

# Intracranial Hemorrhage Complicating Acute Stroke: How Common Is Hemorrhagic Stroke on Initial Head CT Scan and How Often Is Initial Clinical Diagnosis of Acute Stroke Eventually Confirmed?

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**BACKGROUND AND PURPOSE:** Assessment of possible hemorrhage in acute stroke before appropriate therapy remains important. The aim of this study was to determine the frequency with which patients present with clinical stroke and have intracranial hemorrhage on initial noncontrast head CT scan (NCCT). In addition, we sought to determine the frequency with which initial clinical diagnosis acute stroke is confirmed in this group.

**METHODS:** Medical records of 691 consecutive patients with admitting diagnosis of acute stroke were evaluated retrospectively. Results of initial NCCT performed within 24 hours after presentation were assessed. All patients were examined before anticoagulation or thrombolysis. Correlation with treatment and leading differential etiology was made.

**RESULTS:** Twenty-five patients (25/691 [3.6%]) had hemorrhage. Twenty-three patients (23/25 [92%]) had intraparenchymal hemorrhage only. One patient (1/25 [4%]) had a combination of intraparenchymal and subarachnoid hemorrhage. One patient (1/25 [4%]) had subdural hemorrhage only. Twenty-two NCCT scans (22/25 [88%]) were performed within 6 hours of presentation. Seventeen NCCT scans (17/25 [68%]) were performed within 3 hours of presentation.

**CONCLUSION:** Despite frequent concerns for intracranial hemorrhage complicating acute stroke and treatment, a low percentage of patients had this complication. Moreover, our frequency is much lower than the wide ranges reported elsewhere. The most common type of intracranial hemorrhage in this cohort was intraparenchymal, but subarachnoid and subdural hemorrhages were also diagnosed and must also be considered. Twenty-eight percent of patients with initial suspicion of acute ischemic stroke are eventually given other diagnoses. These results may have implications for use of CT imaging.

Despite a large amount of clinical interest and numerous prior studies, it remains unclear how often patients with clinical acute stroke upon initial evaluation have intracranial hemorrhage on their screening head CT scan. According to the literature, intracra-

nial hemorrhage is associated with 10%–65% of strokes (1–7). Prior studies involve small numbers of patients, patients imaged as long as several days after ictus, and imaging performed before the widespread use of “modern” CT techniques such as multidetector arrays and soft-copy interpretation. Approximately 15% of these patients have clinical lacunar stroke syndromes with hemorrhage, affecting the basal ganglia, internal capsule, thalamus, and pons (8). As many as 20%–40% of patients suffer hemorrhagic transformation of ischemic infarct within 1 week of ictus (9), but these patients would not be considered within the acute stroke timeframe. Previous reports also cover a wide variety of stroke etiologies; for example, some previous studies include petechial hemorrhages, whereas others do not.

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In many urgent care settings, the initial evaluation of suspected stroke is performed with noncontrast head CT (NCCT; 10–13). The primary indication for performance of NCCT in this patient population is to “exclude intracranial hemorrhage.” (12) The conventional thinking and teaching is that NCCT is as sensitive as—if not more sensitive than—other radiologic methods (such as MR imaging sequences) used for the diagnosis of intracranial hemorrhage.

In this study, a large number of emergency department (ED) patients admitted to our hospital with suspected acute stroke were identified, and their initial (screening) NCCT results were evaluated for intracranial hemorrhage. Our aim was to determine, with reference to the literature, the frequency with which intracranial hemorrhage occurs in a large patient population, with modern CT techniques including performance and interpretation, and to maintain the study group to the early timeframe after presentation. We have included a large cohort in the hopes of reducing potential bias, eliminated petechial hemorrhages because neurologists at our hospital do not change treatment on the basis of that result, and limited the diagnosis of intracranial hemorrhage to the initial scan because this would be the examination on which the initial therapy would be based. We feel that these parameters make our study potentially superior to those previously published. As potential stroke interventions such as thrombolysis become more available and decisions regarding patient candidacy are based on initial imaging, we felt these issues were timely.

## Methods

### *Patient Demographics*

The study population included 691 subjects drawn from 733 consecutive patients admitted from the ED with clinical diagnosis of acute stroke during a 12-month period, a 5-month hiatus, and then a 17-month period. The data from the hiatus period were excluded because the service coordinator was unavailable and records were incomplete. Two additional patients were also excluded for incomplete records. Another 40 patients who received discharge diagnoses of transient ischemic attack (TIA) were considered separately, and are not included in this study; patients with TIA were excluded, because radiologic imaging in this patient cohort is believed to be variable. In all instances, the patient was seen by at least an ED attending physician and a neurology house staff officer assigned to the ED, and the admission diagnosis was based on their assessment as documented in the medical record.

### *CT Acquisition*

A routine head CT was performed without intravenous contrast on a GE scanner (General Electric, Waukesha, WI) with 5-mm contiguous axial sections: 140 kVp, 340 mAs, and 1-second scan time. Interpretations were performed after review of filmed images at standard window and level settings.

### *Data Review*

Hospital records were reviewed retrospectively to determine sex, age, triage date and time, admitting diagnosis, and discharge diagnosis. Primary discharge neurologic diagnoses taken from the medical record were used as the standard

against which the diagnostic results were compared; in instances with multiple diagnoses, stroke or lacunar stroke was considered to be the primary neurologic discharge diagnosis, if present. Radiology reports were reviewed for interpretations and to determine the timing of first NCCT (performed within 24 hours of presentation to the ED).

The exact time of CT scanning and the radiologist's signed reports indicating the scan findings were obtained from the IDX RAD V9.7.1 electronic radiologic record system maintained by the radiology department (IDX Systems Corporation, Burlington, VT). The reports were searched with a standard keyword subroutine (Folio; Camberly Systems, Cambridge, MA) for the words “hemorrhage,” “hemorrhagic” and “blood.” Patients with intracranial hemorrhage diagnosed following the first 48 hours were excluded to tailor the cohort to evaluation of acute stroke only and not complications of prolonged treatment or subacute stroke evolution. All candidate images were reviewed individually and unblinded to additional radiologic imaging examination findings or the final neurologic discharge diagnosis. Patients with only petechial hemorrhage were excluded, because our stroke service has indicated to us that treatment decisions would not be altered by the identification of this type of intracranial hemorrhage alone. All other patients with a report specifying intracranial hemorrhage were included in the cohort.

According to general convention in stroke imaging, presumed hypertensive hemorrhages were included in the cohort. Moreover, nonspecific intraparenchymal hemorrhages were also included. Patients with clear, noninfarct-related hemorrhage on initial imaging, such as arteriovenous malformation on CT scan or MR imaging or amyloid angiopathy on MR imaging, were also excluded.

### *Temporal Assignments*

Because, for most patients, a precise time of onset of symptoms cannot be confirmed, we chose the time of presentation to the ED as “time = 0” and calculated the interval from this time until diagnostic imaging.

## Results

Of the 691 patients enrolled (Table 1), 495 patients eventually had a primary neurologic discharge diagnosis of acute territorial stroke (495/691 [72%]). The second most common diagnosis was multisystem organ failure (36/691 [5%]). Intracranial hemorrhage ranked third, followed by lacunar stroke. None of the patients within the excluded group, with final discharge diagnosis of TIA had intracranial hemorrhage.

Twenty-five patients (25/691 [3.6%]) admitted to the hospital with suspected acute stroke were identified with intracranial hemorrhage on initial CT scan after presentation to the ED (Table 2). Initial NCCT was performed at a mean of 2 hours following presentation to the ED. Twenty-two examinations (22/25 [88%]) were performed within 6 hours of presentation. Seventeen examinations (17/25 [68%]) were performed within 3 hours of presentation. All patients were examined by initial NCCT before therapy with heparinization and thrombolysis.

Within the group of 25 patients with diagnosed hemorrhage, the mean patient age was 70 years. The youngest patient was 21 years of age, and the oldest was 91 years of age. There were 12 men and 13 women.

Twenty-three (23/25 [92%]) patients had intrapa-

**TABLE 1: Primary neurologic discharge diagnoses with incidence in group of 691 consecutive patients with admitting diagnosis of clinical acute stroke**

Primary Neurologic Discharge Diagnosis	Patients
Stroke	495
Multisystem organ disorder/failure	36
Intracranial hemorrhage	25
Lacunar stroke	24
Brain tumor	9
Weakness (not otherwise specified)	8
Cerebrovascular disease	8
Vertigo (idiopathic)	5
Vertebrobasilar syndrome	5
Gait disorder (not otherwise specified)	5
Encephalitis	5
Syncope (idiopathic)	4
Migraine	4
Labyrinthitis	4
Ataxia (idiopathic)	4
Psychiatric disturbance (DSM IV axis I)	3
Multiple sclerosis and/or optic neuritis	3
Head trauma (closed head injury)	3
Dehydration	3
Bell's palsy	3
Pneumonia	2
Peripheral neuropathy	2
Numbness (not otherwise specified)	2
Hypoglycemia	2
Dizziness (idiopathic)	2
Delirium	2
Confusion (not otherwise specified)	2
Atypical angina	2
Sepsis	1
Seizure	1
Speech abnormality (not otherwise specified)	1
Degenerative disease of the spine	1
Polyneuropathy	1
Overdose	1
Multi-infarct dementia	1
Myoclonus (not otherwise specified)	1
Meningitis	1
Lyme disease	1
Hydrocephalus	1
Congestive heart failure	1
Headache (idiopathic)	1
Gastrointestinal bleed	1
Failure to thrive	1
Dysequilibrium (idiopathic)	1
Cerebral infarction with transient symptoms	1
Cholecystitis	1
Amnesia	1
Total	691

renchymal hemorrhage only. One patient (1/25 [4%]) had a combination of intraparenchymal and subarachnoid hemorrhage. One patient (1/25 [4%]) had subdural hemorrhage only.

In patients with intracranial hemorrhage (Table 2), 23 (23/25 [92%]) had normal coagulation profiles, one patient (1/25 [4%]) was being treated with warfarin, 16 (16/25 [64%]) were being treated with aspirin (doses variable from 81 mg to >325 mg per day by mouth), and no patients were on any other antiplatelet medications. Ten patients (10/25 [40%]) were

thought to have embolic stroke with hemorrhage on the basis of imaging results and all available clinical data from before, during, and after acute presentation.

## Discussion

### *Discussion of Findings*

This cohort represents the largest evaluated for hemorrhage complicating acute stroke. Moreover, the cohort is more homogeneous than those in previous communications, with patients diagnosed with TIA considered separately. The timing of imaging was more realistic for the evaluation of hemorrhage complicating acute stroke—that is, imaging within the initial 24 hours is considered, whereas some previous studies report cohorts based on the first 7 days.

Our results support that approximately 72% of patients with suspected acute territorial stroke, on the basis of clinical criteria in the ED, eventually are confirmed to have that diagnosis by the time of discharge from the hospital. Thus, 28% of patients suspected of clinical stroke at first evaluation are not proved to have a diagnosis of ischemic territorial infarct as their primary diagnosis. Although intracranial hemorrhage is one of the contributors, many other diagnoses may function as stroke mimics (Table 1). Our results have implications for the radiologist assigned the task of performing and interpreting these initial examinations. More specifically, many other disease processes may be seen in this setting, including infection, inflammation, and brain tumor. Clinical history may improve the interpretive process (14). Moreover, these findings may have implications for use of resources, especially imaging modalities, by ED staff.

Despite the frequently illustrated concern for intracranial hemorrhage in the patient with suspected stroke, intracranial hemorrhage remained a rare (3.6%) complication of the acute time period, and our results support the assertion that the actual value is likely much lower than those previously and frequently quoted (that is, 15%, with a range of 10%–65%; 5). Only one patient in 691 (0.14%) was diagnosed with subarachnoid hemorrhage, and that patient also had an intraparenchymal hemorrhage, putatively the source of the subarachnoid blood. An additional patient (0.14%) had subdural hemorrhage only.

The most common type of intracranial hemorrhage in this cohort was intraparenchymal. Primary, or intraparenchymal, intracranial hemorrhage in a patient with appropriate symptoms is considered a stroke subtype (15). This type would be the most ominous and potentially devastating if undiagnosed before therapy with anticoagulation or thrombolysis. Intracranial hemorrhage remains difficult to diagnose without appropriate imaging, but certain clinical scores have shown promise (15–18).

**TABLE 2: Results from 691 consecutive patients with acute stroke and intracranial hemorrhage on initial computed tomography scan**

Patient No./ Sex/Age (y)	Time (h:min)*	Type	Embolic	Character and Etiology of Infarct <sup>†</sup>
1/F/21	1:40	IPH	Yes	HI
2/M/49	1:16	IPH	No	Hypertensive HI
3/M/52	1:08	IPH	No	Hypertensive HI
4/M/56	3:47	IPH	No	Hypertensive HI
5/F/58	1:36	IPH	Yes	HI
6/F/61	5:06	IPH	Yes	Septic emboli with HI
7/F/61	2:24	SAH, IPH	Yes	Lung cancer with hemorrhagic metastasis and separate infarct
8/M/66	0:48	IPH	No	Coagulopathy related to CLL with HI
9/M/68	6:30	IPH	Yes	HI
10/F/68	2:37	IPH	No	Hypertensive HI
11/F/70	0:55	IPH	No	Coagulopathy (anticoagulation)
12/M/70	2:00	IPH	Yes	HI
13/M/71	1:16	IPH	Unlikely	NED
14/F/74	6:46	IPH	Yes	HI
15/M/74	14:32	IPH	Yes	HI
16/M/76	1:52	IPH	Yes	HI
17/F/81	3:07	IPH	No	Amyloid angiopathy
18/F/82	0:29	IPH	No	Hypertensive HI
19/F/84	3:21	IPH	No	Hypertensive HI or vascular
20/F/84	1:27	IPH	No	Hypertensive HI
21/F/86	1:22	IPH	No	NED
22/F/88	1:54	IPH	Yes	HI
23/M/88	1:15	IPH	No	Hypertensive HI
24/M/88	1:23	IPH	Unlikely	NED
25/M/91	3:03	SDH	Unknown	NED

Note.—No patient in this group had a lacunar stroke. CLL indicates chronic lymphoid leukemia; IPH, intraparenchymal hemorrhage; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage; HI, hemorrhagic infarct; NED, no etiology determined despite follow-up.

\* Computed tomography time after presentation to the emergency department.

† Comments on the character of the infarct and the most likely etiology based on imaging characteristics and clinical and follow-up data.

### Discussion of NCCT and Stroke Mimics

Additional controversies remain regarding the rate of hemorrhagic stroke and rate of hemorrhagic stroke mimics in patients with suspected acute stroke (19, 20). This information is salient to the individualized course of treatment that each patient is offered based on clinical and imaging findings (21). For example, Motto et al reported in 1999 that on CT scanning, cerebral edema and extraparenchymal but not intraparenchymal hemorrhage was independently associated with unfavorable outcome (22). The information is also time-sensitive, in that the window of opportunity is typically narrow to begin thrombolysis (23), anticoagulation, or neuroprotective agent administration. Bonaffini et al point out that while CT may have a sensitivity as high as 100% for intracranial hemorrhage, that it remains relatively poor in determining ischemic injury in the early hours after symptom onset, possibly delaying therapeutics (24).

Molina et al reported that as many as 90% of patients with cardioembolic stroke have hemorrhages within the initial week postictus (4). Lyden and Zivin reviewed the literature in 1993 and determined that animal and clinical human data supported the hypothesis that hemorrhagic infarct occurs in relation to augmented collateral circulation into the ischemic tissue area, possibly in association with hypertension (2). In 2001, Molina et al found that delayed recanalization after 6 hours postictus was an independent

predictor of hemorrhagic transformation (4). In addition, Smith et al reported in 2002 that leukoariosis was independently associated with hemorrhage following warfarin treatment for stroke (25). In 1989, Okada et al reported that the incidence of hemorrhagic infarction increased with age and was highest for those patients 70 years of age and older and in large infarct size (1). Furthermore, they found that in 160 patients thrombolytic and/or anticoagulant therapy did not increase the rate of intracranial hemorrhage but did result in massive hemorrhage when bleeding occurred (1). In 2002, Obajimi et al reported that spontaneous intracranial hemorrhagic stroke is highest in Ghanaians (at 52.9% of 1172 patients studied; 7). In their large cohort, intraparenchymal hemorrhage encompassed 83.6%, and subarachnoid hemorrhage was found in 8.1% (7).

### Discussion of the Incidence of Nonintraparenchymal Hemorrhage

In 2001, van Gijn and Rinkel reviewed the literature and determined that the incidence of subarachnoid hemorrhage is approximately 6 cases per 100,000 patient years, with similar risk factors to stroke and etiologies composed of ruptured aneurysm (85%), nonaneurysmal perimesencephalic hemorrhage (10%), and other rare causes, including stroke (5%; 26).

Notwithstanding the issue of delaying or obviating

treatment with anticoagulants and thrombolytics, several types of intracranial hemorrhage may be identified in stroke patients and what if any prognostic value this holds remains unclear. Motto et al described 4 primary types of intraparenchymal hemorrhage that possibly relate to clinical outcome and are used to communicate a description: type I (petechial), type II (medium-sized, high attenuation, within an infarct area), type III (large-sized, high attenuation, encompassing an infarct area), and type IV (large-sized, high attenuation, exceeding an infarct area) (3). In 2001, Berger et al reported that, in 790 patients, parenchymal hematoma only resulted in clinical deterioration and worsened prognosis if it encompassed >30% of the infarct volume, was attenuated and homogeneous on CT scan, and had significant volume and mass effect (27).

### Limitations

Our study has limitations, including its retrospective design. We have based our results on the signed radiologic reports. This may introduce bias if findings were identified by the radiologists interpreting the examination but not communicated in the report. We have limited hemorrhage diagnosis to the initial 24 hours, whereas it is possible that more patients with hemorrhagic complication may be identified later in their course. We have limited the scope of this surveillance to facilitate a useful and manageable period of time in acute stroke. The study was not designed to evaluate the sensitivity of NCCT for hemorrhage, and thus patients with hemorrhage not identified on radiologic imaging or on discharge summaries during their admission to the hospital were not identified. It is our impression that these instances would be few if any but could theoretically increase the number of patients with intracranial hemorrhage. Patients were obtained from those admitted to the hospital and not all patients presenting to the ED or on the patient care floors with suspected stroke. Thus, the group is biased toward more serious findings, including hemorrhage. It is likely then that the actual rate of intracranial hemorrhage in the population at large is even lower than that reported herein. Also, the distribution of intracranial hemorrhage may be biased. It is our impression that patients with subarachnoid and extra-axial hemorrhage typically present with a different constellation of findings than do patients with stroke—for example, worst headache of life versus aphasia. We have included presumed embolic infarcts, lacunar infarcts, and hypertensive hemorrhages by convention, and, although this may introduce potential bias in terms of heterogeneity of etiologies, we feel that the design more closely mirrors actual practice, when a radiologist is faced with a patient with clinical stroke and the object is to diagnose intracranial hemorrhage on the initial examination. Finally, patients who were eventually diagnosed with TIA were excluded, which is typical and by convention; none of these patients had intracranial hemorrhage and the final hemorrhage prevalence would

be smaller if these patients were included within the patient group.

### Summary

In summary, frequent clinical concerns to avoid the potentially serious adverse consequences of stroke therapy or delay to accurate diagnosis, especially for intraparenchymal hemorrhage, remain. The prevalence of intracranial hemorrhage in this patient cohort, however, was much lower than the previously reported, varied results within the literature. Moreover, the prevalence of subarachnoid hemorrhage was particularly and remarkably low. Our data support the conclusion that, although 72% of patients with initially suspected ischemic acute stroke eventually are given that diagnosis, 28% are not and suffer a wide variety of alternative diagnoses that function effectively as stroke mimics. This result may have implications for radiologists interpreting screening examinations for these patients in the emergency setting and for ED use as well. Our study represents the largest reported to date, most homogeneous and most homogeneously imaged early after stroke onset, most modern, most closely approximating the typical day-to-day acute practice and, in contradistinction to other studies, is most closely addressed to the time period that is most closely aligned with treatment decision making.

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