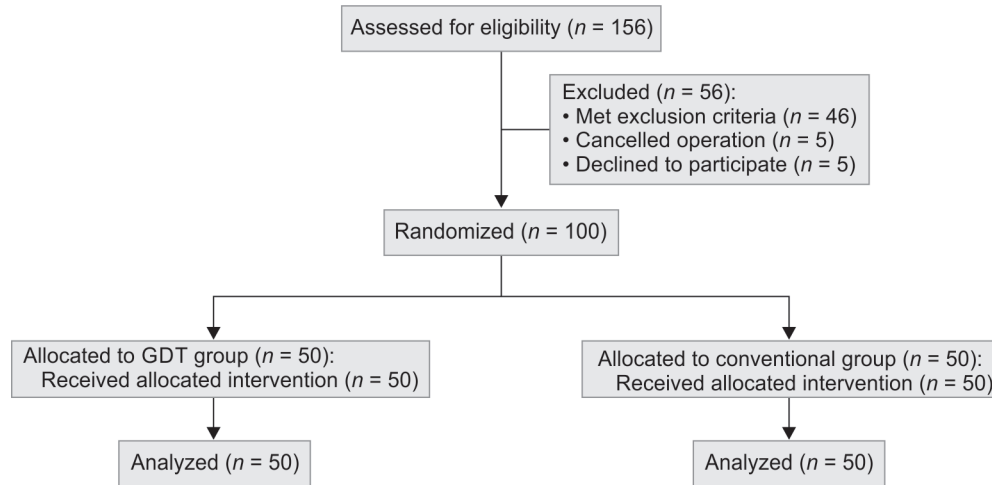


Fig. 1: The study flowchart

### Data Collection

Baseline blood pressure, heart rate, cardiac index, and SVV were recorded. Arterial blood was sent for arterial blood gas analysis and lactate levels after arterial line cannulation were completed. Fluid intake and output were recorded hourly. Hypotensive events and treatment of hypotension were also recorded. At the end of the operation, arterial blood gas analysis results, lactate level, total fluid balance, and operative time were recorded. Brain relaxation was graded by the surgeon and was classified on a 1–4 scale (relax = 1, satisfied = 2, firm = 3 or bulging = 4).

Fluid balance in the first 24 hours, ICU, and hospital length of stay (supplemental digital content 4), intubation time (immediately after surgery until extubation), postoperative complications, and mortality rate were recorded during the postoperative period.

### Statistical Analysis

Based on the results from a previous study,<sup>18</sup> a median ICU length of stay of 6 days was used to calculate the sample size with an aim to detect 2 days difference in ICU length of stay. With type I error of 5% and type II error of 20%, the calculated sample size was 43 patients per group. To compensate for a 10% loss during follow up, 50 patients per group were determined to be needed.

Descriptive statistics, including frequency and percentage, were used for categorical variables. Normality was checked using the Kolmogorov–Smirnov test. Continuous variables were reported as mean  $\pm$  standard deviation for normally distributed variables and median (interquartile range or IQR; Q1, Q3) for non-normally distributed variables. Comparisons of categorical variables between patients in control and GDT group were performed using Chi-square test or Fisher’s exact test. Continuous variables were compared using independent *t*-test or Mann–Whitney test. For all tests performed, a *p*-value  $< 0.05$  was considered statistically significant. STATA/IC 14.0 was used to perform all statistical analyses.

## RESULTS

One hundred patients were randomized into two groups. Patients were equally assigned to GDT group and control group (Fig. 1). Baseline patient characteristics showed no significant differences between the two groups including preoperative fluid intake, P-POSSUM score, and Edmonton frail scale (Table 1). Hemodynamic

variables and laboratory data at baseline and immediately after surgery are given in Table 2. There were also no significant differences between the two groups.

### Outcome Variables

Results showed that the ICU length of stay was comparable between two groups: GDT group [14 (12, 16.75) hours] vs control group [15 (13, 18) hours] ( $p = 0.116$ ). The hospital length of stay was also similar between groups: 7 (6, 10) days in the GDT group vs 8 (6, 11) days in the control group ( $p = 0.582$ ). There was no difference in intubation time between both groups; 0 (0, 0) hours in GDT group vs 0 (0, 0) hours in the control group ( $p = 0.697$ ) (Table 3).

Patients in the GDT group received significantly less crystalloid compared with the control group 1311.5 (823, 2018) mL vs 2080 (1420, 2690) mL ( $p < 0.001$ ). Patients in the GDT group also had better fluid balance than in the control group 342.5 (23, 607) mL vs 771 (462, 1269) mL ( $p < 0.001$ ). There were no significant differences in urine output and blood loss when comparing the GDT group with the control group: 700 (460, 1005) mL vs 877.5 (620, 1200) mL ( $p = 0.069$ ) and 350 (150, 650) mL vs 375 (200, 800) mL ( $p = 0.529$ ), respectively. Patients in the GDT group received significantly more ephedrine than the control group: 18 (36%) vs 28 (56%) ( $P = 0.045$ ) (Table 4).

Brain relaxation scores were found comparable between the two groups (Table 4). There were also no significant differences in lactate levels between two groups at the end of surgery ( $2.46 \pm 1.37$  in GDT vs  $2.31 \pm 1.33$  in control;  $p = 0.597$ ).

The postoperative fluid balance was also similar between groups. No significant differences were observed in the occurrence of postoperative complications and mortality rate between groups (Table 5).

## DISCUSSION

In this study, we were unable to demonstrate a reduction in the ICU length of stay using goal-directed fluid therapy based on SVV in elderly patients undergoing elective craniotomy. There were also no significant differences in postoperative complications between our two groups. Patients in GDT group did receive a significantly lower amount of crystalloid during the intraoperative period and exhibited better fluid balance.

**Table 1:** Baseline characteristics of the patients

Variables	GDT (n = 50)	Conventional (n = 50)	p-value
Age (years)	66.4 ± 5.33	67.74 ± 5.44	0.216
Sex			
Female	18 (36%)	24 (48%)	0.224
Male	32 (64%)	26 (52%)	
Diagnosis			
Supratentorial mass	34 (68%)	32 (64%)	0.673
Infratentorial mass	11 (22%)	14 (28%)	0.488
Cerebral aneurysm	5 (10%)	4 (8%)	0.727
Operation			
Tumor removal	45 (90%)	46 (92%)	1
Clipping aneurysm	5 (10%)	4 (8%)	
Weight (kg)	60.78 ± 10.71	62.7 ± 11.05	0.379
Height (cm)	158.02 ± 8.51	159.7 ± 7.15	0.288
BMI (kg/cm <sup>2</sup> )	24.06 ± 3.22	24.67 ± 4.29	0.428
ASA physical status			
2	45 (90%)	43 (86%)	0.538
3	5 (10%)	7 (14%)	
P-POSSUM physiological score	18.1 ± 3.38	17.6 ± 3.14	0.445
P-POSSUM operative severity score	12.28 ± 3.45	13.16 ± 3.01	0.178
Edmonton frail scale			
Not frail	15 (30%)	11 (22%)	0.637
Vulnerable	15 (30%)	20 (40%)	
Mild frailty	13 (26%)	14 (28%)	
Moderate frailty	7 (14%)	5 (10%)	
GCS	15 ± 0	14.98 ± 0.14	0.322
Underlying disease			
Hypertension	30 (60%)	30 (60%)	1
Diabetes mellitus	9 (18%)	13 (26%)	0.334
Malignancy	8 (16%)	9 (18%)	0.79
Previous stroke	6 (12%)	4 (8%)	0.505
Preoperative dexamethasone	36 (72%)	41 (82%)	0.235
Tumor size (cm)	3.89 ± 1.65	3.81 ± 1.64	0.816
Number of tumors			
1	44 (88%)	45 (90%)	0.987
2	1 (2%)	1 (2%)	
Aneurysm size (cm)	0.39 (0.14, 0.7)	0.25 (0.14, 1)	0.724
WFNS	5 (10%)	4 (8%)	0.727
Hunt and Hess scale			
0	4 (8%)	3 (6%)	0.358
1	1 (2%)	0 (0%)	
2	0 (0%)	1 (2%)	
Fisher scale			
0	0 (0%)	1 (2%)	0.308
1	4 (8%)	2 (4%)	
3	1 (2%)	0 (0%)	
4	0 (0%)	1 (2%)	
Preoperative fluid administration (mL)	474.28 ± 233.22	527.82 ± 244.01	0.265

Value presented as mean ± SD, or median (IQR) and *n* (%). *p*-value corresponds to independent *t*-test or Mann-Whitney test and Chi-square test. ASA, indicates American Society of Anesthesiologists; GCS, Glasgow Coma Score; P-POSSUM, Portsmouth-POSSUM score; WFNS, World Federation of Neurosurgeon Grading Scale

**Table 2:** Hemodynamic variables and laboratory data at baseline and end of surgery

Variables	Baseline			End of surgery		
	GDT (n = 50)	Control (n = 50)	p-value	GDT (n = 50)	Control (n = 50)	p-value
MAP (mm Hg)	87.56 ± 16.95	83.58 ± 15.47	0.223	86.18 ± 13.36	89.5 ± 16.85	0.278
Heart rate (bpm)	62.02 ± 12.96	67.22 ± 14.09	0.058	76.06 ± 14.27	83.82 ± 17.23	0.016*
Cardiac index (L/min/m <sup>2</sup> )	2.66 ± 0.62	-	-	2.82 ± 0.68	-	-
SVV	7.82 ± 3.82	-	-	10.26 ± 2.81	-	-
PH	7.31 ± 0.85	7.44 ± 0.07	0.292	7.43 ± 0.06	7.41 ± 0.04	0.058
PaCO <sub>2</sub> (mm Hg)	31.75 ± 2.64	31.1 ± 3.21	0.275	32.73 ± 3.36	33.77 ± 3.26	0.121
PaO <sub>2</sub> (mm Hg)	228.26 ± 45.51	234.61 ± 60.31	0.554	214.88 ± 54.62	218.5 ± 57.39	0.747
P/F ratio	474.64 ± 97.57	468.6 ± 118.68	0.781	458.45 ± 103.46	432.89 ± 106.24	0.226
HCO <sub>3</sub> <sup>-</sup>	21.56 ± 1.76	21.01 ± 1.86	0.133	22.14 ± 1.73	21.58 ± 1.92	0.131
Base excess	-2.83 ± 1.89	-3.51 ± 2.05	0.088	-2.46 ± 1.9	-3.26 ± 2.33	0.061
Lactate	1.6 ± 0.79	1.59 ± 0.74	0.990	2.46 ± 1.37	2.31 ± 1.33	0.597
Hematocrit (%)	38.16 ± 2.92	37.91 ± 4.19	0.728	35.32 ± 5.82	35.03 ± 3.61	0.770
Hemoglobin (gm/dL)	12.73 ± 1.07	12.63 ± 1.36	0.678	12.01 ± 1.21	11.63 ± 1.18	0.113

Value presented as mean ± SD. p-value corresponds to independent t-test. p < 0.05

**Table 3:** Length of ICU stay; hospital stay and intubation time

Variables	GDT (n = 50)	Conventional (n = 50)	p-value
ICU length of stay (hours)	14 (12, 16.75)	15 (13, 18)	0.116
Hospital length of stay (days)	7 (6, 10)	8 (6, 11)	0.582
Intubation time (hours)	0 (0, 0)	0 (0, 0)	0.697

Value presented as median (IQR). p-value corresponds to Mann-Whitney test

**Table 4:** Intraoperative data

Variables	GDT (n = 50)	Conventional (n = 50)	p-value
Crystalloid (mL)	1311.5 (823, 2018)	2080 (1420, 2690)	<0.001*
Colloid (mL)	0 (0, 0)	0 (0, 0)	0.122
Packed red cells (mL)	0 (0, 0)	0 (0, 205)	0.163
Fresh frozen plasma (mL)	0 (0, 0)	0 (0, 0)	1.000
Urine output	700 (460, 1005)	877.5 (620, 1200)	0.069
Fluid balance	342.5 (23, 607)	771 (462, 1269)	<0.001*
Estimated blood loss (mL)	350 (150, 650)	375 (200, 800)	0.529
Hypotension	1 (0, 3)	2 (0, 5)	0.144
Ephedrine	18 (36%)	28 (56%)	0.045*
Norepinephrine	15 (30%)	12 (24%)	0.499
Operative time (hours)	240.8 ± 106.59	247.59 ± 82.4	0.725
Anesthesia time (hours)	308.57 ± 108.62	310.22 ± 91.82	0.935
Brain relaxation score			
1	37 (74%)	29 (58%)	0.191
2	10 (20%)	12 (24%)	
3	3 (6%)	7 (14%)	
4	0 (0%)	2 (4%)	

Value presented as mean ± SD. or median (IQR) and n (%). p-value corresponds to independent t-test or Mann-Whitney test and Chi-square test. \*p < 0.05

**Table 5:** Postoperative data

Variables	GDT (n = 50)	Conventional (n = 50)	p-value
Crystalloid (mL)	1821.5 (1338, 2063)	1761.5 (1346, 2208)	0.956
Colloid (mL)	0 (0, 0)	0 (0, 0)	0.080
Packed red cells (mL)	0 (0, 0)	0 (0, 0)	0.648
Fresh frozen plasma (mL)	0 (0, 0)	0 (0, 0)	0.317
Urine output (mL)	1337.5 (960, 1900)	1402.5 (1040, 1765)	0.855
Fluid balance	308 (-334, 850)	361 (-195, 851)	0.749
GCS	15 ± 0	14.71 ± 1.34	0.142
Surgical complication	2 (4%)	2 (4%)	1
Reoperation	1 (2%)	1 (2%)	1
Cardiac complication	1 (2%)	1 (2%)	1
Respiratory complication	0 (0%)	1 (2%)	0.315
AKI	0 (0%)	1 (2%)	0.315
Other complications	1 (2%)	4 (8%)	0.169
seven-day mortality	0 (0%)	0 (0%)	1
Twenty-eight-day mortality	0 (0%)	0 (0%)	1

Value presented as mean ± SD, or median (IQR) and n (%). p-value corresponds to independent t-test or Mann-Whitney test and Chi-square test. AKI, acute kidney injury; GCS, Glasgow Coma Score

To the best of our knowledge, this is the first study focusing on the effect of goal-directed fluid therapy based on SVV in elderly patients scheduled for craniotomy. A previous study by Luo et al.<sup>20</sup> found that the goal-directed fluid management reduced the ICU length of stay, whereas our study did not find a similar result. This disparity in findings could be explained by differences in the fluid management protocol. Luo et al. chose an SVV of 15% as a cut-off value for fluid responsiveness, resulting in greater restrictions in the fluid management strategy which could have affected the outcome. The cut-off values of SVV can range from 9.5 to 13%.<sup>24–26</sup> We chose an SVV of 12% instead of 15% to avoid the risk of hypovolemia that can lead to cerebral hypoperfusion.

A study by Zheng et al.<sup>21</sup> reported a significant reduction in the intraoperative fluid administration in the goal-directed therapy group, as reported in our study and in the study by Luo et al.<sup>20</sup> This finding showed that the goal-directed fluid management could reduce intraoperative fluid intake and subsequently could improve fluid balance. In addition, our findings suggested that goal-directed fluid therapy could maintain adequate organ perfusion with less fluid intake as the lactate levels did not significantly differ between the two groups. Improved fluid balance could be beneficial in patients who are prone to fluid overload such as patients with severely impaired cardiac function or chronic kidney disease. Further study might be needed in these patients.

A previous study among aneurysmal subarachnoid hemorrhage patients by Bloria et al.<sup>27</sup> also reported that the implementation of goal-directed fluid therapy could reduce intraoperative fluid intake. Results of this study failed to show a reduction in the ICU length of stay and postoperative complication rates. The result was similar to our study as we could not demonstrate the beneficial effect of GDT on the ICU length of stay. We believe that this may be due to the fact that our patients were considered healthy according to the preoperative severity score and the amount of blood loss was not high enough to create a large volume shift. Further research on patients with multiple comorbidities or higher risk surgery might be needed.

Although Ramming et al.<sup>28</sup> observed a significant correlation between the amount of fluid and cerebral edema in a porcine model of brain injury, we did not find such effect in our study as the brain relaxation scores were comparable between groups. However, brain relaxation scores are subjective and may not be sensitive enough to detect a rise in intracranial pressure. Furthermore, Hasanin et al. found that a lower fluid intake in the GDT group resulted in a higher P/F ratio.<sup>29</sup> They proposed this to be a result of less extravascular lung water and less lung congestion in the GDT group. However, we could not demonstrate the same effect in our study.

Results from a study by Benes et al. showed that fewer patients in the GDT group had developed postoperative complications.<sup>30</sup> Similar results have been reported by Luo et al.<sup>20</sup> The reduction of postoperative complications may be explained by a rapid recognition of hemodynamic derangements and prompt treatment of patients in the GDT group.<sup>30</sup> However, such findings were not observed in our study. This could be a result of the inadequate power to detect postoperative complications.

Our study was not without limitations. Firstly, this study was a single-center study conducted at a large tertiary hospital which might be related to low amount of blood loss due to experienced neurosurgeon. Furthermore, the target population was comprised of elderly patients. We believe that generalizability may be affected by these limitations. Secondly, the ICU length of stay reported in this study appeared to be shorter compared with the previous study which we used for initial sample size estimation. Consequently, this study could possess limited statistical power to detect the difference in the ICU length of stay and further larger study might be required to demonstrate any disparities of this crucial outcome. Thirdly, our study did not perform central venous catheterization to measure the central venous pressure, which prevented us from obtaining the systemic vascular resistance value. We used a less invasive method to obtain the cardiac index and SVV. We also attempted to conduct a pragmatic trial. We did not perform central venous catheterization as a routine procedure in neurosurgical patients because most of the patients did not need it. An adverse

event such as pneumothorax can adversely affect the intracranial pressure by reducing the cerebral venous drainage. Finally, the anesthesiologists were not blinded to the treatment allocation. Nonetheless, the primary outcome was an objective outcome, and the outcomes were recorded by a blinded research assistant. Blinding should not have had a significant effect on the outcome measurements.

## CONCLUSION

The intraoperative goal-directed fluid management based on SVV in elderly patients undergoing elective craniotomy did not reduce the ICU length of stay or postoperative complications. However, it resulted in better fluid balance with no evidence of inadequate organ perfusion.

## Availability of Data and Materials

The data of this study are not publicly available due to limitation of ethical approval involving the patient data and anonymity but are available on reasonable request from the corresponding author.

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## SUPPLEMENTARY MATERIALS

All the supplementary materials are available on the website of [www.ijccm.org](http://www.ijccm.org).

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