**Diagnosis of Subarachnoid Hemorrhage**

**Time to Change the Guidelines?**

Jonathan A. Edlow, MD; Jonathan Fisher, MD, MPH

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Although the most concerning diagnosis in patients presenting with thunderclap headache is nontraumatic subarachnoid hemorrhage (SAH), only 8% to 12% of neurologically intact patients with thunderclap headache will have SAH; most have benign causes. Of those with aneurysmal SAH, 40% to 50% of patients will present neurologically intact. Therefore, diagnostic testing beyond history and physical examination is necessary. The initial test of choice is a noncontrast CT scan of the brain.

Although CT is an excellent test for SAH, its sensitivity is both a function of timing from the onset of the headache as well as severity of the hemorrhage. CT sensitivity is extremely high early but rapidly diminishes with time. Clinicians frequently encounter neurologically normal patients with a thunderclap headache and a negative CT scan. Even using third-generation scanners, CT by itself is insufficient to exclude SAH. Therefore, guidelines recommend that a lumbar puncture (LP) be performed in these patients whose CT scans are negative or nondiagnostic. Although LP is a relatively benign test, it adds time, patient discomfort, and, sometimes, diagnostic ambiguity from a traumatic tap.

Prior studies of CT sensitivity do not adequately account for the issue of timing in the earliest hours after the hemorrhage. In this issue of *Stroke*, Backes et al present data suggesting that CT scan is 100% sensitive for SAH if performed within 6 hours of the headache onset and apart from 2 caveats, the authors recommend a change in the guidelines. Are their data strong enough to warrant such a change?

First let us consider the caveats. The first is that the <6-hour rule only applies to patients presenting with headache. This is because they identified a single early-presenting patient with acute neck pain and a negative CT who had SAH due to a cervical arteriovenous malformation. This is an important caveat because up to 8% of patients with SAH will present without thunderclap headache. The second caveat is the study setting; experienced neuroradiologists at a referral center interpreted the scans. Are there any other limitations that we must consider? Aside from its retrospective design, one limitation of this Dutch study is that the incidence of SAH was 42% (50% of those patients presenting within 6 hours). This is far higher than the incidence of SAH in patients with thunderclap headache seen in routine practice. As well, they excluded patients whose SAH was confirmed at the transferring hospital, another factor that could skew their results. That said, their principal findings are compatible with 2 other relevant studies.

The first is a 2010 Danish report that concluded that CT was 100% sensitive if performed within 3 days of the headache. Similar to the current report, this was a referral population to a neurosurgical center; however, unlike the Backes study, the Danish study included patients with focal or generalized neurological deficits. The incidence of SAH in this study was 59% (67% if they presented in the first 24 hours).

Both of these studies are retrospective reports of referral populations whose incidence of SAH is 5 to 6 times what is reported in the literature. Although Backes and colleagues state otherwise, test performance characteristics are in part related to the incidence and severity of the disease that they test for in a given population.

Classic statistical theory teaches that the sensitivity and specificity of a test are fundamental characteristics of the test and independent of disease prevalence. However, there are numerous examples of a diagnostic test performing well in a study population but failing to yield the same results in other populations. In 1978, Rasenhoff and Feinstein described the phenomenon of spectrum bias as the performance of a diagnostic test varying according to the case mix (a combination of disease severity and prevalence) of the population tested. Since that time, a growing body of literature has emerged suggesting that spectrum bias is common, leading to the concept that diagnostic tests perform better in populations of patients with more severe disease or higher prevalence.

As an example of the relationship between prevalence and sensitivity, the prevalence of SAH is higher in early-presenting patients than in those presenting later. So given these issues of spectrum bias, can the Dutch and Danish reports be used to support a change in current guidelines? What will happen when CT is used in a population more reflective of real-world practice in which the severity and prevalence of SAH are much lower?

Fortunately, a third study helps to resolve this conundrum. The 2011 Canadian report by Perry et al is a prospective study of 3132 neurologically intact patients with thunderclap headache presenting to 11 different Canadian emergency departments. Two hundred forty patients (7.7%) had SAH, a
number much more representative of the population of patients to which these results will be applied. Of the 3132 patients, 953 were scanned within 6 hours of onset of headache. All 121 of these early-presenting patients were CT-positive. Like with the other 2 studies, the prevalence of SAH in the earlier presenting group (12.7%) was over twice that of patients who presented >6 hours (5.5%).

Numerous radiologists, both general and neuroradiologists from across multiple institutions, interpreted the scans in the Canadian study. There were 3 instances in which CT scans were read as negative by emergency physicians were later read as positive by a radiologist. In a fourth instance, the false-negative reading was by a radiology trainee. This underscores the importance of having well-trained, experienced physicians interpret the CT scans.

Although not all patients underwent LP after a negative CT, the patients who received an LP did not differ substantially from those who did not. As well, because of the healthcare system in Canada, the researchers were able to obtain healthcare follow-up on >97% of the patients and were able to show that they were alive and had not been subsequently diagnosed with a SAH. We believe that the strengths of this article far outweigh the weaknesses.

As CT technology has become increasingly accurate and available, some have begun to suggest that cerebral CT angiography be performed after a negative CT instead of an LP for the work-up of patients with possible SAH. We believe that this “technology creep” only leads to diagnosis of asymptomatic aneurysms (not the hemorrhage) and has many other unintended negative consequences.12 The Dutch, Danish, and Canadian studies reinforce this notion.

Like with any guideline, it is just as important to know when it does not apply. It does not apply to patients with abnormal neurological examinations. It also does not apply if the history and physical examination suggest other diagnoses beyond SAH (cerebral venous sinus thrombosis, arterial dissections, cerebellar infarction, etc.). Lastly, it only applies to patients who can be scanned within 6 hours of headache onset and specifically does not apply to patients presenting with isolated neck pain. This reinforces both the public health mandate as well as emergency department operations to focus on the rapid recognition and evaluation of patients with symptoms suggesting stroke.

Given this analysis, we believe that practice should change. Neurologically intact patients who present with thunderclap headache and undergo CT scan within 6 hours of symptom onset no longer need an LP to exclude SAH if the CT scan is negative. Physicians and hospitals must ensure the expertise of the individuals who are interpreting these scans.

Disclosures
Dr Edlow has served as an expert witness in medico-legal cases for both defense and plaintiff firms.

References

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