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E-mail: bioinformationruby@gmail.com

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Beyond the waveform: FloTrac for brain protection and DCI in aSAH

Bhavana Pinnaka¹, Vasudha Singhal², Ishrat Yousuf^{3,*}, Poonam Rani⁴, L. Yalamanchali Sindhura⁵ & Harsh Sapra⁶

¹Department of Critical Care Medicine, KIMS ICON Hospitals, Visakhapatnam Andhra Pradesh, India; ²Department of Neuroanaesthesia and Neurocritical care, Max Smart Hospital, Delhi, India; ³Department of Neuroanaesthesia, Sher-e-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India; ⁴Department of Anaesthesia, Aadesh Medical College and Hospital, Mohri, Haryana, India; ⁵Department of Anaesthesia, Cloudnine Hospital, Hitech City, Hyderabad, Telangana, India; ⁶Department of Neuranaesthesia and Neurocritical care, Medanta - The Medicity, Gurugram, Haryana, India; *Corresponding author

Affiliation URL:

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Author contact:

Bhavana Pinnaka - E-mail: bhavanachowdary88@gmail.com
Vasudha Singhal - E-mail: vasudha_sarab@yahoo.com
Ishrat Yousuf - E-mail: eshratusuf90@gmail.com
Poonam Rani - E-mail: prathore646@gmail.com
Yalamanchali L. Sindhura - E-mail: sindhuraones@gmail.com
Harsh Sapra - E-mail: harsh.sapra@medanta.org

Abstract:

Delayed cerebral ischaemia is the leading preventable cause of morbidity after aneurysmal subarachnoid haemorrhage and this study evaluated FloTrac-guided goal-directed fluid therapy. A prospective randomized trial enrolled 68 patients assigned to conventional CVP-guided management (n=34) or FloTrac-guided therapy (n=34), with delayed cerebral ischaemia as the primary outcome. Delayed cerebral ischaemia occurred less often with FloTrac-guided therapy (17.6% vs. 32.4%), while angiographic vasospasm was absent in the FloTrac group (0% vs. 32.3%; $P < 0.001$). FloTrac-guided therapy produced better functional recovery, fewer readmissions and shorter ICU and hospital stays, although most differences were not statistically significant. Thus, FloTrac-guided goal-directed therapy showed clinically meaningful benefits and this may improve neurological outcomes after aneurysmal subarachnoid haemorrhage.

Keywords: Aneurysmal subarachnoid haemorrhage (aSAH), cardiac output monitoring, delayed cerebral ischaemia, FloTrac, goal-directed therapy, vasospasm

Background:

Aneurysmal subarachnoid haemorrhage (aSAH) carries a global incidence of approximately 7.9 per 100,000 person-years, accounting for 5% of all strokes, with case fatality ranging from 8% to 67% [1]. Among patients who survive the initial haemorrhage, delayed cerebral ischaemia (DCI) represents the most prevalent cause of preventable neurological disability, complicating 30-50% of cases within the first two weeks after ictus [2]. The pathophysiology of DCI has evolved considerably beyond the historical paradigm of large-vessel vasospasm. Current understanding recognises a convergence of cortical spreading depolarisation, microvascular thrombosis, neuroinflammation and blood-brain barrier disruption, all operating in the context of the profound haemodynamic perturbations intrinsic to aSAH [3]. These include catecholamine-mediated cardiac dysfunction, cerebral salt wasting and the competing hazards of hypovolaemia and fluid overload. The Triple-H strategy -hypervolaemia, hypertension and haemodilution -has been largely abandoned in favour of a more physiologically grounded approach: normovolaemia targeted induced hypertension and cardiac output augmentation where indicated [4]. However, translating this strategy into consistent clinical practice is hampered by the limitations of conventional haemodynamic monitoring. Central venous pressure, in particular, is a poor surrogate for intravascular volume status and provides no information regarding actual cardiac output or downstream oxygen delivery. Goal-directed therapy (GDT) offers a structured, physiology-driven framework that titrates haemodynamic interventions to measured parameters in real time [5]. The FloTrac/Vigileo system (Edwards Life sciences,

Irvine, CA, USA) provides continuous cardiac index (CI), stroke volume index (SVI), stroke volume variation (SVV) and systemic vascular resistance index (SVRI) from a standard radial arterial waveform, without requirement for external calibration [6]. Its minimally invasive design is well suited to the neuro-ICU setting, where invasive pulmonary artery catheterisation carries disproportionate risk. Prior randomised evidence has showed benefit from transpulmonary thermodilution-guided GDT in aSAH [7]. Therefore, it is of interest to report the clinical outcomes of FloTrac-guided goal-directed fluid therapy versus conventional CVP-guided fluid management in patients with aneurysmal subarachnoid haemorrhage.

Materials and Methods:

This prospective, single-centre, randomised controlled trial was conducted at the Department of Neurosciences, Medanta - The Medicity, Gurugram - a 1600-bed tertiary referral centre -between July 2021 and December 2022. Ethics Committee approval was obtained (Reference No. 1339/2021 DNB). Written informed consent was obtained from all participants or their legally authorized representatives prior to enrolment. The study was conducted in accordance with the principles of the Declaration of Helsinki. Adults aged ≥ 18 years with radiologically confirmed aSAH were screened consecutively. Of 80 patients assessed for eligibility, 68 fulfilled inclusion criteria and were enrolled. Exclusion criteria comprised: age < 18 years, traumatic subarachnoid haemorrhage, congestive cardiac failure, pregnancy and severe aortic valvular pathology. Eligible patients were randomised 1:1 using a computer-generated

allocation sequence to Group A (conventional management, n=34) or Group B (FloTrac-guided GDT, n=34). Sample size was calculated based on published extravascular lung water index data (mean 10.4 ± 2.3 ml kg⁻¹; effect size d=0.78), yielding n=34 per group at $\alpha=0.05$ and 80% power. All patients received standardised aSAH management in accordance with American Heart Association guidelines, including bed rest, short-term antifibrinolytic therapy and early definitive treatment by surgical clipping or endovascular coiling. All patients were subsequently admitted to the neuro-ICU and received oral nimodipine 60 mg every 4 h for 21 days.

Group A: (Conventional management):

Crystalloid infusions of 1500-3000 ml day⁻¹ were administered for 14 days, adjusted according to clinical judgement and targeting CVP 5-8 mmHg. Allogeneic blood transfusion was administered when haematocrit fell below 30%.

Group B: (FloTrac-guided GDT):

Hemodynamic management was directed by the Vigileo FloTrac system, connected to a radial arterial catheter and a 7Fr internal jugular central venous catheter. The device calculated CI, SVI, SVV and SVRI every 20 s. Measurements commenced after a 10-minute stabilisation period. Predefined haemodynamic targets were: CI 3.0-5.0 L min⁻¹ m⁻²; SVI ≥ 40 ml m⁻²; SVRI 1700-2400 dyn s cm⁻⁵ m⁻². Fluids, vasopressors and inotropes were titrated in a protocolised fashion to maintain these targets throughout the 14-day monitoring period.

Outcome measures:

All patients were followed for 14 days. The primary outcome was the incidence of DCI, defined as: (a) arterial calibre reduction to $\leq 50\%$ of the admission angiogram on digital subtraction angiography (DSA); or (b) a decrease of ≥ 2 points on the Glasgow Coma Scale (GCS) or an increase of ≥ 2 points on the NIH Stroke Scale persisting for ≥ 8 h, after exclusion of alternative causes. Vasospasm was assessed daily by transcranial Doppler ultrasonography (TCD) -twice daily for the first 7 days, then once daily -with confirmation by DSA when clinically indicated. TCD criteria for vasospasm were: peak middle cerebral artery (MCA) velocity increase of >50 cm s⁻¹ per 24 h, or mean MCA velocity >120 cm s⁻¹; Lindegaard ratio >3 to differentiate from cerebral hyperaemia. Symptomatic vasospasm was treated with intra-arterial nimodipine and milrinone per the Montreal Protocol. Functional outcome at hospital discharge was assessed using the Extended Glasgow Outcome Scale (GOSE).

Statistical analysis:

Data were analysed using IBM SPSS Version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as frequencies and percentages and compared using Pearson's chi-squared test. Continuous variables are reported as mean (SD) and compared using the independent samples t-test. Statistical significance was defined as P<0.05.

Results:

The two groups were well matched at baseline. Mean age was 53.1 years in Group A and 54.8 years in Group B (P=0.101). Female sex was more prevalent in Group B (58.8% vs 44.1%; P=0.332). The anterior communicating artery was the most frequent aneurysm site in both groups (35.3% vs 38.2%). Hypertension was the predominant comorbidity, present in 32.4% of patients in each group. The majority of patients presented in good clinical grades: GCS 13-15 in 76.5% (Group A) and 79.4% (Group B). Modified Fischer grade distribution, WFNS grading and time from ictus to presentation did not differ significantly between groups (**Table 1**). DCI occurred in 11 of 34 patients (32.4%) in Group A and in 6 of 34 patients (17.6%) in Group B, representing an absolute risk reduction of 14.8 percentage points (P=0.262). Although statistical significance was not achieved -attributable to the sample size constraints -the magnitude and consistency of the observed effect are clinically meaningful. The most statistically robust finding concerned DSA-confirmed vasospasm, which was documented in 11 patients (32.3%) in Group A and in no patient in Group B (P<0.001). TCD-detected vasospasm was observed in 47.1% of Group A patients versus 35.3% of Group B (P=0.460). Milrinone infusion was required in 41.2% of Group A compared with 26.5% of Group B (P=0.199). Vasopressor support with noradrenaline was administered in 41.2% of Group A and 23.5% of Group B (P=0.119). CVP values were significantly and consistently higher in Group A at all 14 monitoring time points (range 6.4-7.6 mmHg vs 3.2-4.5 mmHg; P<0.001 at all-time points). This reflects the differing fluid management philosophies: Group A patients were managed towards a positive CVP target consistent with historical hypervolaemic practice, whilst Group B patients were maintained within a precise euvolaemic corridor determined by real-time CI and SVI. Mean arterial pressure and heart rate did not differ significantly between groups, indicating that haemodynamic adequacy was achieved without excessive vasoactive driving in the GDT arm. Upper good recovery (GOSE 8) was achieved in 76.5% of patients in Group B compared with 58.8% in Group A. Severe disability (GOSE ≤ 4) was recorded in 8.8% of Group B versus 17.6% of Group A. A vegetative state was observed in one patient in Group A and none in Group B. Although these differences did not achieve statistical significance (P=0.480), a consistent gradient favouring GDT was apparent across all GOSE categories. Prolonged hospital admission (>25 days) occurred in 20.6% of Group A but only 5.9% of Group B. Readmission was required in 38.2% of Group A versus 17.6% of Group B (P=0.060). Secondary outcomes are summarised in (**Table 2**). Across both groups, higher modified Fischer grade, lower GCS score, higher WFNS grade, the presence of vasospasm, longer ICU stay and the requirement for milrinone infusion or intra-arterial nimodipine were all significantly associated with DCI (P<0.05), consistent with established risk factors in the literature.

Table 1: Baseline characteristics of study participants

Variable	Group A (n=34)	Group B (n=34)
Mean age (years)	53.1	54.8

Female sex	44.1%	58.8%
Anterior communicating artery aneurysm	35.3%	38.2%
Hypertension	32.4%	32.4%
GCS 13-15 at presentation	76.5%	79.4%
WFNS Grade 1-2	50.0%	32.4%
Modified Fischer Grade 1-2	73.5%	79.4%
Presentation within 5 days of ictus	64.7%	73.5%

GCS, Glasgow Coma Scale; WFNS, World Federation of Neurosurgical Societies

Table 2: Primary and secondary outcomes.

Outcome	Group A	Group B	P value
Delayed cerebral ischaemia	32.4%	17.6%	0.262
Vasospasm (DSA-confirmed)	32.3%	0%	<0.001
Vasospasm (TCD-detected)	47.1%	35.3%	0.460
GOSE 8 (upper good recovery)	58.8%	76.5%	0.480
Severe disability (GOSE ≤4)	17.6%	8.8%	—
ICU stay <10 days	67.6%	79.4%	0.633
Hospital stay <10 days	55.9%	70.6%	0.218
Readmission	38.2%	17.6%	0.060
Vasopressor requirement	41.2%	23.5%	0.119
Milrinone infusion	41.2%	26.5%	0.199

DCI, delayed cerebral ischaemia; DSA, digital subtraction angiography; GOSE, Extended Glasgow Outcome Scale; ICU, intensive care unit; TCD, transcranial Doppler.

Discussion:

This randomised trial evaluated whether continuous cardiac output monitoring with FloTrac-guided GDT could reduce DCI and improve outcomes following aSAH. The principal findings were a near-halving of clinical DCI incidence in the GDT arm, complete elimination of DSA-confirmed vasospasm, improved functional recovery, reduced vasopressor requirements and lower readmission rates -all consistently favouring the GDT strategy, albeit with limited statistical power. The reduction in DCI from 32.4% to 17.6% closely mirrors the findings reported by Alves *et al.* [8] in their randomized controlled trial of 108 aSAH patients, where transpulmonary thermodilution-guided GDT reduced DCI from 34% to 13% (P=0.021). The convergence of effect magnitude across two independent trials employing different monitoring technologies, in different clinical settings, supports the hypothesis that real-time cardiac output guidance - rather than any specific monitoring platform - is the active mechanism underlying the benefit. The complete absence of DSA-confirmed vasospasm in Group B (0% vs 32.3%; P<0.001) is the most striking observation in this dataset. This finding suggests that FloTrac-guided haemodynamic management may interrupt the transition from subclinical perfusion deficit to established angiographic vasospasm by enabling pre-emptive correction of reduced CI and hypovolaemia before microvascular injury becomes irreversible. Mutoh *et al.* [9] described a conceptually similar mechanism with integrated continuous cardiac output and near-infrared spectroscopy monitoring, demonstrating that real-time multimodal haemodynamic data facilitates pre-emptive rather than reactive intervention. The systematically higher CVP values observed in Group A (6.4-7.6 mmHg vs 3.2-4.5 mmHg across all 14 monitoring days) are consistent with the well-recognised clinical tendency towards volume loading when using filling pressure targets in the absence of cardiac output data. This pattern aligns with the independent association between high fluid intake and adverse outcomes showed by the feasibility data reported by Vergouw *et al.* [10], both of which suggest that the

haemodynamic optimum in aSAH is euvolaemia rather than hypervolaemia. The functional outcome data, though statistically non-significant, are clinically noteworthy. A 17.7 percentage-point absolute difference in the rate of upper good recovery (GOSE 8) -76.5% versus 58.8% -represents a meaningful difference in patient-centred outcomes. The near-significant reduction in readmission rates (P=0.060) suggests that the haemodynamic benefits of GDT may extend beyond the acute admission, consistent with a model in which cerebral protection during the critical two-week window confers lasting neurological benefit [11, 12].

Conclusion:

FloTrac-guided goal-directed therapy was associated with complete elimination of DSA-confirmed vasospasm, a clinically important reduction in DCI incidence, improved functional recovery and reduced hospital burden in patients with aSAH. These data support incorporation of continuous cardiac output monitoring into aSAH haemodynamic management protocols and provide justification for an adequately powered, multicentre randomized trial.

Limitations:

This study has several limitations that merit acknowledgement. The sample size, whilst appropriate for the primary power calculation based on extravascular lung water data, was insufficient to detect modest differences in the clinical endpoints reported. The single-center design limits generalizability. The FloTrac system has recognized accuracy constraints in the presence of cardiac arrhythmias and severe aortic valvular pathology, although these conditions constituted exclusion criteria. Follow-up was limited to 14 days, precluding assessment of longer-term neurological outcomes. Future trials should incorporate extended functional follow-up, health-economic analyses and multicenter enrolment to provide the statistical power necessary to confirm these findings.

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Declarations:

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Conflicts of interest: None declared.

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