Published in final edited form as:

J Crit Care. 2017 February ; 37: 126–129. doi:10.1016/j.jcrc.2016.09.011.

Hematological counts as predictors of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage

Ivan Rocha Ferreira Da Silva, MD^{1,2}, Joao Antonio Gomes, MD³, Ari Wachsman, MD⁴, Gabriel Rodriguez de Freitas, MD, PhD^{1,5}, and Jose Javier Provencio, MD⁶

¹Universidade Federal Fluminense, Niteroi, Brazil

²Americas Medical City, Rio de Janeiro, Brazil

³Summa Health, Akron City Hospital and Northeast Ohio Medical University, Akron, Ohio

⁴Cleveland Clinic-Akron General Medical Center, Akron, OH

⁵Instituto D'Or de Ensino e Pesquisa, Rio de Janeiro, Brazil

⁶University of Virginia, Charlottesville, VA

Abstract

Introduction—Aneurysmal subarachnoid hemorrhage (SAH) is associated with high morbidity and mortality, and ischemic lesion burden is a known predictor of worse outcome. Currently, there is no single clinical method or ancillary test that can reliably predict which subset of patients will develop delayed cerebral ischemia (DCI). Previous animal and human studies suggest that SAH leads to a state of systemic inflammation, with DCI as the most striking manifestation. The aim of this study was to find hematological derangements and clinical factors present during the first seven days after bleeding that could help identify patients at risk for development of DCI.

Methods—Databank analysis of patients with SAH admitted between 2010–2012 in a large quaternary academic center. Data from demographics, imaging, laboratory and clinical factors were collected. Statistical testing was conducted to test for association to the outcome (DCI) and multivariate logistic regression was used to design a predictive model.

Results—Of 55 patients, 14 developed DCI (25%). Anemia and leukocytosis on the third day after bleeding were significantly correlated with the outcome ($p < 0.032$, CI 1.12–15.16, OR 4.12 for anemia and $p < 0.046$, CI 1.03–26.13, OR 5.18 for leukocytosis). Anemia and leukocytosis were still statistically significant after adjustment for age, sex, modified Fisher scale and Hunt-Hess scale.

Conclusion—The presence of leukocytosis and anemia during the third day after SAH was statistically correlated with the occurrence of DCI. Further investigation is needed to assess the broader applicability of these findings.

Introduction

Aneurysmal subarachnoid hemorrhage (SAH) is associated with high morbidity and mortality, with death rates ranging from 25% in contemporary observational series¹ to close to 10% in randomized trials^{2,3}. Roughly 30% of survivors suffer from severe permanent disability⁴, and significant cognitive and psychosocial impairment is present in a large amount of patients⁵⁻⁷. In patients with aneurysmal SAH, ischemic lesion burden is a known predictor of worse outcome^{8,9}. Currently, there is no single clinical method or ancillary test that can reliably predict which subset of patients will develop delayed cerebral ischemia (DCI). The ability to stratify patients into high- and low-risk categories at the onset of hemorrhage would be useful in guiding early aggressive care. Transcranial doppler ultrasonography (TCD) has been used for decades as a tool for screening patients at risk of developing cerebral vasospasm, but the method lacks sensitivity and suffers from high interobserver variability^{10,11}. Fisher and modified Fisher grades are based on the amount of subarachnoid blood on CT brain scan on admission and can fairly predict development of DCI, but with lower positive predictive values in patients with small amounts of blood¹²⁻¹⁵. Previous animal and human studies suggest that SAH leads to a state of systemic inflammation, with DCI as the most striking manifestation¹⁶⁻¹⁹. At the same time, anemia has been associated to worse outcomes and the occurrence of DCI²⁰⁻²³. Leukocytosis and anemia could represent early markers of bone marrow changes due to systemic inflammation, and serve as early surrogate markers for such a state. The aim of this study was to find hematological derangements and clinical factors present during the first seven days after bleeding that could help identify patients at risk for development of DCI.

Methods

Study population

A databank of aneurysmal subarachnoid hemorrhage was created using patients admitted from 2010 to 2012, in a large quaternary academic center in Cleveland, Ohio, USA. Fifty-five patients with aneurysmal SAH admitted through this period were included in our study. The entry criteria consisted of any patients with confirmed aneurysmal subarachnoid hemorrhage on cerebral angiogram, who stayed at least seven days in the hospital (counted from the day of bleeding) and with information available for all the study variables. We chose to analyze the first seven days after bleeding, as this is the peak period for occurrence of vasospasm in most patients with SAH. Characteristics of participant patients are presented in table 1.

Variables of interest

Data from demographics (age, gender), imaging (transcranial doppler ultrasound, computed tomography and cerebral angiogram, including size and location of the aneurysm), laboratory (white blood cell count, hemoglobin concentration and serum sodium daily for the first seven days, cardiac dysfunction on echocardiography) and clinical factors (fever, occurrence of DCI and radiographic vasospasm, Hunt-Hess and modified Fisher scales on admission, surgical correction of the aneurysm) were collected.

We chose to analyze white blood cell count (WBC) and hemoglobin concentration on day three after bleeding, as this is usually when vasospasm ensues in most patients^{24,25}. We defined anemia as a hemoglobin concentration of <10mg/dL, as this was found to be probably correlated with infarcts secondary to vasospasm and mortality in previous studies^{21,22}. Moreover, positron emission tomography studies in SAH patients indicate that raising hemoglobin concentration with red blood cell transfusion from 8 to 10 g/dL improves cerebral oxygen delivery²⁶, and expert opinion per formal guidelines suggest that levels 8–10mg/dL should be maintained in patients with SAH, depending on the risk of delayed cerebral ischemia²⁴. Leukocytosis is harder to define, as in theory it should be the total WBC count more than two standard deviations above the mean in a normally distributed population; most laboratories have values ranging from 10.000 to 11.000 leukocytes per mm³ as the upper limit for a WBC count²⁷. We defined our cut-off as 10.000 leukocytes per mm³ after a receiver operating curve was done using the data from our study, correlating WBC with DCI, and it was found an area under the curve of 0.68, with values ranging from 10.01 to 10.46 x1000 leukocytes per mm³ to be suggested as with higher sensitivity/specificity. Youden index calculation of the best cutoff using the ROC curve values identified 10.03 as the most accurate value.

For statistical purposes, Hunt-Hess scale was dichotomized in 1–2 and >2 (good neurological grade versus unfavorable grade) and modified Fisher scale was dichotomized in 1–2 and 3–4 (lower risk of vasospasm versus higher risk).

Outcome measures

We defined delayed cerebral ischemia as clinical deterioration deemed secondary to vasospasm (confirmed with digital subtraction angiography) after other causes were eliminated⁸ (such as fever, infection, hyponatremia, seizures, hydrocephalus) and radiographic vasospasm as arterial narrowing diagnosed on digital subtraction angiography²⁴. Moderate narrowing was defined as at least 50% decrease in vessel lumen. In comatose patients, DCI was defined as new infarcts on brain computed tomography or magnetic resonance scans with radiographic vasospasm on digital subtraction angiography, and not deemed to be secondary to endovascular procedures²⁴.

Statistical analysis

First, the chosen metabolic/clinical/radiologic variables were independently tested to check association to the outcome variable (DCI) using Pearson's Chi-Square and Fisher's exact test for categorical variables, t test for normally distributed continuous variables and Mann-Whitney U test for non-parametric continuous variables, as well as univariate logistic regression analysis. Afterwards, the variables with statistical significance (cutoff of $p < 0.05$) were added to a multivariate logistic regression model to assess whether the statistical significance persisted after correction for pre-defined important demographic and clinical variables (Hunt-Hess, modified Fisher Scale, age and sex). Finally, a step-forward logistic regression modeling was performed to assess the best predictive model. All variables were independent, and no collinearity was detected. In the end, Hosmer-Lemeshow test was performed to assess goodness-of-fit of the final model. Statistical software BioStat® (version 5.4, Brazil) was used for all analyses.

Results

Of 55 patients, 14 developed DCI (25%). Anemia and leukocytosis on the third day after bleeding were significantly correlated with the outcome ($p < 0.032$, CI 1.12–15.16, OR 4.12 for anemia and $p < 0.046$, CI 1.03–26.13, OR 5.18 for leukocytosis). The occurrence of fever or hyponatremia, age, sex, size and location of the aneurysm, surgical correction of the aneurysm, Hunt-Hess scale or modified Fisher scale on arrival, presence of cardiac dysfunction, as well middle cerebral artery mean flow velocities > 120 cm/s on transcranial doppler sonography were not correlated with the outcome. Table 2 shows the results for all tested variables. A multiple logistic regression was performed to assess the influence of the other non-significant variables when analyzed concurrently. Anemia and leukocytosis were still statistically significant after adjustment for age, sex, modified Fisher scale and Hunt-Hess scale in a logistic regression model using both variables (adjusted OR 6.3, $p < 0.019$, CI 1.36–30.17 for anemia and adjusted OR 5.68, $p < 0.0367$, CI 1.11–29.01 for leukocytosis). The median hemoglobin concentrations were 10.9 g/dL (SD 1.10) for the patients without DCI and 9.9 g/dL (SD 1.42) for the patients with DCI. Of note, no patients had a hemoglobin concentration of < 10 mg/dL on arrival. For the WBC count, a median value of $10.65 \times 1000/\text{mm}^3$ (SD 2.99) was found for the patients without DCI and $12.29 \times 1000/\text{mm}^3$ (SD 4.06) for the patients with DCI. Figures 1 and 2 show the hemoglobin and WBC counts graphed per population.

The findings remained the case even when retested including only patients with mean flow velocities of the middle cerebral arteries lower than 120 cm/s on TCD sonography performed on the third day after bleeding. Even though our main goal was not to directly compare the diagnostic accuracy of TCD versus inflammatory markers, our data serves as a hypothesis generator that the presence of anemia and leukocytosis was predictive of DCI even among patients deemed of low risk according to TCD criteria.

Discussion

In our study, the presence of hematological derangements on the third day after SAH was statistically correlated with the occurrence of DCI, even after correction for concurrent risk factors.

Some previous studies have noticed a trend for increased mortality and poor prognosis associated to leukocytosis during hospital stay in patients with aneurysmal SAH, but most analyzed the occurrence of blood count changes in any timeframe or even after DCI was established^{28–34}. Also, the presence of leukocytosis was not corrected against other variables in regression models. One study conducted in the United States showed a relationship between peak leukocyte counts (above $15 \times 1000/\text{mm}^3$) and development of DCI, but it analyzed the presence of peaks above this cutoff occurring in any days between 0–5 post bleeding³⁵. Moreover, it used a very high cutoff in a series where DCI developed in 45% of the patients, higher than our cohort and most previous studies^{24,36–38}.

A growing number of animal and human studies suggest that SAH leads to a state of systemic inflammation, with vasospasm as the most striking manifestation^{16–19}.

Leukocytosis and anemia could be early markers of bone marrow changes due to systemic inflammation, and serve as early surrogate markers for this state. A cohort study in Sweden has shown that high leukocyte count at baseline was associated with increased incidence of SAH, mainly in smokers¹⁸. The third day after the initial hemorrhage is suggested to host the initial peak of inflammation in human and animal studies. Cerebral spinal fluid neutrophilia on the third day in patients with SAH was an independent predictor of the later development of DCI in a previous study³⁹, and depletion of neutrophils three days after SAH in a murine model mitigated tissue inflammation, reversed cerebral vasoconstriction and restored memory mechanisms at day 6⁴⁰. Finally, none of the patients from our cohort developed infections during the seven-day period of observation, minimizing the possibility of observing leukocytosis secondary to bacterial infections.

Anemia has been associated to the occurrence of DCI and worse prognosis in previous studies^{21,41,42}, as well as leading to metabolic distress detected by cerebral microdialysis^{20,23,43}. Conversely, studies assessing the impact of blood transfusions in this population have led to conflicting results, not necessarily improving outcomes^{26,44–46}. In critically ill patients, anemia is frequently observed and is hypothesized to occur as a consequence of systemic inflammation leading to myelosuppression, blunted erythropoietin production and erythropoietin response and abnormalities in iron metabolism^{47–49}. It is quite common to detect anemia during the acute phase of SAH^{21,50,51}, even as early as the 3–5th day after bleeding, before the effect of blood loss secondary to multiple blood draws is noticed, suggesting a possible involvement of systemic inflammation.

A point of discussion is that our study showed a statistical correlation, but causal inferences are harder to assert. For example, patients with infections or more frequent blood draws are likely sicker and might be in higher risk of developing DCI. However, in the present study blood samples were collected daily from all patients. Additionally, none of the patients received blood transfusions before day 3, and none were anemic on arrival. SAH is a condition where early diagnosis and aggressive therapy are some of the pillars of therapy, but until today very few data are available on predicting which subset of patients are at higher risk for complications. The modified Fisher and the Hunt-Hess scales are traditionally considered predictors of DCI, but were surprisingly not associated to the outcome in the current study. It might be related to its small sample size, but also to the fact that high scores in both scales could be closely related to the occurrence of early brain injury soon after aneurysm rupture^{52,53}, impacting long-term functional outcomes even before DCI ensues.

Although the current study was retrospective and the cohort relatively small in number, it did disclose a trend for prediction of DCI. To our knowledge, it is the first in the literature to analyze in a very comprehensive way using multiple clinical, radiological and laboratorial variables the early phase of SAH, in regards of prediction of DCI occurrence. Studies on SAH are not easily performed, as the disease is not as common as other forms of acute brain disease; also studies analyzing the early phase soon after arrival of patients with SAH are scarce. We hope that our study could become a hypotheses generator for future investigation.

Conclusion

The presence of leukocytosis and anemia during the third day after subarachnoid hemorrhage was statistically correlated with the occurrence of DCI. Further investigation is needed to assess the broader applicability of these findings.

References

1. Prabhakaran S, Fonarow GC, Smith EE, et al. Hospital case volume is associated with mortality in patients hospitalized with subarachnoid hemorrhage. *Neurosurgery*. 2014; 75(5):500–508. [PubMed: 24979097]
2. Macdonald RL, Higashida RT, Keller E, et al. Clazosentan, an endothelin receptor antagonist, in patients with aneurysmal subarachnoid haemorrhage undergoing surgical clipping: a randomised, double-blind, placebo-controlled phase 3 trial (CONSCIOUS-2). *The Lancet. Neurology*. 2011; 10(7):618–625. [PubMed: 21640651]
3. Molyneux A, Kerr R, Stratton I, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet (London, England)*. 2002; 360(9342):1267–1274.
4. Kreiter KT, Rosengart AJ, Claassen J, et al. Depressed mood and quality of life after subarachnoid hemorrhage. *Journal of the neurological sciences*. 2013; 335(1–2):64–71. [PubMed: 24064259]
5. Al-Khindi T, Macdonald RL, Schweizer TA. Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. *Stroke; a journal of cerebral circulation*. 2010; 41(8):e519–536.
6. Powell J, Kitchen N, Heslin J, Greenwood R. Psychosocial outcomes at 18 months after good neurological recovery from aneurysmal subarachnoid haemorrhage. *Journal of neurology, neurosurgery, and psychiatry*. 2004; 75(8):1119–1124.
7. Springer MV, Schmidt JM, Wartenberg KE, Frontera JA, Badjatia N, Mayer SA. Predictors of global cognitive impairment 1 year after subarachnoid hemorrhage. *Neurosurgery*. 2009; 65(6):1043–1050. discussion 1050–1041. [PubMed: 19934963]
8. Frontera JA, Fernandez A, Schmidt JM, et al. Defining vasospasm after subarachnoid hemorrhage: what is the most clinically relevant definition? *Stroke; a journal of cerebral circulation*. 2009; 40(6):1963–1968.
9. Vergouwen MD, Etminan N, Ilodigwe D, Macdonald RL. Lower incidence of cerebral infarction correlates with improved functional outcome after aneurysmal subarachnoid hemorrhage. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism*. 2011; 31(7):1545–1553.
10. Carrera E, Schmidt JM, Oddo M, et al. Transcranial Doppler for predicting delayed cerebral ischemia after subarachnoid hemorrhage. *Neurosurgery*. 2009; 65(2):316–323. discussion 323–314. [PubMed: 19625911]
11. Marshall SA, Nyquist P, Ziai WC. The role of transcranial Doppler ultrasonography in the diagnosis and management of vasospasm after aneurysmal subarachnoid hemorrhage. *Neurosurgery clinics of North America*. 2010; 21(2):291–303. [PubMed: 20380971]
12. Frontera JA, Claassen J, Schmidt JM, et al. Prediction of symptomatic vasospasm after subarachnoid hemorrhage: the modified fisher scale. *Neurosurgery*. 2006; 59(1):21–27. discussion 21–27. [PubMed: 16823296]
13. Reilly C, Amidei C, Tolentino J, Jahromi BS, Macdonald RL. Clot volume and clearance rate as independent predictors of vasospasm after aneurysmal subarachnoid hemorrhage. *Journal of neurosurgery*. 2004; 101(2):255–261. [PubMed: 15309916]
14. Smith ML, Abrahams JM, Chandela S, Smith MJ, Hurst RW, Le Roux PD. Subarachnoid hemorrhage on computed tomography scanning and the development of cerebral vasospasm: the Fisher grade revisited. *Surgical neurology*. 2005; 63(3):229–234. discussion 234–225. [PubMed: 15734507]

15. Wilson DA, Nakaji P, Abula AA, et al. A simple and quantitative method to predict symptomatic vasospasm after subarachnoid hemorrhage based on computed tomography: beyond the Fisher scale. *Neurosurgery*. 2012; 71(4):869–875. [PubMed: 22801639]
16. Kooijman E, Nijboer CH, van Velthoven CT, et al. Long-term functional consequences and ongoing cerebral inflammation after subarachnoid hemorrhage in the rat. *PloS one*. 2014; 9(3):e90584. [PubMed: 24603553]
17. Provencio JJ. Inflammation in subarachnoid hemorrhage and delayed deterioration associated with vasospasm: a review. *Acta neurochirurgica Supplement*. 2013; 115:233–238. [PubMed: 22890674]
18. Soderholm M, Zia E, Hedblad B, Engstrom G. Leukocyte count and incidence of subarachnoid haemorrhage: a prospective cohort study. *BMC neurology*. 2014; 14:71. [PubMed: 24708536]
19. Tso MK, Macdonald RL. Subarachnoid hemorrhage: a review of experimental studies on the microcirculation and the neurovascular unit. *Translational stroke research*. 2014; 5(2):174–189. [PubMed: 24510780]
20. Kurtz P, Schmidt JM, Claassen J, et al. Anemia is associated with metabolic distress and brain tissue hypoxia after subarachnoid hemorrhage. *Neurocritical care*. 2010; 13(1):10–16. [PubMed: 20383611]
21. Naidech AM, Drescher J, Ault ML, Shaibani A, Batjer HH, Alberts MJ. Higher hemoglobin is associated with less cerebral infarction, poor outcome, and death after subarachnoid hemorrhage. *Neurosurgery*. 2006; 59(4):775–779. discussion 779–780. [PubMed: 17038943]
22. Naidech AM, Jovanovic B, Wartenberg KE, et al. Higher hemoglobin is associated with improved outcome after subarachnoid hemorrhage. *Critical care medicine*. 2007; 35(10):2383–2389. [PubMed: 17717494]
23. Oddo M, Milby A, Chen I, et al. Hemoglobin concentration and cerebral metabolism in patients with aneurysmal subarachnoid hemorrhage. *Stroke; a journal of cerebral circulation*. 2009; 40(4):1275–1281.
24. Diringner MN, Bleck TP, Claude Hemphill J 3rd, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. *Neurocritical care*. 2011; 15(2):211–240. [PubMed: 21773873]
25. Macdonald RL. Delayed neurological deterioration after subarachnoid haemorrhage. *Nature reviews. Neurology*. 2014; 10(1):44–58. [PubMed: 24323051]
26. Dhar R, Zazulia AR, Videen TO, Zipfel GJ, Derdeyn CP, Diringner MN. Red blood cell transfusion increases cerebral oxygen delivery in anemic patients with subarachnoid hemorrhage. *Stroke; a journal of cerebral circulation*. 2009; 40(9):3039–3044.
27. wikipedia. [Accessed July 20th, 2014] Reference ranges for blood tests. 2014. http://en.wikipedia.org/wiki/Reference_ranges_for_blood_tests
28. Kasius KM, Frijns CJ, Algra A, Rinkel GJ. Association of platelet and leukocyte counts with delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage. *Cerebrovascular diseases (Basel, Switzerland)*. 2010; 29(6):576–583.
29. Maiuri F, Gallicchio B, Donati P, Carandente M. The blood leukocyte count and its prognostic significance in subarachnoid hemorrhage. *Journal of neurosurgical sciences*. 1987; 31(2):45–48. [PubMed: 3668657]
30. McMahon CJ, Hopkins S, Vail A, et al. Inflammation as a predictor for delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage. *Journal of neurointerventional surgery*. 2013; 5(6):512–517. [PubMed: 22952245]
31. Niikawa S, Hara S, Ohe N, Miwa Y, Ohkuma A. Correlation between blood parameters and symptomatic vasospasm in subarachnoid hemorrhage patients. *Neurologia medico-chirurgica*. 1997; 37(12):881–884. discussion 884–885. [PubMed: 9465585]
32. Parkinson D, Stephensen S. Leukocytosis and subarachnoid hemorrhage. *Surgical neurology*. 1984; 21(2):132–134. [PubMed: 6701748]
33. Rothoerl RD, Axmann C, Pina AL, Woertgen C, Brawanski A. Possible role of the C-reactive protein and white blood cell count in the pathogenesis of cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Journal of neurosurgical anesthesiology*. 2006; 18(1):68–72. [PubMed: 16369143]

34. Weir B, Disney L, Grace M, Roberts P. Daily trends in white blood cell count and temperature after subarachnoid hemorrhage from aneurysm. *Neurosurgery*. 1989; 25(2):161–165. [PubMed: 2770982]
35. McGirt MJ, Mavropoulos JC, McGirt LY, et al. Leukocytosis as an independent risk factor for cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Journal of neurosurgery*. 2003; 98(6):1222–1226. [PubMed: 12816268]
36. Kassell NF, Sasaki T, Colohan AR, Nazar G. Cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Stroke; a journal of cerebral circulation*. 1985; 16(4):562–572.
37. Oliveira-Filho J, Ezzeddine MA, Segal AZ, et al. Fever in subarachnoid hemorrhage: relationship to vasospasm and outcome. *Neurology*. 2001; 56(10):1299–1304. [PubMed: 11376177]
38. Shimoda M, Takeuchi M, Tominaga J, Oda S, Kumasaka A, Tsugane R. Asymptomatic versus symptomatic infarcts from vasospasm in patients with subarachnoid hemorrhage: serial magnetic resonance imaging. *Neurosurgery*. 2001; 49(6):1341–1348. discussion 1348–1350. [PubMed: 11846933]
39. Provencio JJ, Fu X, Siu A, Rasmussen PA, Hazen SL, Ransohoff RM. CSF neutrophils are implicated in the development of vasospasm in subarachnoid hemorrhage. *Neurocritical care*. 2010; 12(2):244–251. [PubMed: 19967568]
40. Provencio JJ, Swank V, Lu H, et al. Neutrophil depletion after subarachnoid hemorrhage improves memory via NMDA receptors. *Brain, behavior, and immunity*. 2016
41. Kramer AH, Zygun DA, Bleck TP, Dumont AS, Kassell NF, Nathan B. Relationship between hemoglobin concentrations and outcomes across subgroups of patients with aneurysmal subarachnoid hemorrhage. *Neurocritical care*. 2009; 10(2):157–165. [PubMed: 19116699]
42. Stein M, Brokmeier L, Herrmann J, et al. Mean hemoglobin concentration after acute subarachnoid hemorrhage and the relation to outcome, mortality, vasospasm, and brain infarction. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*. 2015; 22(3): 530–534. [PubMed: 25533213]
43. Aaslid R, Huber P, Nornes H. Evaluation of cerebrovascular spasm with transcranial Doppler ultrasound. *Journal of neurosurgery*. 1984; 60(1):37–41. [PubMed: 6689726]
44. Naidech AM, Shaibani A, Garg RK, et al. Prospective, randomized trial of higher goal hemoglobin after subarachnoid hemorrhage. *Neurocritical care*. 2010; 13(3):313–320. [PubMed: 20717750]
45. Smith MJ, Le Roux PD, Elliott JP, Winn HR. Blood transfusion and increased risk for vasospasm and poor outcome after subarachnoid hemorrhage. *Journal of neurosurgery*. 2004; 101(1):1–7.
46. Zygun DA, Nortje J, Hutchinson PJ, Timofeev I, Menon DK, Gupta AK. The effect of red blood cell transfusion on cerebral oxygenation and metabolism after severe traumatic brain injury. *Critical care medicine*. 2009; 37(3):1074–1078. [PubMed: 19237920]
47. Corwin HL. The role of erythropoietin therapy in the critically ill. *Transfusion medicine reviews*. 2006; 20(1):27–33. [PubMed: 16373185]
48. Drews RE. Critical issues in hematology: anemia, thrombocytopenia, coagulopathy, and blood product transfusions in critically ill patients. *Clinics in chest medicine*. 2003; 24(4):607–622. [PubMed: 14710693]
49. Shander A. Anemia in the critically ill. *Critical care clinics*. 2004; 20(2):159–178.
50. Rosenberg NF, Koht A, Naidech AM. Anemia and transfusion after aneurysmal subarachnoid hemorrhage. *Journal of neurosurgical anesthesiology*. 2013; 25(1):66–74. [PubMed: 23047622]
51. Sampson TR, Dhar R, Diringer MN. Factors associated with the development of anemia after subarachnoid hemorrhage. *Neurocritical care*. 2010; 12(1):4–9. [PubMed: 19777386]
52. Claassen J, Carhuapoma JR, Kreiter KT, Du EY, Connolly ES, Mayer SA. Global cerebral edema after subarachnoid hemorrhage: frequency, predictors, and impact on outcome. *Stroke; a journal of cerebral circulation*. 2002; 33(5):1225–1232.
53. Suwatcharakoon S, Meyers E, Falo C, et al. Loss of Consciousness at Onset of Subarachnoid Hemorrhage as an Important Marker of Early Brain Injury. *JAMA neurology*. 2016; 73(1):28–35. [PubMed: 26552033]

Figure 1. Hemoglobin levels per studied population. Horizontal line represents median value, boxes represent standard deviation range and whiskers represent maximum and minimal levels. SVSP: symptomatic vasospasm (delayed cerebral ischemia). ($p < 0.037$)

Figure 2.

WBC count per studied population. Horizontal line represents median value, boxes represent standard deviation range and whiskers represent maximum and minimal levels. SVSP: symptomatic vasospasm (delayed cerebral ischemia). ($p < 0.067$)

Table 1

Population characteristics

Demographics	Patients with delayed cerebral ischemia	Patients without delayed cerebral ischemia	Statistical difference between groups
Age (median)	55 years	55.5 years	P<0.8941
Gender:			P<0.3596
Male	2	13	
Female	12	28	
Modified Fisher scale (most prevalent)	4 (40%)	4 (48%)	P<0.5368
Hunt-Hess scale (most prevalent)	3 (42%)	2 (46%)	P<0.6299
Total:	14 (25.45%)	41 (74.55%)	

Table 2

Results of univariate logistic regression. TCD: transcranial doppler; MFV: mean flow velocity; MCA: middle cerebral artery

Variable	P value	Odds Ratio
Anemia (day 3)	0.032	4.12 (CI 1.12–15.16)
Leukocytosis (day 3)	0.046	5.18 (CI 1.03–26.13)
Age<50	0.65	NA
Gender	0.24	NA
Modified Fisher scale >2	0.08	NA
Hunt-Hess>2	0.09	NA
Aneurysm>7mm	0.61	NA
Anterior circulation aneurysm	0.43	NA
Cardiac dysfunction	0.45	NA
Hyponatremia (day 3)	0.52	NA
Fever	0.65	NA
Surgical correction of the aneurysm	0.66	NA
TCD MFV of MCA>120cm/s (day 3)	0.44	NA