Acta Neurochirurgica (2019) 161:1317–1324
https://doi.org/10.1007/s00701-019-03922-4

ORIGINAL ARTICLE - NEUROSURGICAL INTENSIVE CARE

Transpulmonary thermodilution monitoring–guided hemodynamic management improves cognitive function in patients with aneurysmal subarachnoid hemorrhage: a prospective cohort comparison

Achmet Ali[1] · Taner Abdullah[1] · Mukadder Orhan-Sungur[1] · Gunseli Orhun[1] · Elif Aygun[1] · Evren Aygun[1] · Pulat Akin Sabanci[2] · Yavuz Aras[2] · Ibrahim Ozkan Akinci[1]

Received: 13 February 2019 / Accepted: 18 April 2019 / Published online: 18 May 2019

Abstract

Background The effects of goal-directed hemodynamic management using transpulmonary thermodilution (TPT) monitor on the cognitive function of patients with aneurysmal subarachnoid hemorrhage (aSAH) remain unclear. The present study aimed to determine whether hemodynamic management with TPT monitor provides better cognitive function compared with standard hemodynamic management.

Methods Patients with aSAH who were admitted to the intensive care unit in 2016 were assigned to cohort 1, and those admitted in 2017 were assigned to cohort 2. In cohort 1, hemodynamic and fluid management was performed in accordance with the traditional pressure-based hemodynamic parameters and clinical examination, whereas in cohort 2, it was performed in accordance with the TPT monitor-measured flow-based parameters. The incidence of delayed cerebral ischemia (DCI) and pulmonary edema (PE) was determined. The functional outcome of patients was assessed using the modified Rankin scale (mRS) score and Montreal cognitive assessment (MoCA) test at 1 year following aSAH.

Results Cohort 1 included 45 patients and cohort 2 included 39 patients who completed the trial. The incidence of DCI (38% versus 26%) and PE (11% versus 3%) was comparable between the cohorts ($p > 0.05$). The mRS score was similar between the cohorts ($p = 0.11$). However, the MoCA score was 20.2 (19.2–21.4) and 23.5 (22.2–24.8) in cohort 1 and cohort 2, respectively ($p < 0.001$). Accordingly, the occurrence of poor MoCA score (38% versus 18%) was significantly lower in cohort 2 ($p = 0.045$).

Conclusions TPT monitor-based hemodynamic management provides better cognitive outcome than standard hemodynamic management in patients with aSAH.

Keywords Subarachnoid hemorrhage · Fluid therapy · Hemodynamic management · Cognitive function · Transpulmonary thermodilution monitor

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a life-threatening neurological condition with high mortality and morbidity [2]. Delayed cerebral ischemia (DCI) is a frequent complication of aSAH in patients who survive initial ictus. DCI typically develops within 4 to 14 days following aSAH due to arterial vasospasm, microcirculatory dysfunction, and microembolism [3, 19, 21]. The clinical features of DCI can be reversible or irreversible and progressing to cerebral infarction [23]. Therefore, the occurrence of DCI is an important risk factor for poor neurological outcome and mortality following aSAH [2]. The frequency and severity of DCI are primarily related to the characteristics and severity of initial hemorrhage and appropriate

This article is part of the Topical Collection on *Neurosurgical intensive care*

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00701-019-03922-4) contains supplementary material, which is available to authorized users.

✉ Achmet Ali
a_achmet@hotmail.com

[1] Department of Anesthesiology and Reanimation, Istanbul University, Istanbul Medical Faculty, Turgut Ozal cad. Fatih, Istanbul, Turkey

[2] Department of Neurosurgery, Istanbul University, Istanbul Medical Faculty, Istanbul, Turkey

hemodynamic management following hemorrhage [5]. Volume status, cardiac output, and mean arterial pressure (MAP) of patients directly affect cerebral perfusion. Current evidence recommends maintaining normovolemia and normal circulating blood volume for preventing DCI. Moreover, the induction of hypertension is recommended if DCI occurs [2]. Generally, conventional clinical variables, such as arterial blood pressure, heart rate (HR), central venous pressure (CVP), and fluid balance, are used to assess the volume status and hemodynamics of patients [24]. However, these traditional pressure-based parameters are insufficient for hemodynamic evaluation and do not provide adequate information on the cardiac performance and risk of pulmonary edema (PE) [6, 13]. Transpulmonary thermodilution (TPT) systems can measure flow-based hemodynamic parameters, such as cardiac index (CI), global end-diastolic index (GEDI), systemic vascular resistance index, and extravascular lung water index (ELWI). Recent studies used TPT monitor in patients with aSAH and suggested that their use could provide better hemodynamic optimization than standard monitoring methods and could potentially improve neurological outcome [10, 11, 22]. However, the effect of TPT monitor-guided hemodynamic management on long-term cognitive function remains unelucidated.

In the present prospective cohort comparison study, we aimed to compare traditional and TPT monitor-guided hemodynamic management with regard to the cognitive function of patients at 1 year following aSAH as the primary outcome, and the incidence of DCI, PE, and persistent cerebral infarct as secondary outcomes.

Materials and methods

Study design and population

This prospective cohort comparison, single-center study was approved by the Ethics Committee of the Istanbul Medical Faculty, Turkey (no. 849) and conducted in accordance with the guidelines of the Helsinki Declaration. Enrollment of patients was done based on the year of admission. All patients with aSAH who were admitted to our neurosurgery intensive care unit (neuro ICU) between 2016 and 2017 were screened for the present study. Those who were admitted between January 2016 and December 2016 were assigned to cohort 1 (traditional parameter-guided hemodynamic management), and those admitted between January 2017 and December 2017 were assigned to cohort 2 (TPT monitor-guided hemodynamic management).

Fifty-six and 52 patients with aSAH were admitted to our neuro ICU in 2016 (cohort 1) and 2017 (cohort 2), respectively. Among these, 48 patients in cohort 1 and 41 patients in cohort 2 were enrolled in the study for meeting the following inclusion criteria (Fig. 1). The present study inclusion criteria were (1) age > 18 years; (2) non-traumatic SAH and the presence of an aneurysm identified on diagnostic cerebral angiography (DSA); (3) score < 4 on the informant questionnaire on cognitive decline in the elderly short form (IQCODE-SF; this questionnaire was provided to patients' relatives on the first day of admission to evaluate if the patient had dementia prior to aSAH; (4) admission to neuro ICU ≤ 2 days following ictus; (5) neuro ICU follow-up until the 14th day following aSAH; and (6) acceptance to participate.

General management of cohort 1 and cohort 2

Patients in both cohorts were evaluated with head computed tomography (CT) and CT angiography on the admission day. All patients were followed up in the neuro ICU until at least the 14th day following aSAH. Ruptured aneurysms were treated as soon as possible in the acute phase (< 4 days following ictus) using surgical clipping or coil embolization. All patients were treated with oral nimodipine 6 × 60 mg for 21 days. Hyponatremia (serum sodium level below 135 mEq/l) was

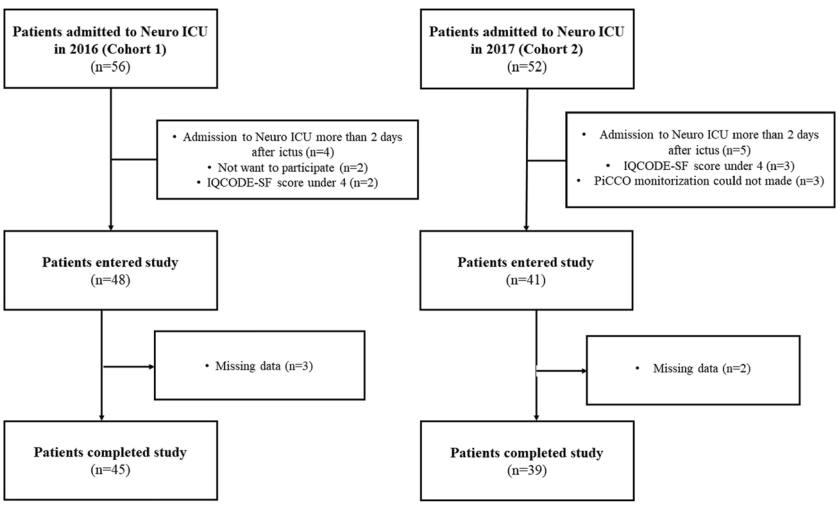

Fig. 1 Study flowchart

corrected by adding an ampule(s) of 10% NaCl (20 ml) to the main fluid bag or by adding hypertonic saline (3%) infusion or a salt capsule (0.5–3 g) to the patients' daily diet. If hyponatremia persisted and cerebral salt loss syndrome was diagnosed, fludrocortisone (300 μg/day) was administered. Blood transfusion was performed when the hematocrit level was below 30%. If patients had signs of elevated intracranial pressure and hydrocephalus, they were treated with external ventricular drainage or intermittent lumbar puncture.

Hemodynamic management of cohort 1

All patients had a 7-Fr central venous catheter inserted into the subclavian vein. During neuro ICU follow-up, normovolemia and MAP were maintained at > 80 mmHg. Volume status was determined based on CVP value, HR, arterial blood pressure, fluid balance, and clinical examination, including dry mouth, urine output, and skin turgor. Patients received a baseline infusion of crystalloid (1500–3000 ml/day). CVP value was maintained between 5 and 8 mmHg, and at least 750 ml of positive daily fluid balance was provided.

When DCI-related neurological deterioration was diagnosed, the maintenance goals were changed to CVP value of 8–12 mmHg and at least 1000 ml of positive daily fluid balance. Volume expansion was provided by additional colloid or crystalloid infusion. Further, arterial blood pressure was increased stepwise until the symptoms of DCI disappeared (maximum allowable systolic blood pressure and MAP were 200 and 140 mmHg, respectively). Noradrenaline (0.01–0.3 μg/kg/min) and/or dopamine (5–20 μg/kg/min) and/or dobutamine (5–20 μg/kg/min) were used for arterial blood pressure augmentation.

Hemodynamic management of cohort 2

Systemic hemodynamics were monitored from days of neuro ICU admission to the 14th day following aSAH using the single-indicator TPT system (PiCCO, Pulsion Medical Systems, Munich, Germany). A 4-Fr PiCCO catheter (Pulsion Medical Systems, Munich, Germany) was inserted into the femoral artery and a 7-Fr central venous catheter was inserted into the subclavian vein of all patients. Both catheters were connected to the PiCCO monitor. Measurements were obtained by injecting 15 ml of ice-cold saline (< 8 °C) bolus into the subclavian vein, with subsequent detection by the thermistor of the PiCCO catheter in the femoral artery. Baseline fluid balance and hemodynamics of patients were managed by the PiCCO monitor that aimed to keep CI value between 3 and 5 l/min/m^2, GEDI value between 680 and 800 ml/m^2, MAP value > 80 mmHg, and ELWI value ≤ 12 ml/kg.

When DCI-related neurological deterioration was diagnosed, additional colloid or crystalloid was administered to the patient to obtain 50 ml/m^2 increase in GEDI value (maximum allowable GEDI value was 900 ml/m^2). Further, CI value was increased stepwise until symptoms of DCI disappeared (maximum allowable CI value was 6 l/min/m^2). If ELWI value was > 14 ml/kg or patients showed any sign of congestive heart failure or PE, fluid loading was stopped and furosemide was administered until the symptoms disappeared, and ELWI value was reduced to 14 ml/kg. Noradrenaline (0.01–0.3 μg/kg/min) and/or dopamine (5–20 μg/kg/min) and/or dobutamine (5–20 μg/kg/min) were used for CI augmentation.

Measurements and definitions

MAP, CVP, CI, GEDI, and ELWI values were recorded three times every day. In the case of neurological deterioration, fluid loading, initiation of vasopressor and vasopressor dose change, and additional measurements were performed. The mean values were calculated for each variable in each of the following four phases: phase 1, 1–3 days following ictus; phase 2, 4–7 days following ictus; phase 3, 8–10 days following ictus; and phase 4, 11–14 days following ictus. DCI was defined as the new focal neurological deficit or global neurological deterioration (a decrease of ≥ 2 points on the Glasgow Coma Scale) lasting for more than 2 h, after the exclusion of intracranial hemorrhage, hydrocephalus, seizures, metabolic derangements, and infection, with or without the radiological signs of cerebral vasospasm [23]. In unconscious patients, DCI was diagnosed using one of the following methods: cerebral vasospasm either on transcranial Doppler, magnetic resonance angiography, or on DSA or perfusion deficit on single photon emission CT [12]. PE was defined as the PaO_2/FiO_2 ratio ≤ 300 and bilateral infiltrative shadows observed on chest radiography. Persistent cerebral infarction was diagnosed as the development of a new lesion consistent with infarction in the vascular territory of angiographic vasospasm using magnetic resonance imaging prior to hospital discharge. One year following aSAH, patients were invited to the hospital for functional outcome assessment using the Montreal cognitive assessment (MoCA) test and modified Rankin scale (mRS). The MoCA test is evaluated on a 30-point scale, and the cut-off value for cognitive impairment is 21 points [17]. A score of < 21 was considered a poor MoCA score. The MoCA test was made by a psychologist who was blinded to subjects. The mRS score ranges from 0 to 6, running from perfect health without symptoms to death, and measures the degree of disability or dependence in the daily activities of patients. mRS was assessed by one of the researchers who were not blinded to patients. A score of 0–3 was considered a good mRS score, and a score of 4–6 was considered poor.

Statistical analyses

The distribution of quantitative data was assessed using the kurtosis and skewness test. All quantitative data were normally distributed except for the duration of hospital stay. Quantitative data with normal distributions are presented as means and 95% confidence interval, while categorical data are presented as frequencies and percentages. Quantitative data between the cohorts were compared using the unpaired Student's t test. Repeated measures in cohorts were compared using the two-way repeated measures ANOVA test with Bonferroni correction. All qualitative data were compared using the chi-square (χ^2) test. The univariate and multivariate binary logistic regression analyses were performed to determine the strength of variables in predicting the number of patients with poor MoCA score in both cohorts separately. Because of fewer cases in each cohort, first, the significant relation was tested using the univariate regression analysis, and then the significant variables in the multiple regression analysis were utilized.

The main aim of the present study was to compare the MoCA score between the cohorts. In our previous studies, we found that the mean MoCA score (obtained 1 year following aSAH) was 20 ± 3 in patients who were monitored using the traditional hemodynamic parameters [1]. It was estimated that using TPT monitor-guided hemodynamic parameters during neuro ICU follow-up would provide at least a 10% (2 points) increase in the MoCA score. The two-tailed power analysis with α of 5% and β of 20% suggested that at least 36 patients were required in each cohort. The average number of patients with aSAH admitted to our neuro ICU over 5 years was 52. Assuming dropout due to missing data and inability to meet the inclusion criteria, 1 year was determined as the patient enrollment period for both cohorts. All p values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of patients

Forty-five patients in cohort 1 and 39 patients in cohort 2 completed the present study (Fig. 1). The characteristics of patients were comparable between the cohorts (Table 1). Five patients in cohort 1 (median, 3 days; min–max, 1–14 days) and 4 patients in cohort 2 (median, 6 days; min–max, 1–14 days) were mechanically ventilated during the study period.

Table 1 Characteristics of patients

Variables	Cohort 1 ($n = 45$)	Cohort 2 ($n = 39$)	p value
Gender (m/f)	18/27	17/22	0.739
Age (years)	52 (47–57)	54 (50–58)	0.457
BMI (kg/m^2)	26 (24–27)	25 (23–27)	0.521
Admission GCS			0.859
15–13	34	29	
12–10	10	8	
9–6	1	1	
Under 6	0	1	
WFNS (good/poor)	34/11	29/10	0.962
Fisher grade (II/III/IV)	21/19/5	20/17/2	0.607
Type of treatment (sur/end)	25/20	23/16	0.752
Time between ictus and treatment (day)	2.4 (2.2–2.7)	2.4 (2.2–2.6)	0.962
Aneurysm location			0.993
ACoA/ACA	16	15	
MCA	14	12	
ICA	10	8	
Other	5	4	
Vasopressor use	21	14	0.318
Hospital stay (days)	26 (16–44)	24 (16–45)	0.055

Quantitative data presented as mean and 95% CI and compared with unpaired Student's t test (except for hospital stay data which is not normally distributed, presented as median, minimum–maximum, and compared with Mann–Whitney test). Qualitative data are presented as number case and compared with chi-square test. *m*, male; *f*, female; *BMI*, body mass index; *GCS*, Glasgow Coma Scale; *WFNS*, World Federation of Neurosurgical Societies score and good WFNS is grades I, II, and III, poor WFNS is grades IV and V; *sur*, surgery; end, endovascular; *ACoA*, anterior communicating artery; *ACA*, anterior cerebral artery; *MCA*, middle cerebral artery; *ICA*, internal carotid artery

Hemodynamics of patients

MAP and CVP values were similar between the cohorts at all measurement times. MAP values at phase 2, phase 3, and phase 4 were significantly higher than those at phase 1 in both cohorts. The CVP value at phase 4 was significantly higher than that at phase 1 in cohort 1 (Supplement Figure 1). The mean daily fluid balance of cohort 1 and cohort 2 was 920 ml/day (95% confidence interval, 835–1005 ml/day) and 773 ml/day (95% confidence interval, 706–840 ml/day), respectively ($p = 0.009$). In cohort 2, CI, GEDI, and ELWI values significantly increased with time (Supplement Figure 2).

Outcome measurements

The frequency of PE was similar between the cohorts (Table 2). In cohort 2, ELWI, GEDI, and CVP values of the patient with PE were 15 ml/kg, 910 ml/m^2, and 12 mmHg, respectively, during diagnosis. In cohort 1, three of five patients with PE had normal CVP value during diagnosis (CVP values of patients with PE were 7, 8, 8, 14, and 15 mmHg). The frequency of occurrence of DCI and persistent cerebral infarction was similar between the cohorts (Table 2). No significant difference was observed between the cohorts on the Kaplan–Meier curve for the occurrence of DCI following aSAH (log rank test: $\chi^2 = 1.58$, $p = 0.208$; Fig. 2).

One year following aSAH, the MoCA score of cohort 1 was significantly lower than that of cohort 2, whereas the occurrence of poor MoCA score was higher in cohort 1 (Table 2). One year following aSAH, the motor neurological deficit incidence, mortality rate, and poor mRS score incidence were similar between the cohorts (Table 2). Histogram of mRS score was presented in Fig. 3. The univariate binary logistic regression analysis was performed to determine the association between poor MoCA score (as the dependent variable) and each independent variable for both cohorts separately. Subsequently, the variables that were determined significant using the univariate binary logistic regression analysis were entered into the multivariate binary logistic regression analysis. The occurrence of DCI and high WFNS grade (WFNS IV and V) were the significant risk factors for poor MoCA score (MoCA score < 21 point) in both cohorts (Table 3).

Table 2 Comparison of outcome measurements between cohorts

Variables	Cohort 1 ($n = 45$)	Cohort 2 ($n = 39$)	p value
PE incidence	5 (11%)	1 (3%)	0.129
Good grade	2 (6%)	0 (0%)	0.184
Poor grade	3 (27%)	1 (10%)	0.314
DCI incidence	17 (38%)	10 (26%)	0.235
Good grade	11 (32%)	6 (21%)	0.299
Poor grade	6 (54%)	4 (40%)	0.505
Persistent CeI incidence	5 (11%)	3 (7%)	0.594
Good grade	3 (9%)	2 (7%)	0.778
Poor grade	2 (18%)	1 (10%)	0.593
MoCA score	20.2 (19.2–21.4)	23.5 (22.2–24.8)	< 0.001*
Good grade	20.8 (19.6–22)	24.1 (22.7–25.6)	< 0.001*
Poor grade	17.4 (15.1–21)	21.5 (19–24)	< 0.001*
Poor MoCA incidence	17 (38%)	7 (18%)	0.045*
Good grade	10 (29%)	5 (17%)	0.258
Poor grade	7 (64%)	2 (20%)	0.044*
Poor mRS score	15 (34%)	7 (18%)	0.110
Good grade	9 (27%)	4 (14%)	0.215
Poor grade	6 (55%)	3 (30%)	0.256
Motor deficit incidence	4 (9%)	3 (8%)	0.843
Good grade	2 (6%)	1 (3%)	0.651
Poor grade	2 (18%)	2 (20%)	0.916
Mortality rate	2 (5%)	1 (3%)	0.643

Quantitative data presented as mean and 95% CI and compared with unpaired Student's t test. Qualitative data presented as number, percentage of case, and compared by chi-square test. Good grade, WFNS I to III; poor grade, WFNS IV to V; *PE*, pulmonary edema; *DCI*, delayed cerebral ischemia; *CeI*, cerebral infarcts; *MoCA*, Montreal Cognitive Assessment test that measured 1 year after aSAH and *mRS*, modified Rankin scale that measured 1 year after aSAH. *$p < 0.05$

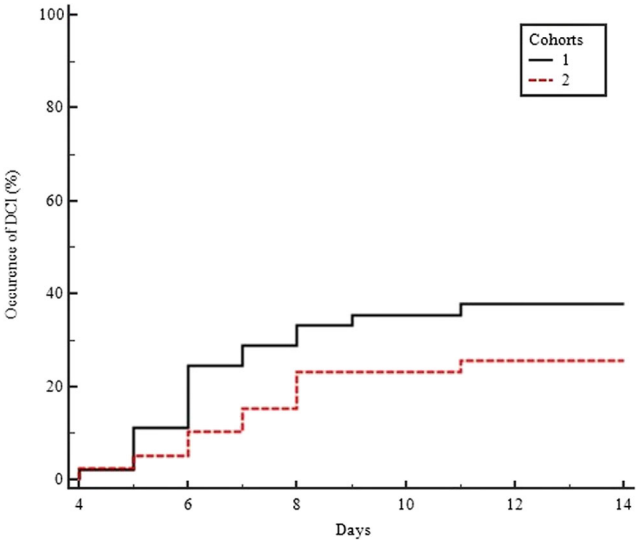

Fig. 2 Kaplan–Meier plots demonstrating the cumulative incidence of delayed cerebral ischemia within 14 days post-ictus. No significant difference was observed between the cohorts (log rank test: $\chi^2 = 1.58$, $p = 0.208$)

Discussion

The present study showed that TPT monitor-guided hemodynamic management that provides CI, GEDI, and ELWI measurements improved the cognitive function at 1 year following aSAH better compared with standard hemodynamic management.

Patients with aSAH who survived the initial bleeding encounter two important complications, namely DCI and cardiopulmonary insufficiency, due to increased sympathetic activity and excessive catecholamine release [18]. Effective hemodynamic and fluid management can reduce the risk of DCI development and prevent its progression to persistent cerebral infarction [5, 16]. Maintaining normovolemia, knowing how much hydration the patients will tolerate, and evaluating cardiac performance are crucial for efficient fluid and hemodynamic management. The traditional hemodynamic parameters, such as CVP, arterial blood pressure, HR, and fluid balance, are insufficient in evaluating the volume status of patients and provide insufficient information on the cardiac performance of patients, as well as the risk of PE [8, 14]. Conversely, TPT monitor estimates volume status more accurately with GEDI measurement and allows for the measurement of cardiac output and extravascular lung volume [8, 11]. Cardiac output measurement is crucial during DCI to obtain adequate cerebral perfusion. High arterial blood pressure does not always indicate high cardiac output. Increase in arterial blood pressure can also be related to increase in systemic vascular resistance. Therefore, cardiac output is a crucial hemodynamic parameter that must be monitored during the treatment of patients with aSAH [24]. Recent studies showed that low GEDI and CI values were a risk factor for DCI, and could increase the severity of DCI [14, 20, 24]. Mutoh et al. found that the occurrence of DCI was lower in the TPT monitor-guided hemodynamic management group compared with that of the classic hemodynamic monitoring group. This difference was more prominent in patients with poor-grade aSAH (WFNS IV and V) [14]. In the present study, we could not find a statistically significant difference between the cohorts in terms of the occurrence of DCI. Presumably, this was due to fewer patients with poor-grade aSAH in our study. However, a clinically important finding from our study was that the occurrence of DCI in cohort 2 was 12% lower than that in cohort 1. PE is not rare during intensive care follow-up. This complication depends on the nature of aSAH

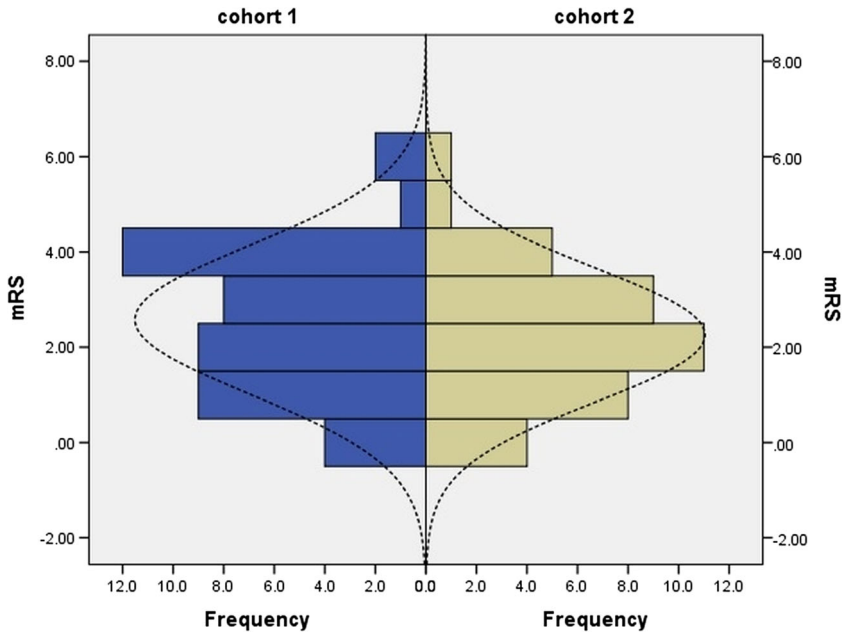

Fig. 3 Histogram of mRS score. Dotted lines show disruption curve. mRS, modified Rankin scale. Cohorts were found similar in terms of 6-point mRS score comparison. Chi-square analysis was used and $p = 0.794$

Table 3 Univariate and multivariate binary logistic regression analyses of the variables associated with low MoCA score in cohort 1 and cohort 2

Regression analyses of poor MoCA in cohort 1				
	Univariate analysis		**Multivariate analysis**	
Variables	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
Gender	0.8 (0.2–2.5)	0.616	–	–
Age	1 (0.9–1.1)	0.493	–	–
WFNS grade poor	2.1 (1.1–3.1)	0.001*	1.4 (0.9–3)	0.023*
Fisher grade IV	0.2 (0.1–1.2)	0.07	–	–
Treatment method	0.6 (0.2–1.9)	0.373	–	–
Occurrence of DCI	2.6 (1.2–3.5)	0.005*	1.5 (1–3.2)	0.012*
MAP at phase 1	1 (0.9–1.2)	0.854	–	–
CVP at phase 1	0.7 (0.5–1)	0.101	–	–
Fluid balance	1 (0.9–1.1)	0.877	–	–
Regression analyses of poor MoCA in cohort 2				
	Univariate analysis		**Multivariate analysis**	
Variables	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
Gender	0.9 (0.1–5)	0.966	–	–
Age	1 (0.9–1.1)	0.319	–	–
WFNS grade poor	1.9 (0.8–2.7)	0.007*	1.3 (0.7–3)	0.02*
Fisher grade IV	0.3 (0.1–1.4)	0.102	–	–
Treatment method	1.9 (0.3–11)	0.465	–	–
Occurrence of DCI	2.6 1(1–3.2)	0.007*	1.4 (0.7–2.6)	0.02*
MAP at phase 1	0.9 (0.8–1.2)	0.976	–	–
CVP at phase 1	1.3 (1–1.7)	0.072	–	–
Fluid balance	1 (0.9–1.1)	0.566	–	–
CI at phase 1	9.6 (1–15)	0.108	–	–
GEDI at phase 1	1 (0.9–1.1)	0.265	–	–

Data are presented as odds ratios (OR) with 95% confidence intervals (95% CI). Variables with $p < 0.05$ as determined by univariate logistic regression analysis were entered into the multivariate logistic regression analysis. *Significant association. *DCI*, delayed cerebral ischemia; *MAP*, mean arterial pressure; *CVP*, central venous pressure; *CI*, cardiac index; *GEDI*, global end-diastolic index. *$p < 0.05$

treatment (hypervolemia and hemodynamic augmentation) and neurogenic stunned myocardium [9, 14, 16, 24]. ELWI measured using the TPT monitor helped us to estimate pulmonary interstitial fluid volume and warned us before the clinical symptoms of PE occurred. However, similar to other studies in the literature, our study also found CVP to be an insufficient parameter in determining the risk of PE [16, 24]. In the present study, PE developed in 1 patient in cohort 2 and in 5 patients in cohort 1. Although this difference was not statistically significant, it is still clinically important.

In the literature, fewer studies have examined the effects of TPT monitor-guided hemodynamic management on long-term outcome following aSAH [11, 14]. Generally, the mRS used in these studies was insufficient for the detailed evaluation of cognitive functions [11, 14, 15]. Mutoh et al. found that at 3 months following ictus, the mRS score was better in the TPT monitor-guided hemodynamic management group compared with that of the classic hemodynamic monitoring group [14]. To the best of our knowledge, the effect of TPT monitor-guided hemodynamic management on cognitive function has not been thoroughly addressed in the literature. We evaluated the outcome of patients 1 year following aSAH using the mRS and MoCA tests. We chose the MoCA test to evaluate cognitive outcomes because it has been validated in our language and allows for detailed cognitive examination [17]. We did not observe statistically significant difference between the cohorts in terms of the mRS score. However, the MoCA score was higher in cohort 2 compared with that in cohort 1, and the occurrence of poor MoCA score was significantly lower in cohort 2. We also observed that the occurrence of DCI and poor WFNS grade were the risk factors for poor MoCA score in both cohorts. Previous trials have also showed the negative effect of these factors on outcomes [4, 5]. Additionally, high fluid balance, high blood glucose levels, and blood product transfusion were found to be associated with poor functional outcomes in patients with aSAH [7]. In cohort 2, the frequency of occurrence of DCI, PE (clinically important difference though not statistically significant), and the daily fluid balance were lower in cohort 1. CI and GEDI measurement can assess the effectiveness of hemodynamic augmentation and fluid therapy better than standard parameters. We claim that a combination of the aforementioned benefits resulted in better cognitive outcome in patients who were monitored using the TPT system in our neuro ICU.

The results of this study should be interpreted with caution, considering the limitations. First, this was an observational prospective cohort study wherein the enrollment of patients was not randomized, but instead was done historically. We chose this study method due to the paucity of special TPT catheters which have temperature sensor to obtain thermodilution curve during the planned study period. Second, although our treatment protocol was similar between both cohorts (except for hemodynamic management), our experience could be increased over time and allocation of resources to hemodynamic monitoring in cohort 2 may cause that doctors (and potentially nurses) spent more time with the patients. This issue may contribute better outcome in cohort 2. Third, our study population was not adequately powered for subgroup comparisons, such as poor- and good-grade aSAH. Fourth, the number of patients with high-grade (WFNS IV and V) aSAH was low. Fifth, we could not provide data on heart failure during follow-up because we did not measure B-type natriuretic peptide levels nor performed echocardiography in all patients. Sixth, we choose to compare MoCA score as a primary outcome. However, choosing to compare MoCA poor incidence as a primary outcome instead of MoCA score comparison requires a greater number of patients. Finally, we could not use dynamic parameters, such as pulse pressure variation or stroke volume variation, for the assessment of fluid responsiveness because most of the patients had spontaneous breathing.

In conclusion, the results of the present study show that GEDI- and CI-guided hemodynamic management using TPT monitor provides better cognitive outcome than standard hemodynamic care in patients with aSAH. However, we need randomized controlled trials which can eliminate time course bias to obtain more accurate results.

Acknowledgments We would like to thank the Turkish Neurosurgical Society for its assistance in English editing of the study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Ali A, Bitir B, Abdullah T, Sabanci PA, Aras Y, Aydoseli A, Tanirgan G, Sencer S, Akinci IO (2018) Gray-to-white matter ratio predicts long-term recovery potential of patients with aneurysmal subarachnoid hemorrhage. Neurosurg Rev. https://doi.org/10.1007/s10143-018-1029-y
2. Bederson JB, Connolly ES Jr, Batjer HH et al (2009) Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 40:994–1025
3. Darkwah Oppong M, Iannaccone A, Gembruch O, Pierscianek D, Chihi M, Dammann P, Köninger A, Müller O, Forsting M, Sure U, Jabbarli R (2018) Vasospasm-related complications after subarachnoid hemorrhage: the role of patients' age and sex. Acta Neurochir 160:1393–1400
4. de Rooij NK, Rinkel GJ, Dankbaar JW, Frijns CJ (2013) Delayed cerebral ischemia after subarachnoid hemorrhage: a systematic review of clinical, laboratory, and radiological predictors. Stroke. 44:43–54
5. Francoeur CL, Mayer SA (2016) Management of delayed cerebral ischemia after subarachnoid hemorrhage. Crit Care 20:277
6. Hoff RG, van Dijk GW, Algra A, Kalkman CJ, Rinkel GJ (2008) Fluid balance and blood volume measurement after aneurysmal subarachnoid hemorrhage. Neurocrit Care 8:391–397
7. Kissoon NR, Mandrekar JN, Fugate JE, Lanzino G, Wijdicks EF, Rabinstein AA (2015) Positive fluid balance is associated with poor outcomes in subarachnoid hemorrhage. J Stroke Cerebrovasc Dis 24:2245–2251
8. Kumar A, Anel R, Bunnell E et al (2004) Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Crit Care Med 32:691–699
9. Muroi C, Keller M, Pangalu A, Fortunati M, Yonekawa Y, Keller E (2008) Neurogenic pulmonary edema in patients with subarachnoid hemorrhage. J Neurosurg Anesthesiol 20:188–192
10. Mutoh T, Kazumata K, Ajiki M, Ushikoshi S, Terasaka S (2007) Goal-directed fluid management by bedside transpulmonary hemodynamic monitoring after subarachnoid hemorrhage. Stroke 38:3218–3224
11. Mutoh T, Kazumata K, Ishikawa T, Terasaka S (2009) Performance of bedside transpulmonary thermodilution monitoring for goal-directed hemodynamic management after subarachnoid hemorrhage. Stroke 40:2368–2374
12. Mutoh T, Ishikawa T, Suzuki A, Yasui N (2010) Continuous cardiac output and near-infrared spectroscopy monitoring to assist in management of symptomatic cerebral vasospasm after subarachnoid hemorrhage. Neurocrit Care 13:331–338
13. Mutoh T, Kazumata K, Kobayashi S, Terasaka S, Ishikawa T (2012) Serial measurement of extravascular lung water and blood volume during the course of neurogenic pulmonary edema after subarachnoid hemorrhage: initial experience with 3 cases. J Neurosurg Anesthesiol 24:203–208
14. Mutoh T, Kazumata K, Terasaka S, Taki Y, Suzuki A, Ishikawa T (2014) Early intensive versus minimally invasive approach to postoperative hemodynamic management after subarachnoid hemorrhage. Stroke 45:1280–1284
15. Mutoh T, Kazumata K, Yokoyama Y, Ishikawa T, Taki Y, Terasaka S, Houkin K (2015) Comparison of postoperative volume status and hemodynamics between surgical clipping and endovascular coiling in patients after subarachnoid hemorrhage. J Neurosurg Anesthesiol 27:7–15
16. Okazaki T, Kuroda Y (2018) Aneurysmal subarachnoid hemorrhage: intensive care for improving neurological outcome. J Intensive Care 6:28
17. Ozdilek B, Kenangil G (2014) Validation of the Turkish version of the Montreal Cognitive Assessment Scale (MoCA-TR) in patients with Parkinson's disease. Clin Neuropsychol 28:333–343
18. Rabinstein AA (2015) Critical care of aneurysmal subarachnoid hemorrhage: state of the art. Acta Neurochir Suppl 120:239–242
19. Rowland MJ, Hadjipavlou G, Kelly M, Westbrook J, Pattinson KT (2012) Delayed cerebral ischaemia after subarachnoid haemorrhage: looking beyond vasospasm. Br J Anaesth 109:315–329
20. Tagami T, Kuwamoto K, Watanabe A et al (2014) Optimal range of global end-diastolic volume for fluid management after aneurysmal subarachnoid hemorrhage: a multicenter prospective cohort study. Crit Care Med 42:1348–1356
21. van Gijn J, Kerr RS, Rinkel GJ (2007) Subarachnoid haemorrhage. Lancet 369:306–318
22. Vergouw LJM, Egal M, Bergmans B et al (2017) High early fluid input after aneurysmal subarachnoid hemorrhage: combined report of association with delayed cerebral ischemia and feasibility of cardiac output-guided fluid restriction. J Intensive Care Med 1: 885066617732747
23. Vergouwen MD, Participants in the International Multi-Disciplinary Consensus Conference on the Critical Care Management of Subarachnoid Hemorrhage (2011) Vasospasm versus delayed cerebral ischemia as an outcome event in clinical trials and observational studies. Neurocrit Care 15:308–311
24. Watanabe A, Tagami T, Yokobori S, Matsumoto G, Igarashi Y, Suzuki G, Onda H, Fuse A, Yokota H (2012) Global end-diastolic volume is associated with the occurrence of delayed cerebral ischemia and pulmonary edema after subarachnoid hemorrhage. Shock 38:480–485