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Clinical Investigation

CLINICAL INVESTIGATION

Comparison of two stroke volume variation-based goal-directed fluid therapies for supratentorial brain tumour resection: a randomized controlled trial

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Abstract

Background: The optimal volume status for neurosurgery has yet to be determined. We compared two fluid protocols based on different stroke volume variation (SVV) cut-offs for goal-directed fluid therapy (GDFT) during supratentorial brain tumour resection.

Methods: A randomized, single-blind, open-label trial was conducted. Eighty adult patients undergoing elective supratentorial brain tumour resection were randomly divided into a low SVV and a high SVV group. The SVV cut-offs were used to determine when to initiate colloid infusion. Clinical outcomes and perioperative changes in serum neuronal biomarkers, including S100β, neurone-specific enolase (NSE) and glial fibrillary acidic protein (GFAP), were compared.

Results: Patients in the low SVV group received a higher volume of colloid [869 (SD 404) *vs* 569 (453) ml; $P=0.0025$], had a higher urine output [3.4 (2.4) *vs* 2.5 (1.7) ml kg^{-1} h^{-1}; $P=0.0416$] and a higher average cardiac index [3.2 (0.7) *vs* 2.8 (0.6) litres min^{-1} m^{-2}; $P=0.0204$]. Patients in the low SVV group also had a shorter intensive care unit stay [1.4 (0.7) *vs* 2.6 (3.3) days, $P=0.0326$], fewer postoperative neurological events (17.5 *vs* 40%, $P=0.0469$), attenuated changes in the NSE and GFAP levels, lower intraoperative serum lactate and a higher Barthel index at discharge (all $P<0.05$).

Conclusions: During GDFT for supratentorial brain tumour resection, fluid boluses targeting a lower SVV are more beneficial than a restrictive protocol.

Clinical trial registration. NCT02113358.

Key words: brain tumour; goal-directed fluid therapy; stroke volume variation

Despite previous research that advocates the application of intraoperative goal-directed fluid therapy (GDFT) in major abdominal surgery,[1] recent studies have shown neutral or detrimental outcomes in comparison with protocols with restrictive fluid balance,[2–5] possibly because of risks of unnecessary fluid. This ambiguity also exists during craniotomy, because fluid therapy may augment both cardiac output and cerebral blood flow,[6] but an elevated net fluid balance may result in poor neurological outcomes.[7 8] Whether a fluid protocol aiming for cardiac output augmentation or fluid restriction is

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Editor's key points

- Stroke volume variation (SVV) is a measure of fluid responsiveness used in goal-directed fluid therapy strategies.
- The optimal volume status during neurosurgery is not known.
- Patients undergoing supratentorial tumour excision were randomized to a protocol using a high or low SVV cut-off.
- Patients assigned to the low SVV group received more fluid but had better outcomes.

favourable to post-craniotomy neurological outcomes remains uncertain.

Stroke volume variation (SVV) is one of the dynamic fluid parameters that predicts fluid responsiveness for various surgical settings,[9] including brain surgery.[10] However, there is a 'grey zone' of two cut-offs within which the validity is inconclusive.[11] For instance, fluid boluses based on the lower SVV cut-off exclude fluid responsiveness with near certainty, resulting in cardiac output augmentation; by contrast, those based on the higher SVV cut-off include fluid responsiveness with near certainty, resulting in a restrictive fluid balance. Application of two SVV cut-offs in the grey zone may provide clinical insights regarding the ambiguity of GDFT for craniotomy. Therefore, we investigated the effects of the GDFT protocols based on the two SVV cut-offs in the grey zone (a low SVV and a high SVV) in patients undergoing craniotomy for supratentorial brain tumour resection. The effects of the fluid bolus protocols on postoperative neurological outcomes were compared, and the changes in serum neuronal markers were investigated as biochemical evidence.

Methods

Study design and participants

In this single institution, single-blind study, two parallel arms were enrolled, namely low SVV and high SVV. This trial was approved by the Research Ethics Committee of National Taiwan University Hospital and was registered at clinicaltrials.gov with the identifier NCT02113358. We enrolled patients older than 20 yr who had undergone elective craniotomy for supratentorial brain tumour resection during May 2014–February 2017. Patients who met any of the following criteria were excluded: age >70 yr; recurrent tumours; BMI <18.5 or >27.0 kg m^{-2}; a history of cardiac dysfunction, such as coronary artery diseases, New York Heart Association Functional Classification (NYHA) class II or higher heart failure, and arrhythmia; renal insufficiency with an estimated glomerular filtration rate of <60 ml min^{-1} 1.73 m^{-2}; and chronic obstructive pulmonary disease and surgery in the prone position (Fig. 1).

All patients provided written informed consent on the day before surgery from an investigator who was unaware of the randomization result. On arrival at the operating theatre, patients were allocated to the study arms in a 1:1 ratio according to a predefined block randomization list with blocks randomly sized between four and six patients. Only the attending anaesthesiologist and research nurse were aware of patient allocation.

Anaesthesia

General anaesthesia was induced through total i.v. anaesthesia comprising a combination of target-controlled infusion of propofol using the Schnider model for induction (4 mg ml^{-1}), and maintaining a plasma concentration of 3–5 mg ml^{-1},[12] as well as fentanyl and cisatracurium. Patients were ventilated in a volume-controlled mode with a tidal volume of 8 ml kg^{-1}, an air:oxygen ratio of 1:1 and a total flow rate of 1 litre min^{-1}. A respiratory rate was set to maintain Pa_{CO_2} between 25 and 30 mm Hg to improve the operating conditions.[13] For analgesia, each patient received a scalp nerve block containing 10–20 ml of levobupivacaine 0.5% before head clamp placement and skin incision. In addition, neurophysiological monitoring techniques were used to enhance resection safety.

Haemodynamic monitoring

After anaesthesia induction, a 20-G radial arterial line was inserted and connected to the fourth-generation Vigileo/Flotrac system (Edwards Lifesciences, Irvine, CA, USA) to obtain the SVV and cardiac index. The Vigileo/Flotrac system analyses the pressure waveform 100 times s^{-1} over 20 s, capturing 2000 data points for analysis and performing calculations by using data obtained in the most recent 20 s. The SVV was calculated as the variation in beat-to-beat stroke volume (SV) from the mean value obtained during the most recent 20 s: $SVV = (SV_{max} - SV_{min}/SV_{mean})$. A large-bore i.v. catheter (16-G) in the forearm or a double-lumen 5.5-Fr catheter (Arrow central venous catheter; Teleflex Life Sciences Ltd, Athlone, Ireland) was inserted into the femoral vein for fluid infusion.

GDFT protocols and fluid bolus indications

Before conducting this study, a grey zone was created for the fourth-generation Vigileo/Flotrac-derived SVV to predict a 10% increase in the cardiac index of 124 fluid boluses [using 250 ml of tetrastarch (Voluven; Fresenius Kabi, Uppsala, Sweden) within 15 min] from 45 patients who underwent supratentorial brain tumour resection through retrospective analysis of a prospectively maintained database by a bootstrapped resampling method.[11] The grey zone resampling results showed that the median cut-off was 13%, with a 95% confidence interval of the distribution of optimal cut-offs ranging between 9 and 17% (Supplementary File S1). Therefore, the threshold SVV values of ≥10 and ≥18% for the low SVV and high SVV groups, respectively, were selected to initiate fluid boluses.

Figure 2 presents the GDFT protocols. The haemodynamic goal was evaluated every 15 min. The administration of fluid bolus using 250 ml of tetrastarch, for a better volume-sparing effects than crystalloid during craniotomy,[14] within 15 min was on the basis of two different SVV threshold values. The attending anaesthesiologist was allowed to infuse a supplementary colloid fluid bolus to prevent inadvertent hypovolaemia if a ≥10% decrease in cardiac index concurrent with a ≥5% increase in SVV from baseline states was observed because of its highly possible association with hypovolaemia.[15 16]

The SVV-based protocol was temporarily suspended when a blood transfusion was required. I.V. ephedrine (4–8 mg per bolus) was administered at the discretion of the attending anaesthesiologist to maintain the cardiac index when patient SVV was within the threshold limit; dopamine was considered to be infused if the total ephedrine dose was >40 mg. Maintenance of oxygenation, haemoglobin, blood glucose, core temperature and haemodynamics, such as minimal cardiac