Balkan Med J 2022;39:351-7

Comparison of Stroke Volume Variation-based goal-directed Therapy Versus Standard Fluid Therapy in Patients Undergoing Head and Neck Surgery: A Randomized Controlled Study

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Background: Perioperative fluid therapy is used to avoid dehydration and hypovolemia. Optimum perioperative fluid administration may improve postoperative outcomes after major surgery, and the optimal strategy remains controversial and uncertain.

Aims: The primary outcome was the total amount of intraoperative fluids given between perioperative goal-directed fluid therapy (GDFT) guided by a hemodynamic monitoring system and standard fluid therapy based on "mean arterial pressure-diuresis" data in patients undergoing head and neck surgery. The secondary outcomes were the hemodynamics and laboratory variables, postoperative complications, length of mechanical ventilation, intensive care unit and hospital stay.

Study Design: A randomized controlled study

Methods: Sixty patients were scheduled and randomized into two groups of 30 patients each: in the study group, an arterial pressure catheter was inserted and connected to the FloTrac system, whereas in the control group, an arterial pressure catheter was inserted and integrated into the hemodynamic monitoring system with a special transducer. The control group had fluids administered at the discretion of the anesthesiologist according to the mean arterial pressure >65 mmHg and diuresis >0.5 ml/kg/h. In the study group, fluid management was administered to achieve a target value of ≤13% through the stroke volume variation.

Results: The total amounts of fluid in the intraoperative period were different between the groups, with the study group receiving significantly more fluids ($P = 0.0455$). The length of hospital stay was significantly longer in the study group than in the control group ($P = 0.012$), but prolonged oxygen demand was significantly more frequent in the control group than in the study group ($P = 0.017$). No difference was found in hemodynamics, lactate kinetics, and vasoactive agent requirements.

Conclusion: The standard fluid therapy guided by conventional circulatory parameters appears sufficient for patients with low-to-moderate risk during head and neck surgery.

INTRODUCTION

Perioperative fluid therapy is used to correct dehydration and treat hypovolemia and provide maintenance fluid and electrolyte requirements postoperatively. The question is probably one of the most controversial issues in anesthesia practice. Evidence suggests that optimum perioperative fluid administration may improve postoperative outcomes after major surgery.[1,2] Several studies have been conducted concerning the issue, but the optimal strategy remains controversial and uncertain.[3,4]

Individualized goal-directed fluid therapy (GDFT) protocols guided by dynamic parameters such as stroke volume variation (SVV) or pulse pressure variation (PPV) were conducted to determine the optimal dose of fluids[5-7] in recent years. An improvement in postoperative outcomes in patients undergoing high-risk surgery has been obtained with this approach.[8-13]

The pulse-contour cardiac-output measuring system (FloTrac, Vigileo, Edwards Life Sciences Corp., CA, USA) preferred in this study is a minimally invasive monitoring technology working

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Received: February 09, 2022 Accepted: July 19, 2022 Available Online Date: September 09, 2022 • DOI: 10.4274/balkanmedj.galenos.2022.2022-1-88

Available at www.balkanmedicaljournal.org

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Cite this article as:
Turkut N, Altun D, Canbolat N, Uzuntürk C, Şen C, Çamcı AE. Comparison of Stroke Volume Variation-based goal-directed Therapy Versus Standard Fluid Therapy in Patients Undergoing Head and Neck Surgery: A Randomized Controlled Study. *Balkan Med J.*; 2022; 39(5):351-7.

on the principle of arterial waveform analysis to calculate SV without requiring a transpulmonary thermodilution-based external calibration. The device can guide fluid therapy and the selection of inotropes and vasopressors through a clinical algorithm to optimize cardiac-output and oxygen delivery to the tissues.[14]

This prospective randomized study aimed to compare perioperative GDFT guided by this hemodynamic monitoring system with standard fluid therapy based on "mean arterial pressure-diuresis" data in patients undergoing head and neck surgery. The primary outcome was the difference in intraoperative fluid balance, and secondary outcomes were the hemodynamics and laboratory variables, postoperative complications, duration of mechanical ventilation, and length of stay (LOS) in the intensive care unit (ICU) and hospital stay.

MATERIAL AND METHODS

After receiving approval from the local institutional ethics committee (2017/1122) and written informed consent, 60 patients aged 18-80 years, with American Society of Anesthesiology (ASA) I-III states, undergoing head and neck surgery consisting of oncological laryngeal and hypopharyngeal surgeries were enrolled in this study. This clinical trial was registered at ClinicalTrials.gov (Registration no. NCT04728178). Patients with congestive heart failure (ejection fraction ≤35%), cardiac arrhythmias, kidney disease (glomerular filtration rate <30 ml/kg/min), peripheral vascular disease, body mass index (BMI) >40 kg/m^2 were excluded from the study.

Following premedication with midazolam 0.05 mg/kg administered intravenously 15 min before the induction of anesthesia, standard monitoring of electrocardiography (ECG), noninvasive blood pressure, peripheral oxygen saturation (SpO_2) was applied upon arrival to the operating room. Additionally, the Bispectral Index Monitoring (BIS) (Covidien, Medtronic Medical, MI, USA) system was applied to adjust the anesthetic depth among patients. Crystalloid infusion at 7 ml/kg/h was started in both groups. Standard anesthetic techniques including propofol 2-3 mg/kg and fentanyl 1.5 μg/kg were given to all patients. A BIS level of 40-60 was targeted and maintained during anesthetic induction and in the entire study period. When this level was obtained, 0.6 mg/kg rocuronium was administered to facilitate endotracheal intubation. All patients were ventilated in a volume-controlled mode with a tidal volume of 8 ml/kg based on their ideal body weight. The respiration rate was adjusted to keep the end-tidal carbon dioxide ($ETCO_2$) level at 35-40 mmHg. Positive-end expiratory pressure (PEEP) was set at 5 cm H_2O. If the driving airway pressure was <20 cm H_2O with these settings, those patients were excluded from the study.

The patients were randomly allocated into two groups (study group, group S; control group, group C) using computer-generated numbers on the operation day after anesthetic induction. After randomization, patients underwent radial arterial cannulation. In group S, the arterial cannulas were attached to the hemodynamic monitoring system (EV1000 Clinical Platform-Edwards Lifesciences Corp.) with a special transducer (FloTrac Sensor, Edwards Lifesciences Corp). After entering the demographic data of the patient, the system starts the monitoring process and displays the SV index (SVI), cardiac index (CI), and SVV during the respiratory cycle. The intraoperative fluid management was planned to achieve a target value of ≤13% through SVV monitoring in group S. In group C, fluid management was settled according to standard goals as maintaining mean arterial pressure (MAP) of 65 mmHg and diuresis of 0.5 ml/kg/h and above.

Intraoperative Fluid Therapy

In addition to the maintenance fluid at 7 ml/kg/h, in group S, when the SVV value exceeded 13%, 250 ml of crystalloids was given in the first stage, and if the situation continued, 250 mL of colloid bolus (hydroxyethyl starch 6%, HES) was added. Colloid boluses were given until the increase in SVV was within 13% up to a maximum of 20 ml/kg. If the need persisted, fluid boluses were performed using crystalloid solutions. Norepinephrine infusion was started when the MAP was <65 mmHg even if the SVV remained below 13%. Group C was given 250 ml of crystalloids in the first stage if the MAP was <65 mmHg, and if the hypotensive episode continued, 250 ml of colloid bolus up to 20 ml/kg was given. If hypotension persisted despite these fluid boluses, a norepinephrine infusion was initiated. In addition, when diuresis was at 0.5 ml/kg/h or less, 250 ml of colloid bolus was administered. The intraoperative transfusion threshold was determined as a hemoglobin level of 7 g/dl in all patients.

Hemodynamic measurements (MAP, HR, and SVI in group S) were completed and recorded at the following time intervals (T_1, after general anesthesia induction; T_2, at the end of the operation; T_3, postoperative 1st hour; and T_4, postoperative 12th hour). The need for additional fluid or vasoactive agents was recorded. Arterial blood gas parameters were recorded from all patients at the same measurement times. Finally, creatinine and lactate levels and urinary output were surveyed throughout the study.

The primary aim of this study was to compare the amount of intraoperative total fluid balance (crystalloid, colloid, and blood products) between the groups. The secondary outcomes were the hemodynamics and laboratory variables and the number of interventions to achieve the specified target. The following parameters were also recorded: postoperative respiratory (hypoxia [PaO_2 <60 mmHg] and hypercarbia [$PaCO_2$ >45 mmHg]), prolonged mechanical ventilation requirement lasting >6 h, prolonged need for oxygen support (oxygen supplementation by mask >24 h and pneumonia), and cardiac complications (refractory hypotension, bradycardia [<40 bpm], tachycardia [>100 bpm] myocardial ischemia and infarction, and hypertensive attack). The length of mechanical ventilation and ICU and hospital stay were also compared.

Statistical Analysis

To determine the number of samples, a power analysis was performed using the G*Power (v3.1.9.2) program. The power of the study is expressed as 1-β (β = probability of type II error); in general, studies should have 80% impact power. In the two-group

comparisons according to the total amount of fluid, the result of the calculation made with the assumption that a minimum difference of 600 ml (SD, 800 ml) of fluid will be clinically significant, the effect size was calculated as d = 0.750. To obtain 80% power at an $\alpha = 0.05$ level, there should be at least 29 people in each group and 58 people in total. Considering that there might be losses during the working process, 30 people were recruited for each group.

Data normality was verified with the Shapiro-Wilk test and was presented as mean ± standard deviation for parametric variables. Non-parametric values are presented as median (range), frequency, percentage, minimum, and maximum. In compliance with the distribution of data, Student's t-test for normally distributed data or Mann-Whitney's U-test and Wilcoxon signed-rank test were used for intergroup comparisons of quantitative variables that did not show normal distribution. The Pearson chi-square test, Fisher-Freeman-Halton test, and Fisher exact test were used to compare qualitative data between groups. Significance was accepted as $p < 0.05$.

RESULTS

Sixty-eight patients requiring general anesthesia for head and neck surgery were screened for eligibility. Three patients refused to participate, and 65 consenting patients were finally enrolled. Two patients who developed cardiac arrhythmia during the study period and three patients who had an intraoperative surgical plan modification caused by histopathological study were excluded from the study. The targeted BIS level was obtained and maintained in all patients, and no patients were excluded because of inappropriate anesthetic depth. Data from the remaining 60 patients were included in the statistical analysis, and each group included 30 patients, as shown in the flow diagram (Figure 1).

Demographic data of the patients and some biochemical information are presented in Table 1 and were comparable between the two groups with respect to age, sex, BMI, ASA status, and coexisting systemic diseases. The average duration of surgery was 385.8 ± 97.8 min for all patients.

Intraoperative fluid administration data revealed that although the total fluid amount (ml) was different between the groups and significantly more fluids were administered to group S ($P = 0.0455$), no significant difference was found in the total amounts of fluid and additional amounts of fluids administered between the groups when the results were compared in ml/kg/h. However, this difference was attributed to the duration of surgery, which was significantly different between the groups. In group S, the mean duration of surgery was 415.2 ± 106.8 min, whereas in group C, the surgery lasted 358.8 ± 82.8 min ($P = 0.028$). Therefore, maintenance fluid administration was accepted as comparable between the groups.

The amounts of additional crystalloid and colloid administered in the case of "hypotension/oliguria" in group C or SVV increase in group S were not different between the groups. Group C received 531 ± 221 ml of additional crystalloids and 375 ± 130 ml of colloid boluses to treat hypotension, whereas group S received 477 ± 352 ml and 366 ± 129 ml of crystalloid and colloid

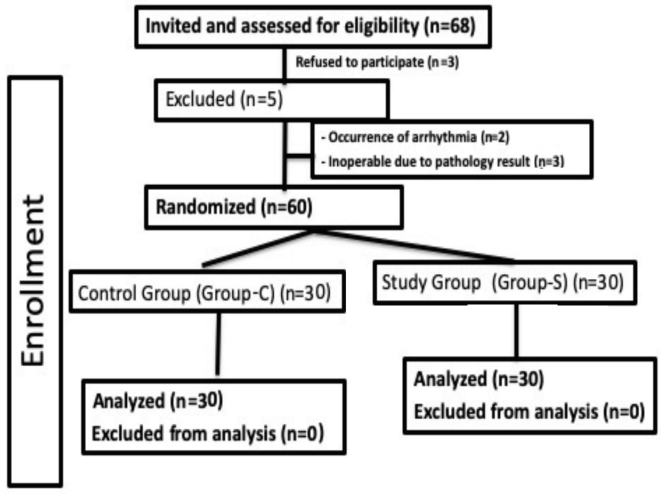

FIG. 1. Flow diagram of the study

TABLE 1. Demographic, Biochemical Data, and Duration of Surgery

	Group C (n = 30)	Group S (n = 30)	P value
Age (year)	58.07 (11.24)	58.80 (13.2)	**0.818**
Sex (M/F)	10/20	3/27	**0.028***
BMI (kg/m^2)	26.9 (4.51)	25.9 (4.83)	**0.431**
ASA status (I/II/III)	2/18/10	3/20/7	**0.712**
Comorbidities (Y/N)	20/10	15/15	**0.190**
Hypertension	15	8	**0.063**
Coronary disease	6	3	**0.472**
Diabetes	4	3	**1.000**
Creatinine (mg/dl)	0.87 ± 0.23	0.93 ± 0.61	**0.341**
Lactate (mmol/dl)	1.54 ± 0.85	1.69 ± 0.61	**0.486**
Duration of surgery (min)	358.0 ± 83.0	415.0 ± 106**	**0.042***

*$P < 0.05$
M, male; F, female, min: minimum

boluses, respectively, to reduce the SVV values within the target limits. In group C, 14 patients received additional crystalloids at 23 different times, whereas in group S, 12 patients received them at 28 occasions. Regarding the incidence of additional colloid administration, 13 patients in group C and 12 patients in group S received additional colloids at 18 times for both groups. Intraoperatively, data concerning the fluid regimen are presented in Table 2. Two participants in group C received a single unit of red blood per patient during the operation, whereas none of the patients in group S needed any blood product.

Vasoactive agent requirement was comparable between the groups: eight patients in group C and two patients in group S needed norepinephrine infusion to achieve and maintain the targeted MAP after adequate volume therapy (P = 0.08 *Fisher exact test*). Hemodynamic data (HR, MAP, and SVI [group S]) and blood gas analysis results are presented in Table 3. None of the aforementioned data showed a significant difference between the groups at any measurement time. Creatinine and lactate levels obtained pre- and postoperatively were comparable between the groups. Parallel to this finding, the maximum lactate level reached during perioperative period was comparable. Data concerning lactate and creatinine are presented in Figure 2a and 2b.

In the analysis of postoperative undesired events, the overall rate for incidents was 60% for group C and 80% for group S, without significant difference. The complications are shown in Table 4. Postoperative respiratory complications occurred in 70% (n = 42) of the cases, and prolonged oxygen demand is observed at the highest rate [61.7% (n = 37)], which was significantly more frequent in group C than in group S (P = 0.017). The duration of mechanical ventilation and ICU LOS were comparable between the groups. The hospital LOS of group S was significantly longer than that of group C (P < 0.012) No mortality was observed during the study period.

DISCUSSION

In the present study conducted on patients undergoing head and neck surgery, we did not observe any significant difference between SVV-guided GDFT (study) and the standard fluid therapy (control) in terms of the additional amounts of fluid administered intraoperatively. Additionally, no difference was found in the hemodynamic profile, lactate kinetics, and vasoactive agent requirement during the study period. The postoperative course was fairly comparable between groups S and C, except for the prolonged oxygen support needed in group C. On the contrary, a longer hospital LOS was observed in group S.

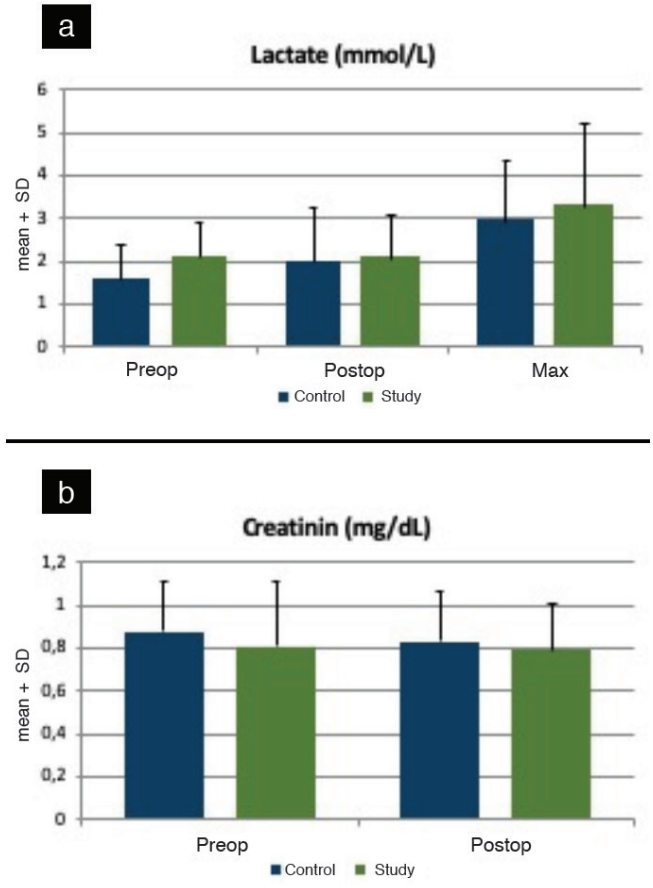

FIG. 2. a) Lactate levels between the groups, b) creatinine levels between the groups

TABLE 2. Data of Intraoperative Fluid Status

	Group-C (n=30)	Group-S (n=30)	*P* value
Total fluid (ml)	3370 ± 902	3955 ± 1282	***0.045****
Total fluid (ml/kg/h)	9.16 ± 2.50	8.55 ± 1.55	***0.549***
Additional crystalloid (ml)	531.25 ± 221.27	477.27 ± 352.79	***0.167***
Additional crystalloid (ml/kg/h)	0.88 ± 1.15	0.61 ± 0.69	***0.495***
Additional colloid (ml)	375 ± 130.56	366.67 ± 129.1	***0.866***
Additional colloid (ml/kg/h)	0.43 ± 0.47	0.33 ± 0.45	***0.423***
Urinary output (ml)	664.0 ± 427	534.0 ± 344	***0.240***
Fluid balance at the end of surgery (ml)	3291.0 ± 1062	2835.0 ± 899	***0.273***
Fluid balance at the end of surgery (ml/kg/h)	6.59 ± 1.46	6.31 ± 0.83	***0.378***
Used norepinephrine	8 (27 %)	2 (6.7 %)	***0.080***

**P = 0.045*

Several meta-analyses and recommendations have been published to guide clinicians for an optimal strategy of perioperative fluid therapy and to determine its effectiveness on postoperative outcomes.[15-17] Nevertheless, a few studies have analyzed the perioperative effects of GDFT on patients undergoing head and neck surgery. Possible reasons for the lack of data in this field could be attributed to the different characteristics of other oncological surgeries that produce serious fluid and blood loss when compared with head and neck surgery that results in minimal fluid shift and bleeding. Anatomical restrictions caused by the operation zone could be another factor limiting central venous access and related monitoring techniques. The effects of these difficulties on monitoring praxis have been documented by a survey conducted by the British Association Oral and Maxillofacial Surgeons and revealed that only 9% (3 of over 40) of the anesthesia departments monitor SV intraoperatively during head and neck surgery.[18] However, SV, especially SVV, is an accurate predictor of fluid responsiveness and may help clinicians in initiating fluid therapy in the early period of volume requirement and can improve the outcomes.[19,20] Additionally, data can be obtained from an arterial catheter and sensor without requiring any additional intervention, which makes it suitable for head and neck surgery.

In a retrospective study, Lahtinen et al.[20] demonstrated that the SVV-guided fluid management reduced fluid administration in head and neck surgery with shorter hospital LOS but without a difference in the postoperative complication rate. Kim et al.[21] stated contradictory results in a prospective randomized study, and they concluded that hospital LOS was comparable between the conventional hemodynamic therapy and GDFT groups, but low amounts of crystalloids were used during surgery in the GDFT group. Finally, Hand et al.[22] found more frequent use of vasoactive agents and shorter ICU LOS in the GDFT group after free tissue transfer surgery for head and neck cancer, but no significant difference was observed in terms of the amount of administered fluids between the groups. Our primary outcome was the amount of fluid given intraoperatively, which was found comparable between the SVV-guided GDFT group and the standard therapy group. The secondary endpoints, as vasoactive agent administration, ICU LOS, and number of complications, were approximately comparable, and hospital LOS was longer in the GDFT group, but this was caused by one patient, who had an esophageal fistula requiring long-term hospital care. The amount of crystalloid and colloid fluids administered intraoperatively in group S was slightly higher than that in group C, but it was not significantly similar to those of Hand et al.[22] However, we did not observe a major significant

TABLE 3. Hemodynamic Variables During Study Period

		T1 Post-induction	T2 End of surgery	T3 Post-op 1st hour	T4 Post-op 12th hour
MAP (mmHg)	**C**	77.6 ± 8.7	74.5 ± 7.3	92.3 ± 12.8	85.8 ± 12.1
	S	77 ± 10.3	75.1 ± 7.8	94.3 ± 14.6	87.8 ± 11.4
HR (beat/min)	**C**	72 ± 11	69.9 ± 12	76.3 ± 14	75.6 ± 11
	S	72.3 ± 10	69.4 ± 13.4	81 ± 13	79.9 ± 13.5
SVI (ml/m^2)	**S**	47.7 ± 3.44	41.8 ± 6.5*	45.1 ± 7.7	44.2 ± 5.1

MAP: mean arterial pressure; HR: Heart rate; SVI: stroke volume index
C: control; S: study
*$P < 0.001$ compared to T1

TABLE 4. Postoperative Course of the Patients

	Group S (n = 30)	Group C (n = 30)	*P* value
Prolonged oxygen demand	14 (46.7%)	23 (76.7%) *	**0.017***
Hypercarbia	5 (16.7%)	4 (13.3%)	**1.000**
Infectious complications	2 (6.7%)	0	**0.492**
Hypertensive episode	9 (30%)	14 (46.7%)	**0.184**
Hypotensive episode	5 (16.7%)	4 (13.3)	**1.000**
Rhythm disturbance	9 (10%)	3 (6.7%)	**1.000**
Mechanical ventilation (hours)	4 (036)	3 (0-15)	**0.860**
ICU stay (hours)	18 (14-40)	19 (15-20)	**0.936**
Length of hospital stay (day)	14.5 (5-60)	10 (3-26) **	**0.012****

*$P < 0.017$
**$P < 0.012$

difference in the frequency of postoperative complications between our groups, as stated by Lahtinen et al.[20]

The ambiguous character of those results from different studies is not exceptional and can be considered for all data concerning GDT perioperatively.[23] A recent meta-analysis revealed that perioperative GDFT reduced morbidity and mortality, but with a low evidence quality due to heterogeneity of protocols and standards of included studies.[24] According to pooled data, GDFT reduced mortality, pneumonia, acute kidney injury, wound infection, and hospital LOS considering all types of surgery. However, the diversity of the devices, protocols, and patients resulted in remarkable clinical heterogeneity.[24] Parallel to this argument, regarding four studies conducted on patients undergoing ENT surgery participating in this meta-analysis, conflicting results were stated concerning fluid balance, vasoactive agent use, and patient outcomes. GDFT was found advantageous over standard therapy in terms of reducing reoperation events,[25] decreasing fluid gain without a change in patient outcomes,[26] discharge from hospital in fewer days,[27] and decreasing ICU LOS by judicious use of vasoactive agents.[22]

A key point for any fluid therapy protocol is the choice of fluid type when planning an appropriate regimen. However, no reported data have clearly demonstrated improved outcomes related to the choice of crystalloids and colloids. In addition, no evidence confirms the benefit when colloids are used instead of crystalloids as a replacement fluid.[28] Specifically, in studies investigating the cost and side effects of colloids in critical patient populations, it would be a rational approach to use them as a second choice.[29] In our study, considering all these factors, we preferred crystalloids as the first option to meet additional fluid requirements and to apply colloids as a second choice if fluid needs persist.

Our study has some limitations. First, the study included a small population consisting of 60 patients with moderate risk; thus, it may make sense to work with larger numbers of patients, both to standardize the group and minimize the differences between them. Second, patient demographics, amount of fluids administered, bolus timing, operation time, hemodynamic data, and blood gas analysis were obtained from anesthesia follow-up forms, ICU records, and patient files. Thus, hemodynamic data were not recorded in real time; therefore, we could only present these data for the recorded intervals (MAP, HR, and $ETCO_2$). At this stage, a digital data collection system could control data quality. Third, a non-calibrated pulse-contour cardiac-output monitor is used in the study. Although the most preferred technique is pulse-contour method calibrated by transpulmonary thermodilution to guide fluid therapy, anatomically possible central venous access areas are within the operating zone, which makes it impossible to use a calibrated method, as well as the esophageal Doppler, due to surgical conditions, and non-calibrated pulse-contour cardiac-output monitors appear to be the sole solution. Finally, we could not apply SV- and SVV-based monitoring in group S to follow the profile without using it for fluid management because of financial issues. Thus, reporting the CO/CI/SV and SVV values for the whole surgical period for both groups would be a stronger study design.

In conclusion, we did not find any significant difference in additional fluid volumes between SVV-based GDFT and blood pressure-diuresis-based standard fluid therapy in patients undergoing head and neck surgery. In addition, intraoperative fluid administration and balance were comparable between the groups. With these data, standard fluid therapy guided by conventional circulatory parameters would be sufficient for patients with low-to-moderate risk undergoing head and neck surgery.

Ethics Committee Approval: İstanbul University Local Ethics Committee (ethical approval no: 2017/1122, date of approval: 13/10/2017).

Informed Consent: Written informed consent was obtained from each patient.

Data Sharing Statement: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author Contributions: Design- D.A.; Materials- N.T.; Data Collection or Processing- C.U., C.Ş.; Analysis or Interpretation- N.C.; Writing- A.E.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Funding: This study was founded by Istanbul University Research Center (IUBAPSIS).

REFERENCES

1. Grocott MP, Mythen MG, Gan TJ. Perioperative fluid management and clinical outcomes in adults. *Anesth Analg.* 2005;100:1093-106. [Crossref]
2. Lobo DN, MacAfee DA, Allison SP. How perioperative fluid balance influences postoperative outcomes? *Best Pract Res Clin Anaesthesiol.* 2006;20:439-455. [Crossref]
3. Holte K, Kehlet H. Fluid therapy and surgical outcomes in elective surgery: a need for reassessment in fast-track surgery. *J Am Coll Surg.* 2006;202:971-989. [Crossref]
4. Bellamy MC. Wet, dry or something else? *Br J Anaesth.* 2006;97:755-757. [Crossref]
5. Vos JJ, Kalmar AF, Struys MM, et al. Comparison of arterial pressure and plethysmographic waveform-based dynamic preload variables in assessing fluid responsiveness and dynamic arterial tone in patients undergoing major hepatic resection. *Br J Anaesth.* 2013;110:940-946. [Crossref]
6. Kim SY, Song Y, Shim JK, et al. Effect of pulse pressure on the predictability of stroke volume variation for fluid responsiveness in patients with coronary disease. *J Crit Care.* 2013;28. [Crossref]
7. Khwannimit B, Bhurayanontachai R. Prediction of fluid responsiveness in septic shock patients: Comparing stroke volume variation by FloTrac/Vigileo and automated pulse pressure variation. *Eur J Anaesthesiol.* 2012;29:64-69. [Crossref]
8. Donati A, Loggi S, Preiser JC, et al. Goal-directed intraoperative therapy reduces morbidity and length of hospital stay in high-risk surgical patients. *Chest.* 2007;132:1817-1824. [Crossref]
9. Venn R, Steele A, Richardson P, et al. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *Br J Anaesth.* 2002;88:65-71. [Crossref]
10. McKendry M, McGloin H, Saberi D, Caudwell L, Brady AR, Singer M. Randomized controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimization of circulatory status after cardiac surgery. *BMJ.* 2004;329:258. [Crossref]
11. Noblett SE, Snowden CP, Shenton BK, Horgan AF. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. *Br J Surg.* 2006;93:1069-1076. [Crossref]
12. Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial [ISRCTN38797445]. *Crit Care.* 2005;9:687-693. [Crossref]
13. Venn R, Steele A, Richardson P, Poloniecki J, Grounds M, Newman P. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. *Br J Anaesth.* 2002;88:65-71. [Crossref]

14. Li J, Ji F.H, Yang J.P. Evaluation of stroke volume variation obtained by the FloTrac™/ Vigileo™ system to guide preoperative fluid therapy in patients undergoing brain surgery. *Int Med Res.* 2012;40:1175-1181. **[Crossref]**
15. Corcoran T, Rhodes JE, Clarke S, Myles PS, Ho KM. Perioperative fluid management strategies in major surgery: a stratified meta-analysis. *Anesth Analg.* 2012;114:640-651. **[Crossref]**
16. Varadhan KK, Lobo DN. A meta-analysis of randomized controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right. *Proc Nutr Soc.* 2010;69:488-498. **[Crossref]**
17. National Institute for Health and Care Excellence (NICE), Intravenous fluid therapy in adults in hospital. National Institute for Health and Care Excellence: Guidelines. NICE 2021. www.nice.org.uk/guidance/cg174. **[Crossref]**
18. Chalmers A, Turner MWH, Anand R, Puxeddu R, Brennan PA. Cardiac output monitoring to guide fluid replacement in head and neck microvascular free flap surgery - What is current practice in the UK? *Br J Oral Maxillofac Surg.* 2012;50:500-503. **[Crossref]**
19. Pearse RM, Harrison DA, MacDonald N, et al. Effect of a perioperative cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. *JAMA.* 2014;311:2181-2190. **[Crossref]**
20. Lahtinen SL, Liisanantti JH, Poukkanen MM, Laurila AP. Goal-directed fluid management in free flap surgery for cancer of the head and neck. *Minerva Anestesiologica.* 2017;83:59-68. **[Crossref]**
21. Kim HJ, Kim EJ, Lee HJ, et al. Effect of goal-directed haemodynamic therapy in free flap reconstruction for head and neck cancer. Acta Anaesth Scand. 2018;62:903-914. **[Crossref]**
22. Hand WR, Stoll WD, Mc Evoy MD, et al. Intraoperative goal-directed hemodynamic management in free tissue transfer for head and neck cancer. *Head Neck.* 2016; 38:1974-1980. **[Crossref]**
23. Gelman S. Is goal-directed haemodynamic therapy dead? *Eur J Anaesthesiol.* 2020;37:159-61. **[Crossref]**
24. Chong MA, Wang Y, Berbenetz NM, McConachie I. Does goal-directed haemodynamic and fluid therapy improve peri-operative outcomes? A systematic review and meta-analysis. *Eur J Anaesthesiol.* 2018; 35:469-483. **[Crossref]**
25. Park S, Kim H, Koo B. Effect of goal directed fluid therapy using stroke volume variation in free flap reconstruction. *Anesth Analg.* 2016;122:302. **[Crossref]**
26. Cordero-Rochet MJ,McCluskey SA, Minkovich L, et al. Goal directed fluid management in free flap reconstructive surgery. *Can J Anesth.* 2014;61:75. **[Crossref]**
27. Kulkarni R, Craske DA, Abdel-Galil K, et al. Haemodynamic optimization in head and neck cancer surgery; Pilot randomized controlled trial of LiDCO rapid. *Eur Arch Oto-Rhino-Laryngol.* 2012;269:4. **[Crossref]**
28. Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database. Syst Rev.* 2013;28:2. **[Crossref]**
29. Saw MM, Chandler B, Ho KM. Benefits and risks of using gelatin solution as a plasma expander for perioperative and critically ill patients: a meta-analysis. *Anaesth Intensive Care.* 2012;40:17-32. **[Crossref]**