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ORIGINAL CONTRIBUTION

# False-negative Interpretations of Cranial Computed Tomography in Aneurysmal Subarachnoid Hemorrhage

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## Abstract

***Objectives:*** Prior studies examining the sensitivity of cranial computed tomography (CT) for the detection of subarachnoid hemorrhage (SAH) have used the final radiology report as the reference standard. However, optimal sensitivity may have been underestimated due to misinterpretation of reportedly normal cranial CTs. This study aims to estimate the incidence of missed CT evidence of SAH among a cohort of patients with aneurysmal SAH (aSAH).

***Methods:*** We performed a retrospective chart review of emergency department (ED) encounters within an integrated health delivery system between January 2007 and June 2013 to identify patients diagnosed with aSAH. All initial noncontrast CTs from aSAH cases diagnosed by lumbar puncture (LP) and angiography following a reportedly normal noncontrast cranial CT (CT-negative aSAH) were then reviewed in a blinded, independent fashion by two board-certified neuroradiologists to assess for missed evidence of SAH. Reviewers rated the CT studies as having definite evidence of SAH, probable evidence of SAH, or no evidence of SAH. Control patients who underwent a negative evaluation for aSAH based on cranial CT and LP results were also included at random in the imaging review cohort.

***Results:*** A total of 452 cases of aSAH were identified; 18 (4%) were cases of CT-negative aSAH. Of these, seven (39%) underwent cranial CT within 6 hours of headache onset, and two (11%) had their initial CTs formally interpreted by board-certified neuroradiologists. Blinded independent CT review revealed concordant agreement for either definite or probable evidence of SAH in nine of 18 (50%) cases overall and in five of the seven (71%) CTs performed within 6 hours of headache onset. Inter-rater agreement was 83% for definite SAH and 72% for either probable or definite SAH.

***Conclusions:*** CT evidence of SAH was frequently present but unrecognized according to the final radiology report in cases of presumed CT-negative aSAH. This finding may help explain some of the discordance between prior studies examining the sensitivity of cranial CT for SAH.

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Nontraumatic subarachnoid hemorrhage (SAH) can be due a variety of underlying causes, including cerebral aneurysms, arteriovenous malformations (both cerebral and spinal), and spontaneous bleeding without a discoverable underlying vascular anomaly (most often observed in the perimesencephalic region). Of these etiologies, aneurysmal SAH (aSAH) is the most common and life-threatening, with high rates of serious morbidity, particularly when diagnosis and definitive treatment is delayed.[1,2] Though the vast majority of aSAH cases are initially detected by cranial computed tomography (CT), in some

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instances CT evidence of SAH is absent, often attributed to delayed clinical presentations allowing for reabsorption of normally hyperattenuating heme products, very small initial volumes of hemorrhage, or a low hematocrit.[3] The diagnosis in these cases of "CT-negative" aSAH is typically made via lumbar puncture (LP) and the presence of red blood cells (RBCs) and/or bilirubin (as established by visual or spectrophotometric analysis for xanthochromia) in the cerebrospinal fluid (CSF). When CSF analysis is positive for these markers of SAH, cerebral angiography is warranted to exclude a ruptured cerebral aneurysm as the cause.[4–11] However, given that CSF analysis in this setting can result in specificities for aSAH as low as 64% to 75%, this approach can result in high rates of extensive and traditionally invasive workups with relatively low yields.[7,8,12,13]

Accordingly, there is great enthusiasm for a potential CT-only approach to the diagnosis of aSAH in the wake of publications reporting 100% sensitivity for aSAH with the use of cranial CT performed within 6 hours of headache onset among patients presenting with a sudden-onset headache and normal mental status.[14–18] However, other studies of nontertiary, nonacademic settings failed to validate these findings.[19,20] Specifically, one recent retrospective study reported a sensitivity of only 95.5% for aSAH when cranial CT was performed within 6 hours of headache onset.[20] These conflicting findings have been hypothesized to be due to selection bias (inclusion of patients with false-positive CSF findings and incidentally discovered cerebral aneurysms) and/or information bias (misinterpreted CT images).[17,21,22] While selection bias in this setting is a well-recognized challenge for both clinicians and researchers, there is no clearly established method to refute or confirm a diagnosis of aSAH in such scenarios, particularly when endovascular therapies are employed, which preclude direct visual inspection for evidence of aneurysm rupture. However, it is possible to assess for errors of CT interpretation, a well-documented issue in SAH diagnosis, which if present would proportionately diminish the selection bias assumption.[3,11,23–25] The objective of this study was thus to retrospectively review, in a blinded independent fashion, CT images from cases of presumed CT-negative aSAH, including several cranial CTs performed within 6 hours of headache onset, for previously unreported CT evidence of SAH.

## METHODS

### Study Setting and Population

This study is an analysis of a case series, derived from a retrospective dataset compiled to examine outcomes following misdiagnosis of aSAH. Electronic health records of patients treated within Kaiser Permanente Northern California (KPNC) between January 2007 and June 2013 were screened for case inclusion if they had an emergency department (ED) or hospital encounter with an associated International Statistical Classification of Diseases and Related Health Problems, Ninth Edition (ICD-9), diagnosis code of SAH (430). Patients were electronically excluded if they had an ICD-9–coded diagnosis of head or neck trauma within 24 hours of the index encounter, lacked continuous health plan membership within the 2 weeks preceding diagnosis (the a priori timeframe for misdiagnosis), were under 18 years of age, or had a prior diagnosis of SAH between 2002 and 2006 (to exclude post aSAH-related encounters). Charts were then manually reviewed and the following study inclusion criteria were abstracted: diagnosis at a KPNC ED, no evidence of SAH on the initial noncontrast cranial CT according to the final radiology report, and angiographic evidence of a cerebral aneurysm thought to be causative of SAH (CT-negative aSAH), resulting in emergent endovascular or surgical treatment during the index hospitalization. The study was approved by the KPNC Institutional Review Board with a waiver of the requirement for informed consent.

### Study Protocol

Two authors (DGM and MVK) conducted a structured explicit chart review and abstraction of records using a standardized paper form as part of a larger outcomes study. For the purpose of this case series analysis, the key information obtained from chart abstraction was confirmation of the inclusion criteria, timing of the initial CT in relation to headache onset, method and details of SAH diagnosis (i.e., CSF analysis and/or magnetic resonance imaging), and the location and size of the culprit aneurysm. Other details regarding abstraction methods and inter-rater reliability have been previously published.[20]

Cranial CT examinations were performed without contrast using multislice cine technology and standard axial imaging protocols to produce slice thicknesses of 5 mm from skull base to vertex. Either general radiologists or neuroradiologists made the final written interpretation of CT images, which were stored in DICOM format on hospital-level secure internal servers. An image review cohort was assembled using the initial CT examinations from patients with CT-negative aSAH, along with several CT examinations from patients with negative ED workups for SAH by both CT and LP to serve as internal controls (randomly selected from an existing control cohort assembled for a prior study).[19] All these CT examinations were anonymized and isolated from any linked follow-up imaging studies using the anonymous export function in iSite PACS (Phillips Healthcare).

### Measurements

Two board-certified neuroradiologists (DCS and PJ), who were blinded to both the study hypothesis and the cohort assembly methods, independently interpreted each CT examination in the image cohort. The neuroradiologists were informed of the reason for referral (acute headache) and asked to interpret the images as either having 1) definitive evidence of SAH (hyperattenuation in the basilar cisterns [suprasellar, lateral pontine, interpeduncular, prepontine or perimesencephalic], Sylvian fissure, anterior interhemispheric fissure, or refluxed blood in the fourth ventricle); 2) probable evidence of SAH (isoattenuation in the basilar cisterns, Sylvian fissures or cortical sulci, with or without hydrocephalus); or 3) no evidence of SAH (Table 1). This

Table 1
Study Definitions for Image Review Interpretations

| | |
|---|---|
| Definite CT evidence of SAH | Hyperattenuation (blood) in any of the following: basilar cisterns (suprasellar, lateral pontine, interpeduncular, prepontine, or perimesencephalic), Sylvian fissure, anterior interhemispheric fissure, or refluxed blood in the fourth ventricle |
| Probable CT evidence of SAH | Isoattenuation in the basilar cisterns, Sylvian fissures or cortical sulci, with or without hydrocephalus |
| No CT evidence of SAH | Hypoattenuation (CSF) in the basilar cisterns, Sylvian fissures, and cortical surfaces |

CT = computed tomography; CSF = cerebrospinal fluid; SAH = subarachnoid hemorrhage

explicit categorization system was prepared by an author (DTS) and agreed to by both neuroradiologists. The category of probable SAH was designed to identify abnormal radiographic findings that are consistent with SAH, which while not clearly diagnostic, would at least prompt further investigations. Original misinterpretation of the CT examination was defined as concordant blinded agreement between the two neuroradiologist reviewers for either definite or probable evidence of SAH.

### Data Analysis

Inter-rater reliability between neuroradiologists was assessed using both inter-rater agreement and unweighted kappa. All statistical analyses were performed using STATA v 13.0 (StataCorp).

## RESULTS

Of a total of 4,121 screened individuals with ICD-9–coded diagnoses of SAH during the study period, there were 452 cases of aSAH identified, of which 18 (4%) were reportedly cases of CT-negative aSAH and met criteria for analysis in this study. Demographic and angiographic characteristics of the CT-positive and CT-negative aSAH subgroups are summarized in Table 2. Of the 18 CT-negative aSAH cases, seven (39%) underwent cranial CT within 6 hours of headache onset, and two (11%) had their initial index encounter CTs interpreted by board-certified neuroradiologists. LP results from the 18 CT-negative aSAH cases revealed a range of CSF RBC counts of 9,960 to 51,7500 cells per μL, with nine (50%) demonstrating visual xanthochromia. Thirteen (72%) patients underwent endovascular aneurysm treatment and the remainder underwent surgical clipping. Other details of the 18 CT-negative aSAH cases and the independent, blinded neuroradiologist reinterpretations of the initial cranial CTs are reported in Table 3.

Table 2
Patient Characteristics

| Variable | CT-positive ($n$ = 434) | CT-negative ($n$ = 18) |
|---|---|---|
| Age (y), median (IQR) | 59 (49–69) | 55 (50–69) |
| Female (%) | 75 | 78 |
| Race (%) | | |
| Caucasian | 49 | 56 |
| Asian | 20 | 22 |
| Black | 14 | 6 |
| Hispanic | 2 | 6 |
| Unknown/other | 15 | 11 |
| Glasgow Coma Score, median (IQR) | 15 (13–15) | 15 (15–15) |
| Hunt-Hess grade at diagnosis (%) | | |
| 1 | 4 | 33 |
| 2 | 49 | 67 |
| 3 | 23 | 0 |
| 4 | 12 | 0 |
| 5 | 12 | 0 |
| Aneurysm location (%) | | |
| ACOM | 26 | 28 |
| PCOM | 16 | 28 |
| MCA | 16 | 11 |
| ICA | 6 | 6 |
| ACA | 4 | 6 |
| Basilar | 5 | 0 |
| PICA | 3 | 6 |
| Vertebral | 2 | 11 |
| Other* | 5 | 6 |
| Unknown | 14 | 0 |
| Aneurysm size (mm), median (IQR) | 5 (4–8) | 5 (3–7) |

ACA = anterior cerebral artery; ACOM = anterior communicating artery; CT = computed tomography; ICA = internal carotid artery; IQR = interquartile range; MCA = middle cerebral artery; PICA = posterior inferior cerebellar artery; PCOM = posterior communicating artery.
*Other locations ($n$) included the vertebral artery (5), superior cerebellar artery (3), pericallosal artery (3), anterior choriodal (3), ophthalmic artery (2), and the superior hypophyseal artery (1).

Concordant agreement for definite evidence of SAH was reported in four (22%, 95% confidence interval [CI] = 7% to 48%) of the CT-negative aSAH cases, and concordant agreement for either definite or probable evidence of SAH (study definition of original misinterpretation) was reported in nine (50%, 95% CI = 27% to 73%) cases (Table 4). Overall, at least one neuroradiologist noted abnormalities concerning for SAH in 14 (78%) of the 18 cases. When cranial CT was performed within 6 hours of headache onset, concordant agreement for either definite or probable SAH was noted in five of the seven cases (71%, 95% CI = 36% to 92%), with at least one neuroradiologist noting definite or probable evidence of SAH in six of the seven (86%) cases. The one discordant case interpreted as negative for SAH by one neuroradiologist was noted to have "possible right tentorial subdural hematoma versus meningitis," an interpretation that would have led to further workup for headache etiology. The remaining case interpreted by both neuroradiologists as negative for SAH had an aneurysm clip from prior SAH that may have obscured CT signs of SAH. Representative

Table 3
CT-negative aSAH Case Details and Retrospective Blinded Interpretations

| Case | Age (y) | HA Onset to CT (h) | CSF RBCs (/μL)* | CSF Xantho† | Aneurysm Location (Side) | Aneurysm Size (mm)‡ | Rater 1 | Rater 2 | Location (s)§ |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 67 | ≤6 | 408,000 | No | PCOM (L) | 6 | No | No | NA |
| 2 | 76 | ≤6 | 517,500 | No | PCOM (R) | 4 | Definite | No‖ | 1, 8 |
| 3 | ≥90 | ≤6 | 280,000 | Yes | ACOM (N) | 5 | Definite | Definite | 1, 2, 7, 8 |
| 4 | 53 | ≤6 | 49,750 | No | PCOM (R) | 2 | Definite | Definite | 2 |
| 5 | 50 | ≤6 | 9,960 | No | ACOM (N) | 9 | Probable | Definite | 1, 2, 4, 8 |
| 6 | 45 | ≤6 | 190,000 | No | ICA (L) | 4 | Probable | Definite | 3 |
| 7 | 70 | ≤6 | 55,000 | Yes | Vert (R) | 2 | Probable | Probable | 1, 8 |
| 8 | 69 | >72 | 205,000 | Yes | ACA (R) | 5 | No | No | NA |
| 9 | 78 | >72 | 28,082 | Yes | PICA (L) | 7 | No | No | NA |
| 10 | 52 | >72 | 23,062 | No | MCA (R) | 2 | No | No | NA |
| 11 | 49 | >72 | NR | Yes | MCA (R) | 4 | No | Probable | 7 |
| 12 | 57 | >72 | 14,500 | No | PCOM (R) | 8 | No | Probable | 2 |
| 13 | 68 | >72 | 321,000 | Yes | ACOM (N) | 8 | Definite | Definite | 7, 8 |
| 14 | 50 | 48–72 | 330,000 | Yes | Vert (L) | 5 | Definite | Definite | 1, 8 |
| 15 | 67 | >72 | 40,000 | Yes | PCOM (R) | 3 | Probable | No | 2, 8 |
| 16 | 37 | 48–72 | 62,280 | No | ACA (R) | 4 | Probable | Probable | 5, 6 |
| 17 | 52 | 48–72 | 20,750 | No | ACOM (N) | 8 | Probable | No | 2 |
| 18 | 30 | 48–72 | 171,380 | Yes | ACOM (N) | 2 | Probable | Probable | 5, 7 |

ACA = anterior cerebral artery; ACOM = anterior communicating artery; aSAH = aneurysmal subarachnoid hemorrhage; CSF = cerebrospinal fluid; CT = computed tomography; HA = headache; ICA = internal carotid artery; L = left; MCA = middle cerebral artery; NA = not applicable; NR = not reported; PCOM = posterior communicating artery; R = right; RBCs = red blood cells; Vert = vertebral artery; xantho = xanthochromia.
*Lowest reported cell count from lumbar puncture analysis.
†Defined as explicit laboratory reporting of CSF color as "xanthochromia" (visual analysis).
‡Maximal diameter as reported at angiography.
§1 = suprasellar cistern, 2 = Sylvian fissure, 3 = interpeduncular cistern, 4 = prepontine, 5 = cortical sulci, 6 = tentorium cerebelli, 7 = intraventricular, 8 = hydrocephalus.
‖Interpreted as right tentorial subdural hematoma versus meningitis.

Table 4
Categorical Cranial CT Interpretations from CT-negative aSAH Cases and Control Patients

| | Reviewer 1 | | Reviewer 2 | | Concordant | |
|---|---|---|---|---|---|---|
| | Definite | Definite or Probable | Definite | Definite or Probable | Definite | Definite or Probable |
| Control ($n$ = 7) | 0/7 (0%) | 0/7 (0%) | 0/7 (0%) | 1/7 (14%) | 0/7 (0%) | 0/7 (0%) |
| aSAH and CT < 6 h after HA onset ($n$ = 7) | 3/7 (43%) | 6/7 (86%) | 4/7 (57%) | 5/7 (71%) | 2/7 (29%) | 5/7 (71%) |
| aSAH and CT > 6 h after HA onset ($n$ = 9) | 2/9 (22%) | 6/9 (67%) | 2/9 (22%) | 6/9 (67%) | 2/9 (22%) | 4/9 (44%) |
| All aSAH ($n$ = 18) | 5/18 (28%) | 12/18 (67%) | 6/18 (33%) | 11/18 (61%) | 4/18 (22%) | 9/18 (50%) |

Definite CT evidence of SAH was defined as hyperattenuation in the basilar cistern, suprasellar cistern, Sylvian fissure, anterior interhemispheric fissure, lateral pontine, interpeduncular, prepontine or perimesencephalic cisterns, or refluxed blood in the fourth ventricle. Probable CT evidence of SAH was defined as isoattenuation in the basilar cisterns, Sylvian fissures, or cortical surface, with or without hydrocephalus.
aSAH = aneurysmal subarachnoid hemorrhage; CT = computed tomography.

images and findings for these seven studies are detailed in the electronic appendix (Figure e1). Inter-rater agreement was 83% for definite SAH and 72% for either probable or definitive SAH (Table 5).

## DISCUSSION

In this retrospective study we found that at least nine of 18 (50%) initial cranial CTs from patients diagnosed with CT-negative aSAH were originally misinterpreted, representing nine of 452 (2%) patients diagnosed with aSAH during our study period. This finding may largely explain the imperfect sensitivity of cranial CT performed within 6 hours of headache onset reported in prior studies from the same practice setting, given that five (or six if considering rater 1 alone) of the seven cranial CTs performed within 6 hours of headache onset in this series do appear to have evidence of SAH.[19,20] Thus the apparent difference in cranial CT test characteristics between this and other practice settings might be attributed to variable expertise among the clinical radiologists, given that the majority of the CTs in this series

Table 5
Percentage Agreement in CT Interpretation Between Neuroradiologists (Kappa)

| | All Interpretations | Definite SAH Only | Either Definite or Probable SAH |
|---|---|---|---|
| Control ($n$ = 7) | 86% (0.00) | 100% | 86% (0.00) |
| Early cranial CT with aSAH ($n$ = 7) | 57% (0.34) | 57% (0.16) | 86% (0.59) |
| All aSAH ($n$ = 18) | 61% (0.42) | 83% (0.61) | 72% (0.40) |

aSAH = aneurysmal subarachnoid hemorrhage; CT = computed tomography.

were interpreted by nonneuroradiologists, implying potential for improved sensitivity with more training and experience. However, the imperfect inter-rater agreement between blinded study neuroradiologists in this study highlights that CT misinterpretation can occur even among clinical experts and is consistent with prior reports examining inter-rater agreements between neuroradiologists.[26]

Discrepancies in cranial CT interpretation between either general radiologists[27,28] or radiology trainees[29,30] and board-certified neuroradiologists have previously been reported to occur in between 1 and 2% of all studies. Research examining misinterpretation of cranial CT for SAH in particular, however, is limited. Both Kowalski et al.[24] and Mayer et al.[25] attributed misdiagnoses of aSAH to misinterpretations of cranial CT in up to 15% of cases, but no further details were provided. A study by Horstman et al.[11] examining the prevalence of cerebral aneurysms among patients with CT-negative SAH reported that four of 30 (13%) cranial CT examinations were misinterpreted as negative for SAH by community radiologists. Another study by Ditta et al.[31] examining the yield of LP in the setting of suspected CT-negative SAH similarly reported that seven of 36 (19%) patients had retrospective radiographic evidence of SAH that was misinterpreted at the referring nontertiary hospitals. Neither of these studies, however, used a blinded or controlled retrospective imaging review process, such that hindsight bias likely played a role in the interpretations.

One recent study did attempt to systematically examine the potential for misinterpretation of early cranial CT for SAH by radiologists practicing in a nonacademic setting, finding one instance of misinterpretation (nonaneurysmal SAH) of 52 patients with CSF xanthochromia (by spectrophotometry) and reportedly normal CT examinations (2% misinterpretation rate).[32] However, the authors concluded that none of the eight of 52 patients (15%) who were ultimately found to have cerebral aneurysms truly suffered from aSAH, thus highlighting specificity issues with the inclusion criteria used by the authors to define CT-negative SAH. Similarly noteworthy is that the study by Perry et al.[15] reporting 100% sensitivity for early cranial CT included one CT that was initially misinterpreted as negative for SAH by a radiology trainee and was only retrospectively reinterpreted as positive after a magnetic resonance angiogram performed several days later revealed an aneurysm. These collective reports, along with our findings, demonstrate that misinterpretations create the potential for missed and/or delayed diagnoses when using CT as a stand-alone test for SAH in clinical practice.

In attempting to explain and remedy the possible drivers of misinterpretation in our patient population and practice setting, several issues arise. The first concerns the fact that radiologists without subspecialization in neuroradiology interpreted nearly all of the CTs found to have evidence of SAH in this series (eight of nine), potentially implying that sensitivity may be improved by uniform interpretation of cranial CTs by neuroradiologists. There is an ongoing debate regarding this issue as it relates to both radiology trainees and general radiologists who routinely interpret cranial CTs.[28,33–38] However, given that inter-rater agreement between neuroradiologists is imperfect to a similar degree as compared to general radiologists, it is unclear that such safeguards would truly improve the overall accuracy of cranial CT interpretation.[26,39] A second issue is that certain locations of hemorrhage may be more likely overlooked, particularly the interpeduncular cistern, such that improved awareness of such specific pitfalls for subtle SAH findings may improve detection.[23,30] The number of misinterpreted cranial CTs with early signs of hydrocephalus in this series (six of nine, specifically with dilatation of the posterior temporal horns and/or the infundibular recess of the third ventricle) might offer another potential target for educational intervention. Of note, posterior temporal horn dilation has previously been noted as a prevalent finding in between 66%–84% of SAH cases, even in the absence of visible hemorrhage.[40,41] Finally, we cannot fully account for unmeasured confounders affecting misinterpretation (years of radiologist experience, clinical workload, fatigue, etc).

Regardless of the factors contributing to misinterpretation, it seems inevitable that subtle cases of SAH will occasionally be overlooked. Accordingly, a redundant testing strategy is appropriate in cases of high clinical suspicion. While LP is capable of definitively ruling out aSAH,[42] false-positives are a major issue.[8,13,31,43,44] Even if one applies a recently suggested cutoff of greater than $2000 \times 10^6$/L CSF RBCs or visual xanthochromia in warranting further investigation for aSAH,[7,45] there is still a false-positive rate of roughly 10%. Assuming both a 1% background prevalence of aneurysms in the general population[46] and a 0.1% major complication rate accompanying diagnostic cerebral angiography,[47] it is debatable whether specific thresholds for post-test probability should drive the decision to perform LP following a reportedly normal cranial CT (i.e., assuming a 10% false-positive LP rate, less than 1 in 1,000 to avoid incidental diagnoses of cerebral aneurysm or less than 1 in 10,000 to avoid iatrogenic complications from angiography). The use of validated clinical decision rules in addition to cranial CT imaging might offer such a pathway to very low-risk stratification and the safe deferral of LP.[20,48]

## LIMITATIONS

We included either definitive or probable evidence of SAH in our final definition of CT misinterpretation. While we required that both neuroradiologist study reviewers record these interpretations independently, it is possible that false-positive interpretations still occurred, particularly when both reviewers rated the scan as showing probable evidence of SAH (three cases). The fact that none of the control CTs were concordantly interpreted by both reviewers as being positive is reassuring in this regard. However, one control scan was rated as "probable" by rater 2, which speaks to the subjective nature of CT interpretation and highlights the potential pitfall of using interpretations from a single reviewer as a gold standard.

Only two neuroradiologists were used for reference readings of the CT scans. It is possible that if more readers were used, the overall agreement of the reference readings would be improved. Inter-rater agreement may have also been constrained by the explicit definitions of definite and probable signs of SAH; however, these definitions were necessary to enable categorization of CT interpretations.

The completeness of our case identification may have been limited by the retrospective nature of the study and the accuracy of the diagnostic coding from hospital and ED encounters. However, we searched databases specific for diagnostic codes assigned during in-system treatment as well as those used to track services billed for out-of-system services, thus making it unlikely that we failed to capture cases of aSAH that were transferred out from the ED. Regardless, given the low numbers of cases identified, although typical for this rare disease entity, the precision of our estimates is limited and should be interpreted with caution.

Although radiographic presence of SAH was retrospectively evident in many cases, coexistence of incidental aneurysms in the setting of nonaneurysmal SAH is still conceivable. However, this is difficult to prove or disprove; while it seems intuitive that SAH should occur in the same location as the cerebral aneurysm, the location of SAH is in fact not a reliable indication of site of aneurysm rupture, with the exception of aneurysms involving the anterior cerebral or anterior communicating arteries.[49] As such, we considered emergent surgical or endovascular treatment of a cerebral aneurysm as a proxy for clinical suspicion of aneurysm rupture, if not explicitly stated otherwise in the clinical record. Finally, we did not include CT images from patients ultimately diagnosed with aSAH who may have been initially misdiagnosed (i.e., presented with symptoms concerning for SAH and had reportedly normal cranial CT imaging but no immediate confirmatory testing), since without confirmatory testing it is impossible to be certain that evidence of SAH would have been otherwise detected at the initial evaluation.

## CONCLUSION

In summary, the findings of our independent, blinded retrospective review by board-certified neuroradiologists suggest an appreciable rate of computed tomography misinterpretation in presumed cases of computed tomography–negative aneurysmal subarachnoid hemorrhage within our multicenter nonacademic community setting, suggesting that, in contemporary practice, the existence of computed tomography–negative aneurysmal subarachnoid hemorrhage cases may be largely due to radiologist misinterpretation. Even though individual radiologist error is unlikely to ever be fully eliminated, awareness of missed computed tomography signs of subarachnoid hemorrhage among radiologists might reduce the misinterpretation rate. Likewise, clinicians should more pointedly question their radiologists regarding subtle computed tomography signs in cases of suspected subarachnoid hemorrhage. These findings also underscore the difficulties in translating test characteristic data for tests with subjective elements, such as computed tomography interpretation, between distinct practice settings. Clinicians should account for such eventualities in their own practice settings through formal validation and/or tailored diagnostic approaches.

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## Supporting Information

The following supporting information is available in the online version of this paper:

**Figure S1.** Representative CT images from the seven cases of CT-negative aSAH with cranial CT performed within six hours of headache onset.