



RESEARCH ARTICLE

# A pilot study on assessing the role of intra-operative Flow 800 vascular map model in predicting onset of vasospasm following micro vascular clipping of ruptured intracranial aneurysms [version 1; referees: 3 approved]

Sunil Munakomi , Deepak Poudel

Neurosurgery, Nobel Teaching Hospital, Biratnagar, 0977, Nepal

**v1** First published: 03 Aug 2018, 7:1188 (doi: [10.12688/f1000research.15627.1](https://doi.org/10.12688/f1000research.15627.1))  
 Latest published: 03 Aug 2018, 7:1188 (doi: [10.12688/f1000research.15627.1](https://doi.org/10.12688/f1000research.15627.1))

**Abstract**

**Objective**

To ascertain the predictive value of intra-operative FLOW 800 vascular map model in predicting onset of post-operative clinical vasospasm and delayed cerebral ischemia among patients undergoing micro-vascular clipping of ruptured intracranial aneurysms.

**Material and methods**

A total of 40 patients were enrolled in the study and their variables such as age, World Federation of Neurological Surgeons (WFNS) grade at presentation, Computerized Tomography (CT) Fisher grading, location of the aneurysms, and Indocyanine Green (ICG) flow status were compared and statistically analyzed along with differences in Absorption Intensities (AI) and difference in time lag values obtained from the FLOW 800 vascular map studies for predicting onset of vasospasm.

**Results**

The Receiver Operating curve (ROC) of the model for predicting post-operative vasospasm was highest (.892) for difference in the AI followed by CT Fisher grading (.778), difference in time lag (.700) and WFNS grading (.699). Analysis of variance for different variables studied in our model for predicting vasospasm was significant for all except for age (.991) and the ICG flow through the parent vessel (.079). Multivariate analysis done for predicting the vasospasm was significant for all variables except for age (.869) and ICG main flow (.196)

**Conclusion**




Our study confirmed the role of FLOW 800 study model in predicting clinical vasospasm. Inclusion of this entity would therefore help in taking timely and correct therapeutics measures to ensure better patient outcomes.

**Keywords**

Aneurysm, vasospasm, ICG study, FLOW 800 study

**Open Peer Review**

Referee Status: 

	Invited Referees		
	1	2	3
<b>version 1</b>			
published 03 Aug 2018	report	report	report

- Guru Dutta Satyarthee**, All India Institute of Medical Sciences, India
- Lekhjung Thapa** , National Institute of Neurological and Allied Sciences, Nepal
- Amit Agrawal** , Narayana Medical College and Hospital, India

**Discuss this article**

Comments (0)

**Corresponding author:** Sunil Munakomi ([sunilmunakomi@gmail.com](mailto:sunilmunakomi@gmail.com))

**Author roles:** **Munakomi S:** Conceptualization, Data Curation, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Poudel D:** Data Curation, Formal Analysis, Methodology, Writing – Review & Editing

**Competing interests:** No competing interests were disclosed.

**Grant information:** The author(s) declared that no grants were involved in supporting this work.

**Copyright:** © 2018 Munakomi S and Poudel D. This is an open access article distributed under the terms of the [Creative Commons Attribution Licence](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Data associated with the article are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC0 1.0 Public domain dedication).

**How to cite this article:** Munakomi S and Poudel D. **A pilot study on assessing the role of intra-operative Flow 800 vascular map model in predicting onset of vasospasm following micro vascular clipping of ruptured intracranial aneurysms [version 1; referees: 3 approved]** *F1000Research* 2018, 7:1188 (doi: [10.12688/f1000research.15627.1](https://doi.org/10.12688/f1000research.15627.1))

**First published:** 03 Aug 2018, 7:1188 (doi: [10.12688/f1000research.15627.1](https://doi.org/10.12688/f1000research.15627.1))

## Introduction

Progressive narrowing of vessels can occur in up to 70% of patients within 2 weeks of intra-cranial aneurysmal rupture, among which 30% develop delayed ischemic neurological deficits<sup>1,2</sup>. Although hypertension, hypervolemia and hemodilution (triple-H) therapy is commonly instituted to counteract this process, there is a paucity of evidence for recommending it for prophylactic purposes<sup>3</sup>. The American Heart Association/American Stroke Association guidelines also recommend induced hypertension targeted euvolemia for managing delayed cerebral ischemia (DCI)<sup>4</sup>. The World Federation of Neurological Surgeons (WFNS) grade of the patient at presentation and the location of epicenter of the subarachnoid bleed has shown to be positively correlated with the onset of vasospasm<sup>5,6</sup>. Since indocyanine green (ICG) flow studies are safe, easily applicable, readily reproducible and now routinely utilized technique during the microvascular clipping of aneurysms, addition of FLOW 800, an automated vascular map study generated by the microscope with the provision for quantitative study of flow velocities and time lag for appearance of the dye between relevant vessels, can help us segregate and outline groups at high-risk of developing post-operative vasospasm and form an evidence-based management algorithm for better therapeutic benefits and clinical outcomes.

## Methods

### Subjects and procedures

A total of 40 patients who underwent microvascular clipping for ruptured intra-cranial aneurysms in the Department of Neurosurgery at Nobel Medical College and Teaching Hospital (Biratnagar, Nepal) between January 2017 and June 2018 were enrolled in the study. Those patients who refused to participate in the study or who left the hospital against medical advice during the course of the study were excluded from the study. Moreover, exclusions were also made in extreme circumstances wherein ICG study was not possible owing to intra-operative brain swelling or inability to visualize the relevant vessels owing to small operating field or close proximities between relevant vessels rendering difficulties in correctly specifying regions of interests (ROI).

### Data acquisition

The retrospective acquisition of data of these patients, with regards to their age, Glasgow coma scale (GCS) during initial presentation, WFNS grade, computerized tomography (CT) Fisher grading<sup>7</sup>, ICG flow status and FLOW 800 mapping (version 2.21) (extrapolated from a Pentero surgical microscope; Carl Zeiss Co., Germany) was conducted and the outcome in terms of occurrence of radiological and clinical vasospasm was analyzed.

To obtain ICG flow status, after the permanent clip was applied, the setting of the microscope was changed from the usual white light to the infrared mode. Next, ICG was injected and visualization was looked for within the desired vessels. This is a qualitative study, but we can record the time lag for appearance of dye. Following this, with the help of the FLOW 800 software, a vascular map was automatically generated from the IR 900 video data. There is also provisions for quantitative analysis of

the flow dynamics in terms of average absorption intensity (AI) and time lag for appearance of the dye by selecting appropriate regions of interests (ROI) within the vessels.

In our study model of FLOW 800 mapping, the lower normal limit for normal difference in average absorption intensity (DfAI) between the parent and the branching vessel was taken at 50%. Similarly, the maximum upper limit for time-lag for appearance of the flow between the parent and the branching vessel was kept at 6 seconds (Figure 1–Figure 4). This time limit was extrapolated from the pooled results of ICG and FLOW 800 studies in patients who did not show any vasospasm in the post-operative period. The average intensity was chosen owing to its easy applicability, calculation and easy reproducibility, thereby minimizing scoring bias. Currently, there is a paucity in the literature with regards to normal values for AIs and time-lag for specific vessels following FLOW 800 study so as to form a specific reference standard. Values from these studies were compared to clinical findings and CT images, which served as the surrogate marker for vasospasm.

To minimize study bias and the post hoc effects, the study was blinded among the investigators who studied the clinical and radiological outcomes from those who analyzed the ICG and FLOW 800 vascular studies. All patients received an intravenous ICG bolus of 25 mg dissolved in 5 ml of 0.9% saline for the study. A Pentero surgical microscope (Carl Zeiss Co., Germany) was utilized for studying ICG as well as FLOW 800 vascular studies.

### Post-operative care

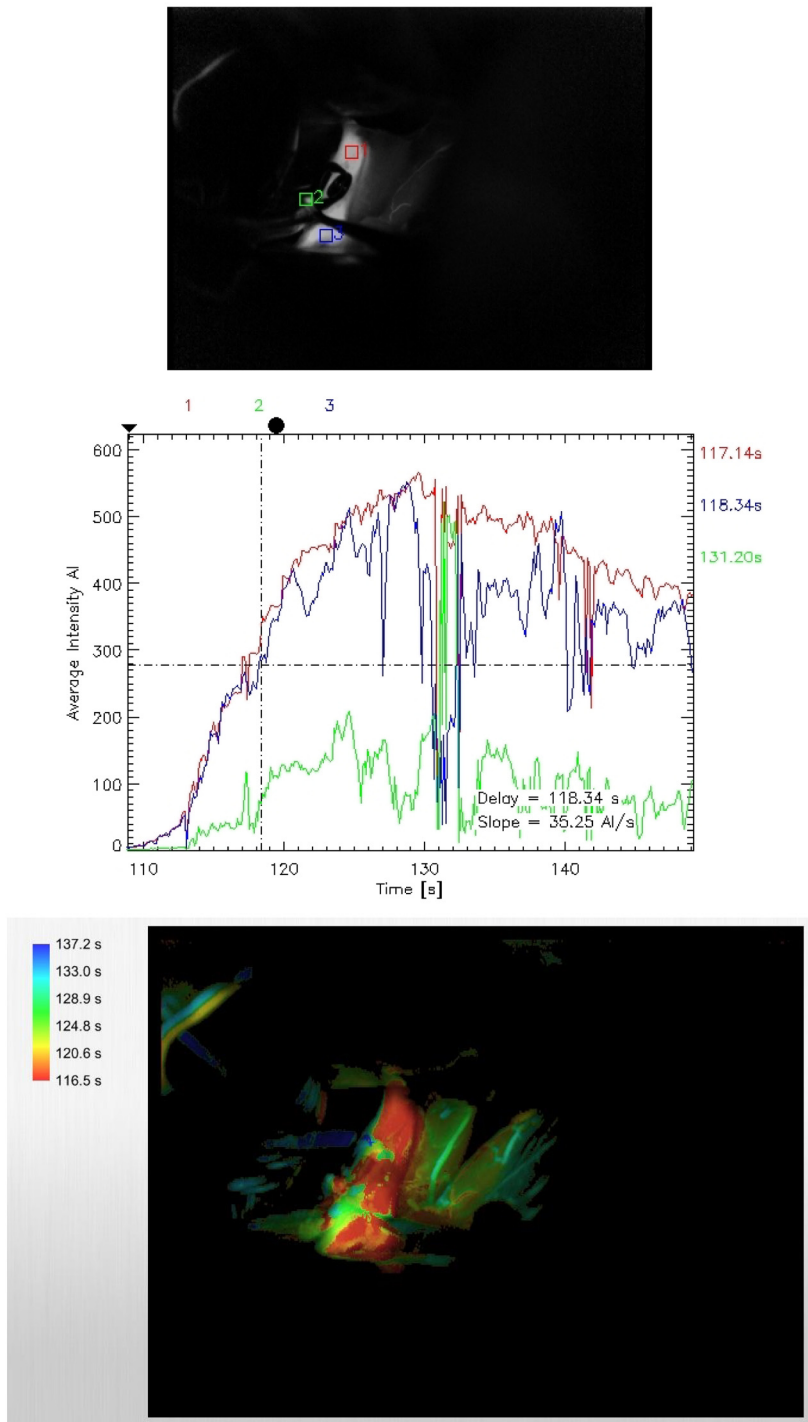
Post-operatively, patients were given 60 mg (oral or via naso-gastric feeding tube) nimodipine every 4 hours and fluid management was titrated to achieve a central venous pressure of 8–12 mmHg, a hematocrit of 30–35% and a mean arterial pressure (MAP) of more than 20 mmHg greater than the preoperative MAP value. Clinical (presence of new onset neurological deficits in the post-operative period) and radiological (presence of features of ischemia or infarction) evidence of vasospasm were stringently assessed and recorded in the post-operative period.

### Ethical considerations

The study was approved by the Institutional Review Committee (IRC) of Nobel Medical College and Teaching Hospital (NMCTH) (approval number 134/2018). Written informed consent was taken from the relatives or next of kin of the patients (owing to the poor neurological status of the patients and the emergent need for operative management) for their inclusions in the study and usage of their relevant clinical data for resource measures.

### Data analysis

Data were recruited and analyzed using the SPSS version 16 software. Statistical analysis was done utilizing receiver operating curve (ROC) with area under curve (AUC) values, Analysis of variance (ANOVA) and multivariate logistic regression analysis along with logistic coefficient curve study among the considered variables applying vasospasm as the final



**Figure 1.** Flow 800 map in the case of a posterior communicating artery (PCOM) aneurysm showing peak flow in PCOM (green) greater than 50% of flow in the internal carotid (red) but significant (>6 seconds) delay in time lag for the flow.

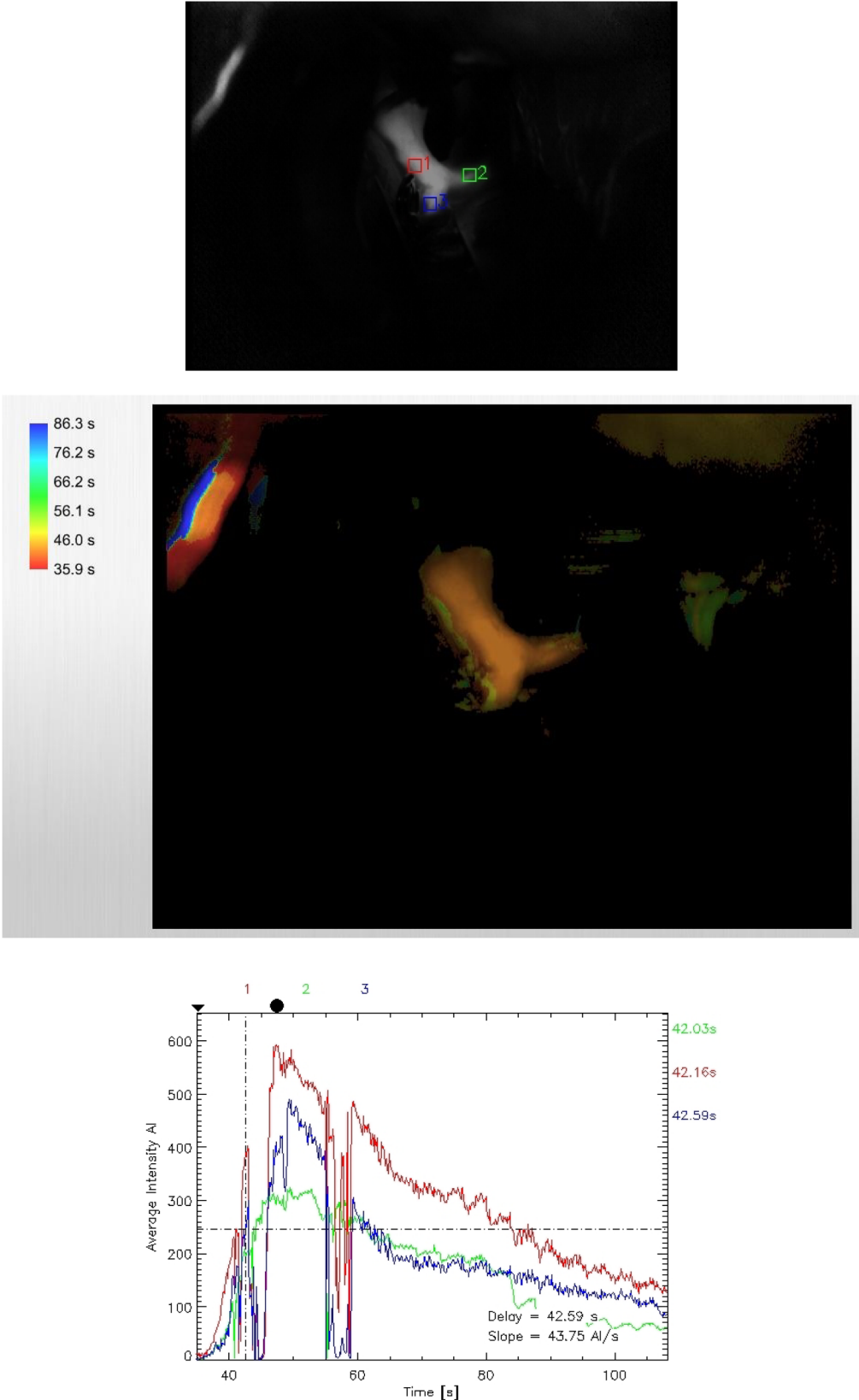
outcome. No post hoc analysis was done beyond those factors pertaining to our study model.

**Results**

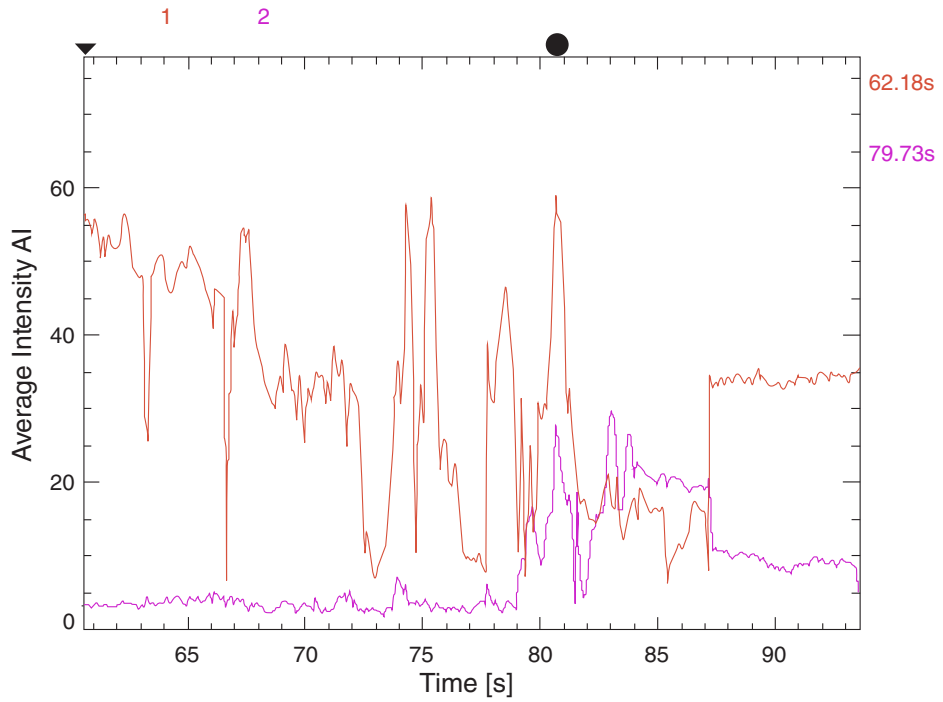
The incidence of clinical vasospasm and delayed cerebral ischemia was 40% in this study. CT Fisher grade 3 was seen in 42.5% of

cases and grade 4 in 37.5% of cases. The incidence of anterior communicating artery aneurysm was observed in 62.5% of cases.

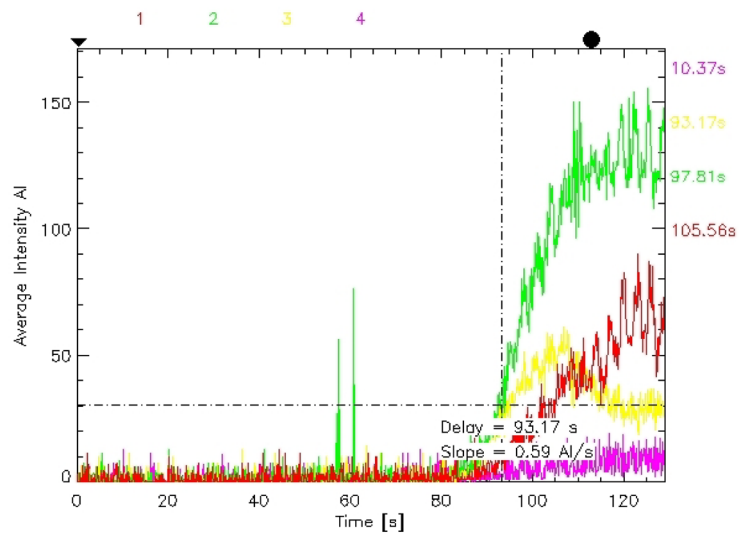
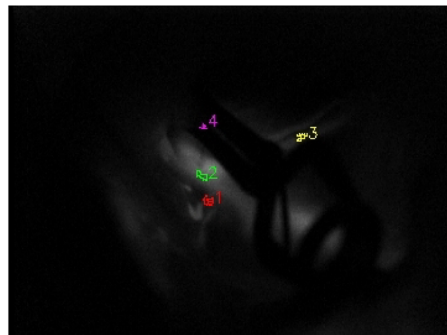
The receiver operating curve (ROC) of the model for predicting post-operative vasospasm was highest (area under the curve (AUC)=0.892) for difference in the AI of FLOW 800 study



**Figure 2.** Flow 800 map in the case of an anterior communicating artery aneurysm showing flow in the A1 segment (green) at 50% of the parent internal carotid artery (red).



**Figure 3.** Flow map in the same patient as in Figure 2 showing flow discrepancy of almost 50% between the two distal A2's as well as significant time delay in flow through them.



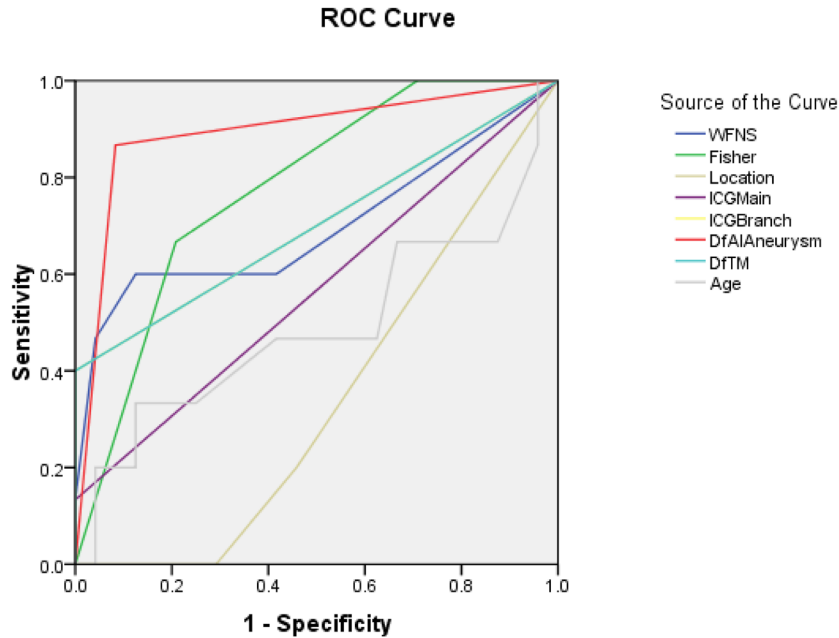
**Figure 4.** Flow map in another anterior communicating artery aneurysm also revealing flow in A2's (yellow) less than 50% of that in the A1 (green).

followed by CT Fisher grading (AUC=0.778), difference in time lag in FLOW 800 (AUC=0.700) and WFNS grading (AUC=0.699) (Figure 5 and Table 1) thereby verifying the aim of our study for its routine inclusion as an intra-operative adjunct to ICG flow study.

ANOVA for variables studied in our model for predicting vasospasm was significant for WFNS grade, CT Fisher grade, location of aneurysms, ICG flow through branching vessels, difference in flow velocities (DfAI) and time lag in dye appearance (DfTM) but not for age of the patients (P=0.991) and the ICG flow through

the parent vessel (P=0.079) (Table 2). Multivariate analysis done for predicting the vasospasm was significant for all variables except for age (P=0.869) and ICG main flow (P=0.196) (Table 3).

The correlation and the coefficient curves between relevant variables and onset of post-operative vasospasm have been shown in the Figure 6 and Figure 7, which are also positively correlated with WFNS, CT Fisher grade, difference in velocities (DfAI) and time lag (DfTM) obtained from the FLOW 800 software in positively predicting the onset of post-operative vasospasm.



Diagonal segments are produced by ties.

Figure 5. Receiver operating curve for different variables in the study for predicting vasospasm.

Table 1. Area under curve values for different variables in predicting vasospasm.

Test result variable(s)	Area	Std. error	Asymptotic significance	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
WFNS	0.699	0.097	0.039	0.508	0.889
Fisher	0.778	0.075	0.004	0.632	0.924
Location	0.342	0.086	0.100	0.173	0.511
ICG main	0.567	0.098	0.488	0.375	0.758
ICG branch	0.700	0.094	0.038	0.516	0.884
Difference (AI)	0.892	0.061	0.000	0.772	1.012
Difference (time)	0.700	0.094	0.038	0.516	0.884
Age	0.490	0.104	0.920	0.286	0.695

WFNS, World Federation of Neurological Surgeons; ICG, indocyanine green; AI, absorption intensity.



**Table 2. Results of analysis of variance for different variables in the study with regards to predicting vasospasm.**

Variable	Comparison	Sum of squares	df	Mean square	F	Sig.
Age	Between groups	0.017	1	0.017	0.000	0.991
	Within groups	5235.583	38	137.779		
WFNS	Between groups	16.017	1	16.017	11.359	0.002
	Within groups	53.583	38	1.410		
Fisher	Between groups	5.192	1	5.192	12.667	0.001
	Within groups	15.167	37	0.410		
Location	Between groups	4.267	1	4.267	4.402	0.043
	Within groups	36.833	38	0.969		
ICG Main	Between groups	0.150	1	0.150	3.257	0.079
	Within groups	1.750	38	0.046		
ICG Branch	Between groups	1.350	1	1.350	13.680	0.001
	Within groups	3.750	38	0.099		
Difference (AI)	Between groups	6.017	1	6.017	63.805	0.000
	Within groups	3.583	38	0.094		
Difference (time)	Between groups	1.350	1	1.350	13.680	0.001
	Within groups	3.750	38	0.099		

df, degrees of freedom; WFNS, World Federation of Neurological Surgeons; ICG, indocyanine green; AI, absorption intensities.

**Table 3. Results of multivariate analysis of various variables for predicting vasospasm.**

Source	Dependent variable	Type III sum of squares	df	Mean square	F	Sig.
Corrected model	Age	39.626	2	19.813	0.141	0.869
	WFNS	14.407	2	7.203	5.036	0.012
	Fisher	5.207	2	2.604	6.186	0.005
	Location	6.574	2	3.287	3.440	0.043
	ICG main	0.164	2	0.082	1.704	0.196
	ICG branch	1.477	2	0.738	7.385	0.002
	Difference (AI)	6.043	2	3.021	34.121	0.000
	Difference (time)	1.477	2	0.738	7.385	0.002

df, degrees of freedom; WFNS, World Federation of Neurological Surgeons; ICG, indocyanine green; AI, absorption intensities.

**Dataset 1. Demographic information and the results of each diagnostic technique performed for each patient**

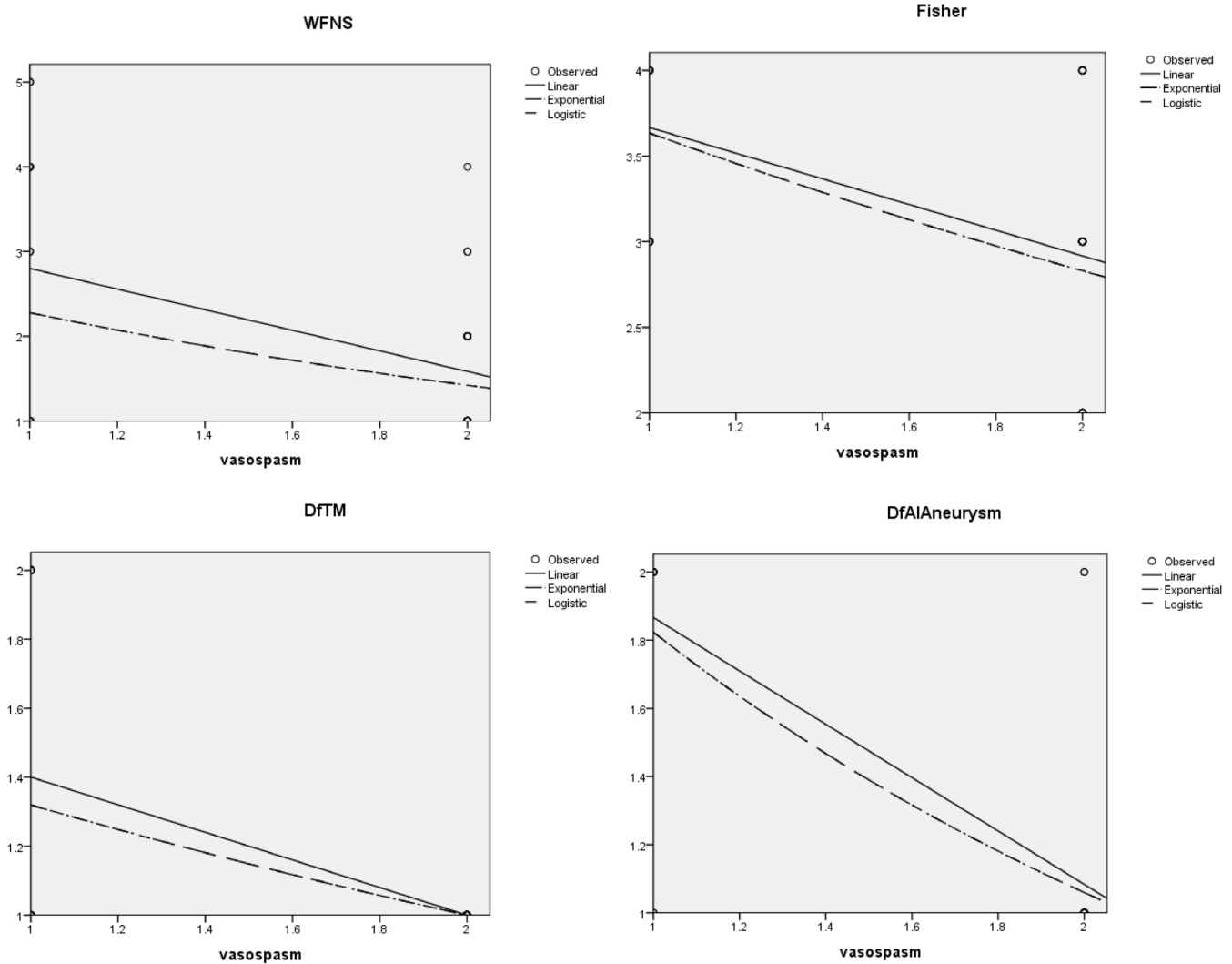
<http://dx.doi.org/10.5256/f1000research.15627.d212875>

**Discussion**

Cerebral vasospasm has surpassed re-bleeding as the main cause of death and major disability among patients with ruptured

intracranial aneurysms<sup>9</sup>. Inadvertent clipping of the parent vessels, its branches or the perforators causing compromised blood flow has been seen in 12–21% of cases, with subsequent occurrence of significant vasospasm in up to 10% of these cases<sup>10,11</sup>. Cerebral vasospasm still leads to mortality in 7% of patients, and to severe disability in another 7% of cases, even in experienced hands and the best neurosurgical care<sup>12–14</sup>. Visual inspection alone does not verify perfect placement of the clips and guarantee the patency of the relevant vessels<sup>10,15</sup>.





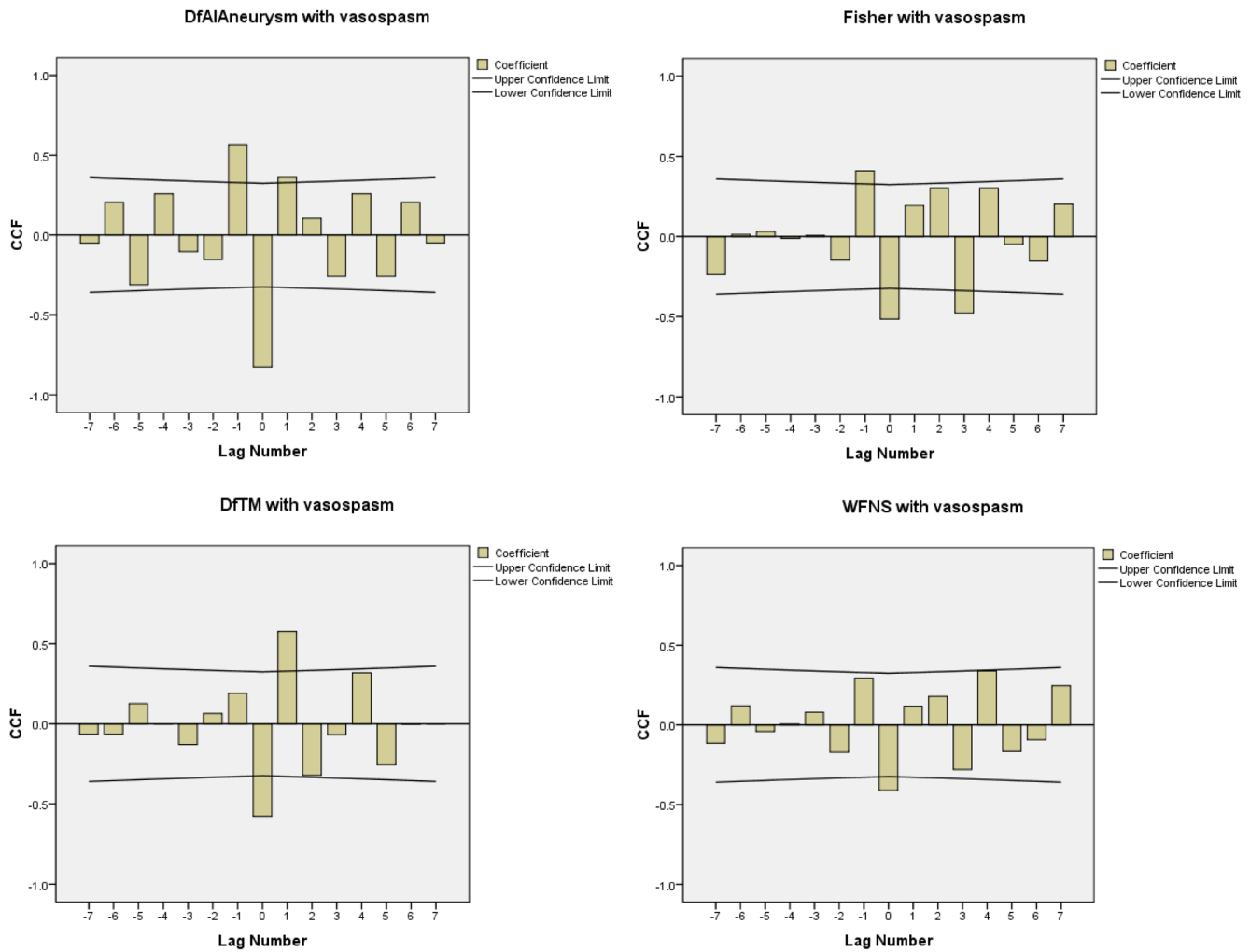
**Figure 6. Logistic correlation curve of various variables with onset of vasospasm.** The specific variable is represented in the 'x' axis and risk of vasospasm in the 'y' axis. DfAI, difference in average absorption intensity between parent and branching vessels; DfTM, difference in time lag for appearance of dye between parent and branching vessels.

In this aspect, intraoperative angiography is still the gold standard in confirming the patency of the parent and their branching vessels along with their relevant perforators<sup>16,17</sup>. Intra-operative angiography has facilitated clip readjustment in almost 44% of cases. However, technical complexities, the risk of radiation hazards and major neurological complications (0.4–2.6%) preclude its frequent intra-operative application<sup>18</sup>. The application of intraoperative angiography also prolongs the operative time by almost 40 minutes<sup>19</sup>.

Microscope-integrated ICG angiography has shown to be a valuable alternative for assessing real-time intra-operative vascular mapping with minimal risks and hazards compared to intra-operative digital subtraction angiography<sup>20,21</sup>. ICG is a near-infrared (NIR) fluorescent dye; its absorption and emission peaks (805 and 835 nm, respectively) are ideally suited for use in vascular studies since confounding absorption from other endogenous chromophores are minimal within these ranges<sup>22</sup>.

The dye remains confined within the vascular compartment after binding to specific plasma proteins. The operating microscope can be integrated with a laser light source (wavelength within the ICG absorption band) and a camera that is capable of exciting, visualizing and subsequently transforming acquired ICG images into real-time vascular road maps<sup>21,23–25</sup>.

FLOW 800 is microscope-integrated software capable of automatically reconstructing time-resolved quantitative analysis of ICG angiography studies. The resulting data can be displayed and stored as either time-to-arrival maps or time-intensity curves specific for selected regions of interests (ROI)<sup>26</sup>. The software reproduces a map graded by the averages of the AIs and the time lag for the same based on time to half maximal fluorescence within the selected ROIs<sup>27</sup>. ICG angiography has complication rate of less than 0.1%<sup>28,29</sup>. The discordance between ICG and intraoperative digital subtraction angiography (DSA) in previous series were reported to be in the range of 10–20%<sup>30–32</sup>. A



**Figure 7. Logistic coefficient curve of various factors with onset of vasospasm.** DfAI, difference in average absorption intensity between parent and branching vessels; DFTM, difference in time lag for appearance of dye between parent and branching vessels.

recent study has shown to be correlating with post-operative DSA findings in almost 97% of cases<sup>23</sup>.

The main limitation of ICG angiography is that it can only study the vascular flow within the field of the operating microscope. Furthermore, blood clots, brain tissue and sometimes applied aneurysm clips can also preclude the proper visualization of the vessels, thereby requiring further adjustments of the microscope. The image quality can also be hindered by calcifications, atherosclerotic plaques or thromboses within the aneurysm<sup>33</sup>.

The limitations of having that microscope in the direct line-of-sight of the region of interest can be counteracted by simultaneous use of an endoscope<sup>25,34</sup>. A recent study suggested the use of intra-arterial ICG at a reduced dosage for better image quality with minimized time-lag between successive studies, owing to its rapid clearance, unlike intravenous studies wherein the ICG remains for around 10 minutes<sup>35</sup>. Micro-vascular Doppler study is a simple and readily applicable alternative

for assessing the vascular patency<sup>36</sup>. A micro-Doppler study, however, lacks quantitative assessment and is also highly influenced on the insonation angles during its placement by the operator<sup>33,36</sup>. The sensitivity and specificity for determining the accurate flow are limited to 85–90%<sup>37,38</sup>. Intraoperative alterations, such as brain shift following retractor removal, probable induced late mechanical thrombosis and sometimes the Coanda effect induced by clips are not detectable by Doppler study<sup>19,39</sup>. Other more recent advancements involve somatosensory evoked potentials (SSEPs)<sup>40,41</sup>. However, they have limitations in predicting ischemia outside the perimeter of the corticospinal tract<sup>25</sup>. The ‘ultimate, all-in-one’ diagnostic tool has not yet been designed<sup>42</sup>.

Prophylactic hypervolaemic therapy is unlikely to confer any additional benefit in minimizing vasospasm<sup>42</sup>. Treatment with triple-H therapy causes complications in 10–20% of patients, with pulmonary edema the most common adverse effect<sup>13,43</sup>. Moreover, there can be exacerbation of cerebral edema and an

added risk of bleeding from unsecured and sometimes hemorrhagic infarctions in ischemic regions<sup>9</sup>.

The advantage of using FLOW 800 intra-operatively is that it facilitates the timely undertaking of corrective measures, such as readjustment of the clips. Calcium overloading, which triggers phosphorylation of the contractile proteins of the arterial smooth muscles thereby leading to vasospasm, can be minimized by using topical sodium nitroprusside (SNP)<sup>44,45</sup>. Moreover, complications such as pulmonary edema due to aggressive medical management can be minimized by placement of a swan gauge catheter to keep the pulmonary capillary wedge pressure below the colloid oncotic pressure (COP)<sup>46</sup>. A serial bedside transcranial Doppler (TCD) study can be utilized in these patients to assess changes in the flow velocities and accordingly modifying the treatment algorithm<sup>47</sup>. Moreover, relevant rescue interventions, such as hemodynamic augmentation or intra-arterial vascular manipulations can be timely initiated for prevention as well as management of refractory vasospasms<sup>48</sup>.

There are some limitations in our study. The results of our study were derived from sample size of only 40 patients, and therefore needs further confirmation from multi-centric randomized control trials with the inclusion of larger cohorts. There is also a prerequisite for an ICG-integrated operating microscope with added facilities for FLOW 800 vascular study. In cases of the repeated use of ICG, there may be bias in the extrapolated results of FLOW 800 owing to false fluorescence from the retained dye. There is also provision for inter-rater bias when

selecting the appropriate ROIs among vessels in close proximities, thereby increased tendency for false results. However, this improves with practice since there is not a steep learning curve.

## Conclusion

The addition of FLOW 800 quantitative mapping following a routinely performed ICG study can precisely help determine patients at high risk of post-operative vasospasm. Timely actions, such as readjusting clips, the local administration of drugs or aggressive medical or interventional management can be undertaken. Additional measures, such as the placement of a swan gauge catheter to minimize complications and TCD for continuous monitoring of these patients can be utilized for better clinical outcomes. Further studies are recommended for confirming the role of FLOW 800 software as a valuable adjunct to intra-operative ICG vascular studies.

## Data availability

Dataset 1. Demographic information and the results of each diagnostic technique performed for each patient. <https://doi.org/10.5256/f1000research.15627.d212875><sup>8</sup>.

## Competing interests

No competing interests were declared.

## Grant information

The author(s) declared that no grants were involved in supporting this work.

## References

- Dorsch NW, King MT: **A review of cerebral vasospasm in aneurysmal subarachnoid haemorrhage part I: incidence and effects.** *J Clin Neurosci.* 1994; 1(1): 19–26. [PubMed Abstract](#) | [Publisher Full Text](#)
- Weir B, Grace M, Hansen J, et al.: **Time course of vasospasm in man.** *J Neurosurg.* 1978; 48(2): 173–8. [PubMed Abstract](#) | [Publisher Full Text](#)
- Awad IA, Carter LP, Spetzler RF, et al.: **Clinical vasospasm after subarachnoid hemorrhage: response to hypervolemic hemodilution and arterial hypertension.** *Stroke.* 1987; 18(2): 365–72. [PubMed Abstract](#)
- Connolly ES Jr, Rabinstein AA, Carhuapoma JR, et al.: **Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** *Stroke.* 2012; 43(6): 1711–37. [PubMed Abstract](#) | [Publisher Full Text](#)
- Charpentier C, Audibert G, Guillemin F, et al.: **Multivariate analysis of predictors of cerebral vasospasm occurrence after aneurysmal subarachnoid hemorrhage.** *Stroke.* 1999; 30(7): 1402–1408. [PubMed Abstract](#)
- Nomura Y, Kawaguchi M, Yoshitani K, et al.: **Retrospective analysis of predictors of cerebral vasospasm after ruptured cerebral aneurysm surgery: influence of the location of subarachnoid blood.** *J Anesth.* 2010; 24(1): 1–6. [PubMed Abstract](#) | [Publisher Full Text](#)
- Fisher CM, Kistler JP, Davis JM: **Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning.** *Neurosurgery.* 1980; 6(1): 1–9. [PubMed Abstract](#) | [Publisher Full Text](#)
- Munakomi S, Poudel D: **Dataset 1 in: A pilot study on assessing the role of intra-operative Flow 800 vascular map model in predicting onset of vasospasm following micro vascular clipping of ruptured intracranial aneurysms.** *F1000Research.* 2018. <http://www.doi.org/10.5256/f1000research.15627.d212875>
- Sen J, Belli A, Albon H, et al.: **Triple-H therapy in the management of aneurysmal subarachnoid haemorrhage.** *Lancet Neurol.* 2003; 2(10): 614–621. [PubMed Abstract](#) | [Publisher Full Text](#)
- Macdonald RL, Wallace MC, Kestle JR: **Role of angiography following aneurysm surgery.** *J Neurosurg.* 1993; 79(6): 826–32. [PubMed Abstract](#) | [Publisher Full Text](#)
- Alexander TD, Macdonald RL, Weir B, et al.: **Intraoperative angiography in cerebral aneurysm surgery: a prospective study of 100 craniotomies.** *Neurosurgery.* 1996; 39(1): 10–7; discussion 17–8. [PubMed Abstract](#) | [Publisher Full Text](#)
- Kivisaari RP, Porras M, Ohman J, et al.: **Routine cerebral angiography after surgery for saccular aneurysms: is it worth it?** *Neurosurgery.* 2004; 55(5): 1015–24. [PubMed Abstract](#) | [Publisher Full Text](#)
- Kassel NF, Torner JC, Haley EC Jr, et al.: **The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: Overall management results.** *J Neurosurg.* 1990; 73(1): 18–36. [PubMed Abstract](#) | [Publisher Full Text](#)
- Pickard JD, Murray GD, Illingworth R, et al.: **Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage: British aneurysm nimodipine trial.** *BMJ.* 1989; 298(6674): 636–42. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Meyer B, Urbach H, Schaller C, et al.: **Immediate postoperative angiography after aneurysm clipping—implications for quality control and guidance of further management.** *Zentralbl Neurochir.* 2004; 65(2): 49–56. [PubMed Abstract](#) | [Publisher Full Text](#)
- Imizu S, Kato Y, Sangli A, et al.: **Assessment of incomplete clipping of aneurysms intraoperatively by a near-infrared indocyanine green-video angiography (Niicg-Va) integrated microscope.** *Mini Inva Neurosurg.* 2008; 51(4): 199–203. [PubMed Abstract](#) | [Publisher Full Text](#)
- Martin NA, Bentson J, Viñuela F, et al.: **Intraoperative digital subtraction angiography and the surgical treatment of intracranial aneurysms and**

- vascular malformations. *J Neurosurg.* 1990; **73**(4): 526–33.  
[PubMed Abstract](#) | [Publisher Full Text](#)
18. de Oliveira JG, Beck J, Seifert V, *et al.*: **Assessment of flow in perforating arteries during intracranial aneurysm surgery using intraoperative near-infrared indocyanine green videoangiography.** *Neurosurgery.* 2007; **61**(3 Suppl): 63–72; discussion 72–3.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  19. Stendel R, Pietilä T, Al Hassan AA, *et al.*: **Intraoperative microvascular Doppler ultrasonography in cerebral aneurysm surgery.** *J Neuro Neurosurg Psychiatry.* 2000; **68**: 29–35.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
  20. Raabe A, Beck J, Gerlach R, *et al.*: **Near-infrared indocyanine green video angiography: a new method for intraoperative assessment of vascular flow.** *Neurosurgery.* 2003; **52**(1): 132–9; discussion 139.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  21. Raabe A, Nakaji P, Beck J, *et al.*: **Prospective evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography during aneurysm surgery.** *J Neurosurg.* 2005; **103**(6): 982–9.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  22. Scerrati A, Della Pepa GM, Conforti G, *et al.*: **Indocyanine green video-angiography in neurosurgery: a glance beyond vascular applications.** *Clin Neurol Neurosurg.* 2014; **124**: 106–13.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  23. Ma CY, Shi JX, Wang HD, *et al.*: **Intraoperative indocyanine green angiography in intracranial aneurysm surgery: Microsurgical clipping and revascularization.** *Clin Neurol Neurosurg.* Elsevier; 2009; **111**(10): 840–846.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  24. Özgiray E, Aktüre E, Patel N, *et al.*: **How reliable and accurate is indocyanine green video angiography in the evaluation of aneurysm obliteration?** *Clin Neurol Neurosurg.* 2013; **115**(7): 870–8.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  25. Mielke D, Malinova V, Rohde V: **Comparison of intraoperative microscopic and endoscopic ICG angiography in aneurysm surgery.** *Neurosurgery.* 2014; **10** Suppl 3: 418–25; discussion 425.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  26. Kamp MA, Slotty P, Turowski B, *et al.*: **Microscope-integrated quantitative analysis of intraoperative indocyanine green fluorescence angiography for blood flow assessment: first experience in 30 patients.** *Neurosurgery.* 2012; **70**(1 Suppl Operative): 65–73; discussion 73–4.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  27. Acerbi F, Cavallo C, Ferroli P: **Letter: Intraoperative Assessment of Blood Flow with Quantitative Indocyanine Green Videoangiography: The Role for Diagnosis of Regional Cerebral Hypoperfusion.** *Neurosurgery.* 2016; **78**(2): E310–E312.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  28. Regillo CD: **The present role of indocyanine green angiography in ophthalmology.** *Curr Opin Ophthalmol.* 1999; **10**(3): 189–96.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  29. Woitzik J, Horn P, Vajkoczy SP: **Intraoperative control of extracranial-intracranial bypass patency by near-infrared indocyanine green videoangiography.** *J Neurosurg.* 2005; **102**(4): 692–8.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  30. Caplan JM, Sankey E, Yang W, *et al.*: **Impact of indocyanine green videoangiography on rate of clip adjustments following intraoperative angiography.** *Neurosurgery.* 2014; **75**(4): 437–43; discussion 444.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  31. Washington CW, Zipfel GJ, Chicoine MR, *et al.*: **Comparing indocyanine green videoangiography to the gold standard of intraoperative digital subtraction angiography used in aneurysm surgery.** *J Neurosurg.* 2013; **118**(2): 420–7.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  32. Doss VT, Goyal N, Humphries W, *et al.*: **Comparison of intraoperative indocyanine green angiography and digital subtraction angiography for clipping of intracranial aneurysms.** *Interv Neurol.* 2015; **3**(3–4): 129–34.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
  33. Cui H, Wang Y, Yin Y, *et al.*: **Role of intraoperative microvascular Doppler in the microsurgical management of intracranial aneurysms.** *J Clin Ultrasound.* 2011; **39**(1): 27–31.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  34. Joo SP, Kim TS: **The Clinical Importance of Perforator Preservation in Intracranial Aneurysm Surgery: An Overview with a Review of the Literature.** *Chonnam Med J.* 2017; **53**(1): 47–55.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
  35. Kuroda K, Kinouchi H, Kanemaru K, *et al.*: **Intra-arterial injection fluorescein videoangiography in aneurysm surgery.** *Neurosurgery.* 2013; **72**(2 Suppl Operative): ons141–150; discussion ons150.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  36. Marchese E, Albanese A, Denaro L, *et al.*: **Intraoperative microvascular Doppler in intracranial aneurysm surgery.** *Surg Neurol.* 2005; **63**(4): 336–342; discussion 342.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  37. Janjua N, Mayer SA: **Cerebral vasospasm after subarachnoid hemorrhage.** *Curr Opin Crit Care.* 2003; **9**(2): 113–19.  
[PubMed Abstract](#)
  38. Lysakowski C, Walder B, Costaza MC: **Transcranial Doppler versus angiography in patients with vasospasm due to a ruptured cerebral aneurysm: a systematic review.** *Stroke.* 2001; **32**(10): 2292–98.  
[PubMed Abstract](#)
  39. Robinson JL, Roberts A: **Operative treatment of aneurysms and Coanda effect: a working hypothesis.** *J Neurol Neurosurg Psychiatry.* 1972; **35**(6): 804–809.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
  40. Kato Y, Sano H, Nagahisa S: **Endoscope-assisted microsurgery for cerebral aneurysms.** *Minim Invasive Neurosurg.* 2000; **43**(2): 91–7.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  41. Manninen PH, Patterson S, Lam AM: **Evoked potential monitoring during posterior fossa aneurysm surgery: a comparison of two modalities.** *Can J Anaesth.* 1994; **41**(2): 92–7.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  42. Lennihan L, Mayer SA, Fink ME, *et al.*: **Effect of hypervolemic therapy on cerebral blood flow after subarachnoid hemorrhage: a randomized controlled trial.** *Stroke.* 2000; **31**(2): 383–91.  
[PubMed Abstract](#)
  43. Solenski NJ, Haley EC Jr, Kassell NF: **Medical complications of aneurysmal subarachnoid hemorrhage: a report of the multicenter, cooperative aneurysm study. Participants of the Multicenter Cooperative Aneurysm Study.** *Crit Care Med.* 1995; **23**(6): 1007–17.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  44. Thomas JE, Rosenwasser RH, Armonda RA: **Safety of intrathecal sodium nitroprusside for the treatment and prevention of refractory cerebral vasospasm and ischemia in humans.** *Stroke.* 1999; **30**(7): 1409–16.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  45. Thomas JE, Nemirowski A, Zelman V, *et al.*: **Rapid reversal of endothelin-1-induced cerebral vasoconstriction by intrathecal administration of nitric oxide donors.** *Neurosurgery.* 1997; **40**(6): 1245–9.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  46. Corsten L, Raja A, Guppy K, *et al.*: **Contemporary management of subarachnoid hemorrhage and vasospasm: The UIC experience.** *Surg Neurol.* 2001; **56**(3): 140–8; discussion 148–50.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  47. Kincaid MS, Souter MJ, Treggiari MM, *et al.*: **Accuracy of transcranial Doppler ultrasonography and single-photon emission computed tomography in the diagnosis of angiographically demonstrated cerebral vasospasm.** *J Neurosurg.* 2009; **110**(1): 67–72.  
[PubMed Abstract](#) | [Publisher Full Text](#)
  48. Durrant JC, Hinson HE: **Rescue therapy for refractory vasospasm after subarachnoid hemorrhage.** *Curr Neurol Neurosci Rep.* 2015; **15**(2): 521.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

# Open Peer Review

Current Referee Status:   

---

Version 1

Referee Report 13 September 2018

doi:10.5256/f1000research.17049.r36816



**Amit Agrawal** 

Department of Neurosurgery, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India

In present study the authors share there preliminary experience with automated vascular mapping to identify sub-group of patient who are high-risk of developing post-operative vasospasm following aneurysmal surgery for spontaneous subarachnoid hemorrhage. It will be beneficial if an evidence based algorithm can be generated and can be used to improve clinical outcomes. Although the article is well written, however the study includes a small number of patients; data were acquired retrospectively and does not include all consecutive cases. As authors have suggested transcranial Doppler study (TCD) at frequent interval can be used as a non-invasive tool to determine the velocity in the cerebral vessels and can be correlated with FLOW 800 studies. Additionally we need to determine the cost-effectiveness of the procedures particularly in settings where the resources are limited. To better understand the benefits of FLOW 800 we need a larger and long term experience.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Referee Report 04 September 2018

doi:10.5256/f1000research.17049.r36812

**Lekhjunga Thapa**

National Institute of Neurological and Allied Sciences, Kathmandu, Nepal

I consider this paper as an excellent report and is an important addition to the existing information on the subject. I personally adored the concept of exploring better markers to identify patients of ruptured intracranial aneurysm at high risk of postoperative clinical vasospasm and delayed cerebral ischemia and the promising findings of components of ICG flow status as one of the important components and predictors as tested by various statistical methods. I hope the author intend to study the concept in larger number of patients with ruptured intracranial aneurysm.

In addition I would like to add few comments:

**Abstract:**

- In the methodology section, the authors can mention ..... (Last line) ....predicting onset of vasospasm and delayed cerebral ischemia, as per the objective of the study.
- In the conclusion section, it may be better to replace word “confirmed” in “our study **confirmed**.....” I feel this study has found/demonstrated the role FLOW 800..... rather than establishing it.

**Introduction:**

1. This section is well written with the emphasis on the potential role of information generated by FLOW 800 vascular mapping. However the last sentence appears to be long. The authors could break up the sentences with pertinent references so that it is easily understood.
- “Indocyanine green (ICG) flow studies are safe, easily applicable, readily reproducible and now routinely used during the microvascular clipping of aneurysms. [Reference?]
  - A note on current status of ICG studies in predicting vasospasm would be better here.

**Methods:**

- The author mentions CLINICAL VASOSPASM in introduction and in methodology section “radiological vasospasm” is also mentioned. Kindly elaborate.
- It is wiser to mention why ANOVA was chosen when multivariate analysis is also done in this case. Why were these tests chosen and how would they help in interpretation in this test.

**Discussion:**

- I think the authors should discuss more about their findings with appropriate reference rather than reviewing about the machine and methods.

**Conclusion:**

- With the limitation explained by the authors, this study obviously may not **precisely** identify patients at high risk of post-operative vasospasm, so it may be prudent to conclude by remaining confined to the objective and the the relevant result of the study.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**



Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Referee Report 29 August 2018

doi:[10.5256/f1000research.17049.r37112](https://doi.org/10.5256/f1000research.17049.r37112)



**Guru Dutta Satyarthee**

All India Institute of Medical Sciences, New Delhi, Delhi, India

Intra-operative Neurosurgical Armamentarium to deal with vasospasm development following aneurysmal subarachnoid hemorrhage.

Authors reported utility of intra-operative FLOW 800 vascular map model with indigo cyanine [ICG] fluoroscopic angiographic images obtained with microscope with appropriate facility in predicting onset of clinical cerebral vasospasm during post-operative period and delayed cerebral ischemic deficit in a cohort of forty patients suffering with aneurysmal subarachnoid hemorrhage and managed microsurgical clipping. Factors predicting risk of vasospasm onset included parameters obtained with FLOW 800 vascular map model like the difference in the absorption intensities and time lag.

However, major disadvantages of the vascular map model include the cost factor as advanced microscope along with appropriate software is a pre-requisite, in addition to the availability of dye, and part of vessel evaluated is very limited to microscope field with direct line of-sight of target vessels but affected by obstructed microscope field by presence of blood clots and aneurysm clips. The anatomical factor of vessel and aneurysm can also impair image quality of atherosclerotic plaques, aneurysmal sac calcifications or thrombosis. Authors rightly advocated vascular model with ICG angiography can act as one of adjunct for aneurysm surgery in neurosurgical armamentarium besides vascular Doppler, endoscope, with capability of predicting vasospasm and appropriate measure can be applied right from intraoperative period like drainage of hematoma, installation of papavarin, Omayya reservoir and installation of papavarin in the post-operative period besides stellate ganglion block, and hemodynamic interventions can definitely aid in improving outcome. However, the size of the cohort sample was modest.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes



**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

---

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact [research@f1000.com](mailto:research@f1000.com)

**F1000Research**