# Low Diagnostic Yield of Non-Invasive Imaging In Angiogram-Negative Subarachnoid Hemorrhage

J Joshi, S Prabhakaran, S John

#### Citation

J Joshi, S Prabhakaran, S John. *Low Diagnostic Yield of Non-Invasive Imaging In Angiogram-Negative Subarachnoid Hemorrhage*. The Internet Journal of Neuromonitoring. 2008 Volume 6 Number 1.

#### **Abstract**

Objectives: We describe the application of fundamental quality improvement methods to medical handoffs in order to improve resident learning and clinical training. Methods: We retrospectively reviewed 226 non-traumatic SAH patients admitted to our institution from January 1, 2007 to June 1, 2009. Imaging data were abstracted from medical charts. Results: Of the 226 SAH patients, 45 (19.9%) had no aneurysm on initial angiography. Of these angiogram-negative SAH patients, 12 (26.7%) were perimesencephalic SAH and 33 (73.3%) were NPAN-SAH. An average of 3.2 non-invasive studies was performed on each patient. In these 142 additional non-invasive studies, there was no additional diagnostic yield in finding the source of SAH. Conclusions: Though non-perimesencephalic angiogram-negative SAH had a worse prognosis compared to perimesencephalic SAH, additional non-invasive neuroimaging provided no diagnostic yield in either patient population.

## **INTRODUCTION**

Subarachnoid hemorrhage (SAH) is an acute, life threatening condition afflicting a significant portion of the emergency room emergency cases and overall patient population.<sup>1</sup> Though many understand the condition as a life threatening condition, SAH is a macrocosm in of itself that encompasses multiple types of hemorrhagic strokes affecting the Sub-Arachnoid region, with varying degrees of urgency and severity. Many prominent seminal studies attempted to classify the types of SAH based on either the prognosis, anatomic origins, pathophysiology, or underlying morbidity and mortality.<sup>2-9</sup> They established the foundation for future studies attempting to determine key correlations and patterns among clinical prognosis, associated clinical symptoms, and either an anatomic or pathophysiologic finding. In current practice, it is common to ascertain SAH patient prognosis upon clinical imaging of either a conventional or DSA angiogram, a computed tomography angiography (CTA) scan of the head, or a magnetic resonance angiography (MRA) of the head. SAH patients whose initial angiogram does not locate a bleeding source are often classified as having perimesencephalic hemorrhages. However, many patients do not fit into this benign picture and are nonperimesencephalic, angiogram-negative SAH (NPAN-SAH). Though the conventional angiogram remains the gold standard for diagnosis, multiple non-invasive imaging tests, beyond a second angiogram, are often performed in the acute evaluation of NPAN-SAH.

When patients are admitted for SAH, it is important to monitor for secondary hematoma formation, hydrocephalus, and hemodynamic stability. These associative conditions are typically more severe in patients with DSA positive imaging for an aneurysm location. <sup>10</sup> If a bleed source, such as an aneurysm, is located, the appropriate treatment can be initiated. Yet, if no bleeding etiology is determined, identifying a potential source becomes one of the principle concerns. <sup>11-14</sup> This risk often precipitates the decision to repeat imaging tests or initiate different modalities.

We determine if such additional non-invasive imaging improves diagnostic yield in identifying a bleeding source, or better characterizing the nature and sub-type of the SAH.

## **METHODS**

With IRB approval, we retrospectively reviewed 226 non-traumatic SAH patients admitted to our institution from January 1, 2007 to June 1, 2009 who underwent SAH imaging protocol at a single tertiary care institution. Patients eligible for the study met the following inclusion criteria per medical records: (1) at least 18 years of age; (2) either non-aneurysmal or indeterminant cause of SAH per initial DSA; (3) the patient was admitted within the acute phase interval of condition; and (4) the patient was treated according to the hospital protocol.

In our study, we began by abstracting imaging data from the medical records detailing the results of the study. We evaluated the DSA study first, and subsequently moved on to CTA and MRA studies, if available. Studies that provided inconclusive results were evaluated on a PACS (picture archiving and communication system) by independent neurologists. Factors considered upon image evaluation include the anatomic location of the bleed, any hematoma formation, and any subsequent bleeding patterns suggestive of rebleeding. We aggregated data on the number of images performed and the number of imaging modalities.

#### **RESULTS**

Of the 226 SAH patients, 45 (19.9%) had no aneurysm on initial angiography. Of these angiogram-negative SAH patients, 12 (26.7%) were perimesencephalic SAH and 33 (73.3%) were NPAN-SAH. There were 4 deaths (8.9%, 95% CI 3.0-21.3), all in NPAN-SAH cohort with 2 (4.4%) deaths due to re-bleeding. Forty-one (91.1%) had repeat angiography within two weeks and 3 (6.7%) had a third angiogram at long-term follow-up. All 33 (100%) NPAN-SAH had repeat angiography. Forty-one (91.1%) had at least 1 CTA of the head, 16 (35.6%) 2 CTAs, and 5 (11.1%) had > 2 CTAs. Forty-two (93.3%) had MRI and MRA of brain and cervical spine, 20 (44.4%) had additional thoracic MRI, and 18 (40.0%) had additional MRI of the entire spine. An average of 3.2 non-invasive studies were performed on each patient. In these 142 additional non-invasive studies, there was no additional diagnostic yield in finding the source of SAH.

#### **DISCUSSION**

Patients with non-perimesencephalic angiogram-negative SAH have worse prognosis compared to patients with perimesencephalic SAH. Our study demonstrates that additional non-invasive neuro-imaging provides no diagnostic yield in either patient population.

The diverse clinical presentation of SAH sub-types makes it difficult to ascertain a set clinical work-up for all patients. And among individual patients, the risk of rebleeding and clinical deterioration warrants continual evaluation and monitoring. Yet our study shows that subsequent testing is not necessarily efficacious. Prior studies demonstrate utility in repeating DSA imaging, but many remain inconclusive about the value of repeat CTA and MRA. <sup>15-22</sup> It is likely that the large disparity in clinical results stem from the uniquely different study types. Having little to no definitional consensus as to what constitutes a specific type of SAH

creates random disparity in each study's categorization of the patient populations' conditions. Though a few studies have attempted to systematically evaluate the decision to undergo a particular type of study or series of imaging studies<sup>23,24</sup>, these studies are largely predicated on the results derived in previously published studies.<sup>23</sup>

Many prior studies have lead to seemingly inconclusive evidence perhaps due to over generalizing. Of late, many studies have focused on studying SAH of a particular anatomic region, a certain blood pattern, or only certain imaging modalities in a specific context. 25-33 Limiting the context of the study to just a certain aspect of angiogram negative patients allows one to better identify key patient presentations making the decision to proceed with imaging modality situation specific. 27,29,32 While the pathophysiology has yet to be fully elucidated, from a clinical standpoint, envisioning each patient's condition as a unique disease allows the physician to make patient specific decisions. Many other cerebrovascular conditions demonstrate different behaviors based on the etiology and anatomic region; and patient management reflects the nuances. 34

In clinical management of angiogram negative SAH, far too often the decision simplifies to determining how significant the risk of re-bleeding is. Though key studies have identified anatomic regions where angiograms are likely to be missed, or where venous-based SAH occur, practical clinical management is reluctant to rely just on those studies. Studies. Studies that corroborate clinical imaging with further surgical evaluation will help strengthen the validity of certain imaging results, but it is difficult to find studies with significant enough patient populations to be heavily relied upon. State of the significant enough patient populations to be heavily relied upon.

Conversely, rather than looking for situation-specific patterns to help guide decision making, better imaging modalities can be used to increase the specificity of a negative angiogram finding.<sup>37</sup> But better technology may not be able to fully eliminate the risk and uncertainty inherent in deciding whether to order further imaging. Part of the issue is the physicians' fear that by not undergoing additional imaging, he or she did not do a comprehensive enough job in patient management. Therefore, extending the standardized protocol of SAH management into imaging based decisions will help alleviate the dilemma faced by physicians.<sup>27</sup>

Limitations in the study include the relatively small sample size. Additionally, we did not distinguish the types of studies from the number of studies. Our focus was to evaluate the absolute number of subsequent studies and assess the utility. Further value could have been gained from assessing the relative value of a subsequent CTA relative to an MRA or DSA. We did not distinguish if certain patient types or anatomic presentations automatically warranted more extensive imaging work-up relative to other presentations either.

Further study must focus on identifying key correlations in an anatomic- or presentation- specific manner. The inconclusiveness and disparity among prior studies assumes that angiogram negative SAH is either one condition, or composed of one or two condition. The spectrum of acuity, mortality, and associative conditions implies that angiogram negative SAH should be viewed as a much broader disease that present as many unique conditions.

#### References

- 1. Ingall T, Asplund K, Mähönen M, Bonita R, WHO MONICA Project. A Multinational Comparison of Subarachnoid Hemorrhage Epidemiology in the WHO MONICA Stroke Study. Stroke 2000;31:1054-1061 2. van Gijn J, van Dongen KJ, Vermeulen M, Hijdra A. Perimesencephalic hemorrhage: a nonaneurysmal and benign form of subarachnoid hemorrhage. Neurology. 1985 Apr;35(4):493-7.
- 3. Brismar J, Sundbärg G. Subarachnoid hemorrhage of unknown origin: prognosis and prognostic factors. J Neurosurg. 1985 Sep;63(3):349-54.
- 4. Eskesen V, Sørensen EB, Rosenørn J, Schmidt K. The prognosis in subarachnoid hemorrhage of unknown etiology. J Neurosurg. 1984 Dec;61(6):1029-31.
- 5. Alexander MS, Dias PS, Uttley D. Spontaneous subarachnoid hemorrhage and negative cerebral panangiography. Review of 140 cases. J Neurosurg. 1986 Apr;64(4):537-42.
- 6. Biller J, Toffol GJ, Kassell NF, Adams HP Jr, Beck DW, Boarini DJ. Spontaneous subarachnoid hemorrhage in young adults. Neurosurgery. 1987 Nov;21(5):664-7.
- 7. Rinkel GJ, Wijdicks EF, Vermeulen M, Hageman LM, Tans JT, van Gijn J. Outcome in perimesencephalic (nonaneurysmal) subarachnoid hemorrhage: a follow-up study in 37 patients. Neurology. 1990 Jul;40(7):1130-2. 8. Rinkel GJ, Wijdicks EF, Vermeulen M, Ramos LM, Tanghe HL, Hasan D, Meiners LC, van Gijn J.

Nonaneurysmal perimesencephalic subarachnoid hemorrhage: CT and MR patterns that differ from aneurysmal rupture. AJNR Am J Neuroradiol. 1991 Sep-Oct;12(5):829-34.

- 9. Rinkel GJ, Wijdicks EF, Hasan D, Kienstra GE, Franke CL, Hageman LM, Vermeulen M, van Gijn J. Outcome in patients with subarachnoid haemorrhage and negative angiography according to pattern of haemorrhage on computed tomography. Lancet. 1991 Oct 19;338(8773):964-8.
- 10. van Gijn J, van Dongen KJ. Computerized tomography in subarachnoid hemorrhage: difference between patients with and without an aneurysm on angiography. Neurology. 1980 May;30(5):538-9.
- 11. Jane JA, Winn HR, Richardson AE. The natural history of intracranial aneurysms: rebleeding rates during the acute and long term period and implication for surgical

- management. Clin Neurosurg. 1977;24:176-84.
  12. Sundt TM Jr, Kobayashi S, Fode NC, Whisnant JP.
  Results and complications of surgical management of 809 intracranial aneurysms in 722 cases. Related and unrelated to grade of patient, type of aneurysm, and timing of surgery. J Neurosurg. 1982 Jun;56(6):753-65.
- 13. Heiskanen O. Risk of bleeding from unruptured aneurysm in cases with multiple intracranial aneurysms. J Neurosurg. 1981 Oct;55(4):524-6.
- 14. Yasui T, Sakamoto H, Kishi H, Komiyama M, Iwai Y, Yamanaka K, Nishikawa M, Nakajima H, Kan M. Management of subarachnoid hemorrhages without detectable aneurysm. No Shinkei Geka. 1997 Oct;25(10):907-12.
- 15. Khan N, Schuknecht B, Yonekawa Y. Presentation and management of patients with initial negative 4-vessel cerebral angiography in subarachnoid hemorrhage. Acta Neurochir Suppl. 2002;82:71-81.
- 16. Houben MP, van Rooij WJ, Sluzewski M, Tijssen CC. Subarachnoid hemorrhage without aneurysm on the angiogram: the value of repeat angiography. Ned Tijdschr Geneeskd. 2002 Apr 27;146(17):804-8.
- 17. Maslehaty H, Petridis AK, Barth H, Mehdorn HM. Diagnostic value of magnetic resonance imaging in perimesencephalic and nonperimesencephalicsubarachnoid hemorrhage of unknown origin. J Neurosurg. 2010 Jul 30. 18. Topcuoglu MA, Ogilvy CS, Carter BS, Buonanno FS, Koroshetz WJ, Singhal AB. Subarachnoid hemorrhage without evident cause on initial angiography studies: diagnostic yield of subsequent angiography and other neuroimaging tests. J Neurosurg. 2003 Jun;98(6):1235-40. 19. Houben MP, van Rooij WJ, Sluzewski M, Tijssen CC. Subarachnoid hemorrhage without aneurysm on the angiogram: the value of repeat angiography. Ned Tijdschr Geneeskd. 2002 Apr 27;146(17):804-8.
- 20. Rogg JM, Smeaton S, Doberstein C, Goldstein JH, Tung GA, Haas RA. Assessment of the value of MR imaging for examining patients with angiographically negative subarachnoid hemorrhage. AJR Am J Roentgenol. 1999 Jan;172(1):201-6.
- 21. Guevara-Dondé JE, Rogel-Ortiz F. Subarachnoid hemorrhage with negative angiography. Gac Med Mex. 1999 Mar-Apr;135(2):107-12.
  22. Curnes JT, Shogry ME, Clark DC, Elsner HJ. MR
- 22. Curnes JT, Shogry ME, Clark DC, Elsner HJ. MR angiographic demonstration of an intracranial aneurysm not seen on conventional angiography. AJNR Am J Neuroradiol. 1993 Jul-Aug;14(4):971-3.
- 23. Ruigrok YM, Rinkel GJ, Buskens E, Velthuis BK, van Gijn J. Perimesencephalic hemorrhage and CT angiography: A decision analysis. Stroke. 2000 Dec;31(12):2976-83.
- 24. Yoshimoto Y, Wakai S. Cost-effectiveness analysis of screening for asymptomatic, unruptured intracranial aneurysms. A mathematical model. Stroke. 1999 Aug;30(8):1621-7.
- 25. Andaluz N, Zuccarello M. Yield of further diagnostic work-up of cryptogenic subarachnoid hemorrhage based on bleeding patterns on computed tomographic scans. Neurosurgery. 2008 May;62(5):1040-6; discussion 1047. 26. Pedraza S, Méndez-Méndez J. The prognostic value of computerized tomography in acute aneurysmal subarachnoid haemorrhages. Rev Neurol. 2004 Aug 16-31;39(4):359-63. 27. Fiebach JB, Schellinger PD, Geletneky K, Wilde P, Meyer M, Hacke W, Sartor K. MRI in acute subarachnoid haemorrhage; findings with a standardised stroke protocol. Neuroradiology. 2004 Jan;46(1):44-8. Epub 2003 Dec 4. 28. Wijdicks EF, Schievink WI, Miller GM. MR imaging in pretruncal nonaneurysmal subarachnoid hemorrhage: is it worthwhile? Stroke. 1998 Dec;29(12):2514-6.

- 29. Maslehaty H, Petridis AK, Barth H, Mehdorn HM. Diagnostic value of magnetic resonance imaging in perimesencephalic and nonperimesencephalic. Subarachnoid hemorrhage of unknown origin. J Neurosurg. 2010 Jul 30. 30. Agid R, Andersson T, Almqvist H, Willinsky RA, Lee SK, terBrugge KG, Farb RI, Söderman M. Negative CT angiography findings in patients with spontaneous subarachnoid hemorrhage: When is digital subtraction angiography still needed? AJNR Am J Neuroradiol. 2010 Apr;31(4):696-705.
- 31. Gaughen JR Jr, Raghavan P, Jensen ME, Hasan D, Pfeffer AN, Evans AJ. Utility of CT angiography in the identification and characterization of supraclinoid internal carotid artery blister aneurysms. AJNR Am J Neuroradiol. 2010 Apr;31(4):640-4.
- 32. Mark DG, Pines JM. The detection of nontraumatic subarachnoid hemorrhage: still a diagnostic challenge. Am J Emerg Med. 2006 Nov:24(7):859-63. Review.
- Emerg Med. 2006 Nov;24(7):859-63. Review.
  33. Curnes JT, Shogry ME, Clark DC, Elsner HJ. MR angiographic demonstration of an intracranial aneurysm not seen on conventional angiography. AJNR Am J Neuroradiol.

1993 Jul-Aug;14(4):971-3.

34. Reichman M, Gold R, Greenberg E, Ivanidze J, Elias E, Comunale J, Tsiouris AJ, Johnson C, Sanelli PC. Validation of a new reference standard for the diagnosis of vasospasm. Acad Radiol. 2010 Sep;17(9):1083-9. Epub 2010 Jun 12. 35. Andaluz N, Zuccarello M. Yield of further diagnostic work-up of cryptogenic subarachnoid hemorrhage based on bleeding patterns on computed tomographic scans. Neurosurgery. 2008 May;62(5):1040-6; discussion 1047. 36. Kokkinis C, Vlychou M, Zavras GM, Hadjigeorgiou GM, Papadimitriou A, Fezoulidis IV. The role of 3Dcomputed tomography angiography (3D-CTA) in investigation of spontaneous subarachnoid haemorrhage: comparison with digital subtraction angiography (DSA) and surgical findings. Br J Neurosurg. 2008 Feb;22(1):71-8. 37. van Rooij WJ, Peluso JP, Sluzewski M, Beute GN. Additional value of 3D rotational angiography in angiographically negative aneurysmal subarachnoid hemorrhage: how negative is negative? AJNR Am J Neuroradiol. 2008 May;29(5):962-6. Epub 2008 Feb 7.

## **Author Information**

# Jay K. Joshi, MD, MBA

Department of Neurological Sciences, Rush University Medical Center

# Shyam Prabhakaran, MD, MS

Department of Neurological Sciences, Rush University Medical Center

# Sayona John, MD

Department of Neurological Sciences, Rush University Medical Center