Diagnostic Accuracy and Yield of Multidetector CT Angiography in the Evaluation of Spontaneous Intraparenchymal Cerebral Hemorrhage

BACKGROUND AND PURPOSE: Multidetector CT angiography (MDCTA) is emerging as the favored initial diagnostic examination in the evaluation of patients presenting with spontaneous intraparenchymal hemorrhage (IPH). This study aims to evaluate the diagnostic accuracy and yield of MDCTA for the detection of vascular etiologies in adult patients presenting to the emergency department with IPH.

MATERIALS AND METHODS: We conducted a retrospective study of 623 consecutive adult patients presenting to the emergency department with IPH, who were evaluated with MDCTA during a 9-year period. CT angiograms were reviewed by 2 neuroradiologists to determine the IPH site and the presence of a vascular etiology. Patients with associated subarachnoid hemorrhage in the basal cisterns were excluded from the study. Medical records were reviewed for risk factors and correlation with final diagnosis. The diagnostic accuracy of MDCTA compared with conventional angiography, intraoperative evaluation, and pathologic findings was determined, when available. Multiple-variable logistic regression analysis was performed to determine clinical and radiologic factors that predict a higher yield of MDCTA.

RESULTS: MDCTA demonstrated a vascular etiology in 91 patients (14.6%), with a sensitivity of 96%, specificity of 99%, and diagnostic accuracy of 98%. We found independent, statistically significant higher yields of MDCTA in patients with the following characteristics: 1) age younger than 46 years (47%); 2) lobar (20%) or infratentorial (16%) IPH, especially lobar IPH with associated intraventricular hemorrhage (25%); 3) female sex (18%); or 4) neither known hypertension nor impaired coagulation at presentation (33%).

CONCLUSIONS: MDCTA is an accurate diagnostic examination in the evaluation of adult patients presenting with spontaneous IPH and should be performed in all patients with the aforementioned clinical and radiologic characteristics.

Spontaneous, nontraumatic intraparenchymal cerebral hemorrhage (IPH) accounts for 10%–15% of cases of acute stroke.1 Although most spontaneous IPHs are caused by hypertension, amyloid angiopathy, or impaired coagulation, many are also caused by vascular lesions such as arteriovenous malformations (AVMs), ruptured intracranial aneurysms, and dural venous sinus thromboses.1-2 Accurate identification of a vascular lesion as the IPH cause is important because these have a high rate of rehemorrhage, with further increased morbidity and mortality, and are potentially treatable.1,2,4-6 Prior studies have identified clinical and noncontrast CT (NCCT) features that increase the likelihood of identifying a vascular etiology with conventional angiography: age younger than 40–50 years,7-10 absence of pre-existing hypertension,7,11,12 presence of associated subarachnoid hemorrhage (SAH) or intraventricular hemorrhage (IVH),8,10,12,14 and temporal or frontal lobe location.8,13 However, Halpin et al15 found vascular abnormalities with conventional angiography in 24% of patients deemed unlikely to have positive findings on angiography based on NCCT features alone, 13% of hypertensive patients, 31% of patients with basal ganglia hemorrhage, and 18% of patients with posterior fossa hemorrhage and, thus, recommended performing conventional catheter angiography in all patients presenting with nontraumatic intraparenchymal hemorrhage. Similarly, Matsumoto et al16 found coexisting unruptured intracranial aneurysms with conventional angiography in 21% of women and 9% of men presenting with hypertensive intracerebral hemorrhage and, thus, recommended performing angiographic investigations in all of these patients, particularly women.

As a result of its increasing availability, rapidity of acquisition, lower cost, favorable risk profile compared with conventional angiography, and diagnostic accuracy for the detection of vascular lesions,17-21 multidetector CT angiography (MDCTA) is emerging as the favored initial diagnostic examination in the evaluation of patients presenting with spontaneous IPH in the emergency department. This study aims to evaluate the diagnostic accuracy and yield of MDCTA for the detection of vascular etiologies in adult patients presenting to the emergency department with spontaneous IPH.

Materials and Methods

Patient Selection

Our study was approved by the institutional review board of the hospital and conducted with Health Insurance Portability and Accountability Act compliance. We conducted a retrospective study of all
consecutive patients who presented to our emergency department from January 1, 2000, until November 1, 2008, with the following inclusion criteria: 1) \( \geq \)18 years of age, 2) evidence of spontaneous IPH on an NCCT examination of the head, and 3) evaluation with a CT angiogram (CTA) of the intracranial circulation within 24 hours of presentation. Patient exclusion criteria were the presence of the following: 1) associated SAH in the basal cisterns, 2) loss of gray-white matter differentiation in a vascular territory suggesting a pre-established acute ischemic stroke, 3) a known intracranial vascular abnormality or mass lesion, or 4) known probable cerebral amyloid angiopathy according to the Boston criteria.  

**Image Acquisition**

NCCT and MDCTA acquisitions were performed according to standard protocols on 16- or 64-section helical CT scanners (LightSpeed; GE Healthcare, Waukesha, Wis). NCCT was performed in a head holder by using an axial technique with 120–140 kilovolt (peak), 170 mA, 2-second scanning time, and 5-mm section-thickness reconstruction. MDCTA was subsequently performed by scanning from the base of the C1 vertebral body to the vertex using the following parameters: pitch, 0.5; collimation, 1.25 mm; maximal mA, 350; kilovolt (peak), 120; FOV, 22 cm; and 65 to 85 mL of nonionic contrast material administered by power injector at 4–5 mL per second into an antecubital vein with either a fixed 25-second delay between the onset of contrast injection and the start of scanning (the delay was increased to 40 seconds in patients with atrial fibrillation), or SmartPrep software, an automatic contrast bolus triggering technique (GE Healthcare). The resulting 1.25-mm-thick axial source images were digitally archived. Standard maximum intensity projection (MIP) images of the major intracranial vessels were created by the 3D laboratory.

**Image Analysis**

The NCCTs were reviewed by 2 neuroradiologists blinded to the clinical data and final diagnosis to determine, by consensus reading, the following: 1) the IPH location (categorized as lobar, deep gray matter, or infratentorial), 2) the presence of associated IVH or SAH, and 3) the probability of an underlying vascular etiology for the IPH (categorized as low, high, or indeterminate). At least 2 weeks after review of the NCCT, the CTA source and MIP images were reviewed by the same 2 neuroradiologists blinded to the NCCT categorization, clinical data, and final diagnosis, to determine, by consensus reading, the presence of an underlying vascular etiology for the IPH.

A “high-probability” NCCT was defined as an examination in which either enlarged vessels and/or a filling defect with associated calcifications along the margins of the IPH or hyperattenuation within a major dural venous sinus and/or a cortical vein potentially draining the region of the IPH was identified. A “low-probability” NCCT was defined as an examination in which none of the findings of a high-probability NCCT were present and the IPH was located within the deep gray matter or pons. An “indeterminate” NCCT was defined as an examination in which the findings of neither a high- nor low-probability NCCT were identified.

A “positive” CTA was defined as a study in which an underlying vascular etiology for the IPH was identified. For the diagnosis of dural venous sinus and/or cortical vein thrombosis, nonopacification of the affected venous structure on the first-pass CTA was confirmed by either persistent nonopacification on delayed images (if obtained) and/or corresponding hyperattenuation in the NCCT.

**Medical Record Review**

Medical records were reviewed for patient age, sex, presence of known hypertension, impaired coagulation, and history of recent cocaine use. Given that prior studies have found significant differences in the yield of conventional angiography according to patient age, 7-10 we divided our patient population into 3 groups according to age: group 1, patients 18–45 years of age; group 2, patients 46–70 years of age; and group 3, patients 71 years of age and older.

Patients were classified as hypertensive if they had a history of hypertension on medical records or were taking antihypertensive medications at presentation. Patients were classified as having impaired coagulation if, at presentation, they were receiving daily antiplatelet therapy with aspirin (at least 81 mg) and/or clopidogrel, 23 had a platelet count of <50,000 cells per cubic millimeter of blood, were on anticoagulation with warfarin and had an international normalized ratio >3.0, 24 or were on anticoagulation with heparin and had an activated partial thromboplastin time of >80 seconds.
Correlation was made with reports of subsequent conventional angiography and MR imaging examinations, as well as surgical and pathologic findings, to establish a final diagnosis. The reports of subsequent conventional angiography examinations and intraoperative and pathologic findings were defined as gold standards for the purpose of evaluation of the diagnostic accuracy of MDCTA. In cases in which no confirmatory examination was performed, if a vascular etiology was identified on the CTA, it was considered the final diagnosis—however, these examinations were not included in the evaluation of diagnostic accuracy.

Statistical Analysis
Statistical analysis was performed utilizing the SAS 9.1 software package (SAS Institute, Cary, NC). After performing univariate statistical analysis using the Pearson $\chi^2$ test, we constructed a multiple variable logistic regression model to determine the correlation of patient age, sex, known hypertension, impaired coagulation, IPH location, and presence of associated IVH, with the identification of a vascular etiology on MDCTA for all patients in the population, the 3 IPH locations separately, and the 3 different age groups separately. A $P$ value $\leq.05$ was considered statistically significant. We calculated standard parameters of diagnostic accuracy for MDCTA compared with defined gold standards along with 95% confidence intervals.

Results
From January 1, 2000 until November 1, 2008, a total of 775 adult patients presented to our emergency department with IPH on an NCCT examination and were evaluated with MDCTA of the intracranial circulation within 24 hours of presentation. One hundred fifty-two patients were excluded from the study (19.6%): 91 due to the presence of associated SAH.
within the basal cisterns, 74 of whom had an underlying vascular etiology (81%); 36 due to the presence of a known vascular or mass lesion; 14 due to loss of gray-white matter differentiation in a vascular territory suggesting a pre-established acute ischemic stroke; and 11 due to known amyloid angiopathy. Hence, a total of 623 patients met the inclusion criteria of our study, with a mean age of 65 years (range, 18–94 years), 335 of whom were men (53.8%) and 288 women (46.2%).

NCCT Examination Categorization and Comparison with Final Diagnosis
Of the 623 NCCTs, 183 were categorized as low-probability for the presence of an underlying vascular etiology (29.4%), 172 due to deep gray matter and 11 due to pontine IPH location) and 19 were categorized as high probability for the presence of an underlying vascular etiology (3%, 8 due to enlarged vessels and/or filling defects with associated calcification along the margins of the IPH and 11 due to hyperattenuation within a dural venous sinus and/or cortical vein overlying the IPH). The remaining 421 NCCTs were categorized as indeterminate for the presence of an underlying vascular etiology (67.6%). Of the 183 low-probability NCCT examinations, 179 were true-negative and 4 were false-negative (1 pontine, 1 thalamic and 2 basal ganglia AVMs). Of the 19 high-probability NCCT examinations, 16 were true-positive and 3 were false-positive. Hence, for the prediction of a vascular etiology for the IPH, high- and low-probability NCCT examinations demonstrated a positive predictive value of 84.2% and a negative predictive value of 93.7%.
value of 97.8%, respectively. However, 72 of the 421 indeterminate NCCTs had an underlying vascular etiology for the IPH (17.1%).

CTA Examination Categorization and Diagnostic Accuracy Compared with Gold Standards

A total of 91 CTAs were categorized as positive for the presence of an underlying vascular etiology for the IPH (14.6%), with the following diagnoses: 40 AVMs (43.9%, Figs 1 and 2), 18 saccular aneurysms with intraparenchymal rupture (19.8%; mean maximum aneurysm sac size, 9.1 mm; range, 5–14 mm, Fig 3), 17 dural venous sinus and/or cortical vein thromboses (18.7%, Fig 4), 8 arteriovenous fistulas (AVFs, 8.8%), 3 pseudoaneurysms (3.3%), 3 cases of vasculitis (3.3%, Fig 5), and 2 cases of Moyamoya disease (2.2%). All patients with false-negative CTAs were younger than 46 years of age, normotensive, and had normal coagulation. One of the false-positive CTAs was interpreted as demonstrating an AVM that was not demonstrated at conventional angiography and was found to be a cavernous malformation with an associated developmental venous anomaly on a subsequent MR imaging examination. The second false-positive CTA was interpreted as demonstrating an AVF overlying the IPH; however, no arteriovenous shunting was demonstrated at conventional angiography, and the enlarged cortical vein was considered to be a normal variant.

Clinical and Radiologic Predictors of a Positive CTA Examination

The results of univariate and multiple variable logistic regression analysis for the diagnostic yield of MDCTA in the entire patient population, patients with lobar IPH, and the 3 different patient age groups are summarized in Tables 2–4, respectively. For infratentorial and deep gray matter IPH, no independent, statistically-significant differences among patients with different characteristics were found. Patients with IPH

### Table 1: Diagnostic accuracy of multidetector CT angiography in IPH

| Findings                  | Confirmed Vascular Lesion* | Confirmed No Vascular Lesion | Total |
|---------------------------|----------------------------|-----------------------------|-------|
| Positive CTA              | 73                         | 2                           | 75    |
| Negative CTA              | 3                          | 132                         | 135   |
| Total                     | 76                         | 134                         | 210   |
| Sensitivity               | 96.1% (89.1%–99.0%)†        |                             |       |
| Specificity               | 98.5% (94.2%–99.7%)†        |                             |       |
| Accuracy                  | 97.6%                      |                             |       |
| PPV                       | 97.3% (89.8%–99.5%)†        |                             |       |
| NPV                       | 97.8% (93.2%–99.4%)†        |                             |       |

Note:—PPV indicates positive predictive value; NPV, negative predictive value; IPH, intraparenchymal hemorrhage; CTA, CT angiography.

* Fifty-one vascular lesions were confirmed by conventional angiography, 54 during direct surgical evaluation of the hematoma cavity and pathologic evaluation of the surgical specimen and 4 at postmortem examination (33 vascular lesions were confirmed by >1 type of examination but counted only once for the purpose of this analysis).

† 95% confidence interval.
and 1) less than 46 years of age (47%), 2) lobar (20%) or infratentorial (16%) IPH location, especially lobar IPH with associated IVH (25%), 3) female sex (18%), or 4) neither hypertension nor impaired coagulation at presentation (33%), had independent, statistically significant higher incidences of vascular etiologies on MDCTA compared to patients without these characteristics (Table 5). Among cases of lobar IPH, those limited to either the parietal (30%) or temporal (29%) lobes had higher incidences of vascular etiologies than IPHs affecting other lobes or >1 lobe. Importantly, patients younger than 46 years of age with infratentorial (67%) or lobar (58%) IPH, with neither hypertension nor impaired coagulation (65%), or female sex (63%) had particularly high incidences of vascular etiologies on MDCTA.

### Summary of Final IPH Etiologies in the Patient Population

In our population of 623 patients presenting to the emergency department, there were a total of 92 patients with a vascular etiology for the IPH (14.8%; mean age, 48 years; range, 18–83 years), 89 of whom were identified on MDCTA (96.7%). Hence, there were 531 patients without a vascular etiology for the IPH (85.2%; mean age, 68 years; range, 18–94 years), 300 of whom underwent subsequent MR imaging (56.5%). Two hundred twenty-three of these MR examinations were negative (74.3%). The remaining MR examinations demonstrated evidence of probable amyloid angiopathy according to the Boston criteria in 47 patients (all with lobar hemorrhage), hemorrhagic cavernous malformations in 12 patients, brain tumors in 11 patients (6 primary and 5 metastatic), septic emboli secondary to bacterial endocarditis in 6 patients, and posterior reversible encephalopathy syndrome in 1 patient. In addition, pathologic examinations demonstrated evidence of amyloid angiopathy in 12 patients, hemorrhagic cavernous malformations in 4 patients, septic emboli in 2 patients, metastases in 2 patients, and a small distal embolic hemorrhagic infarction in 1 patient. A history of recent cocaine use was elicited in 12 patients, 4 of whom had positive CTAs and 1 who had a hemorrhagic cavernous malformation.

Overall, evidence of amyloid angiopathy was demonstrated in 59 of the 221 patients with lobar IPH and no vascular etiology who underwent either subsequent MR imaging and/or pathologic examination (26.7%), with a mean age of 76 years (range, 62–94 years). In addition, the mean age of patients with hemorrhagic cavernous malformations was 44 years (range, 18–77 years) and of those with brain tumors was 59 years (range, 34–76 years).

### Discussion

In our patient population, a vascular etiology for the IPH was identified in 14.8% of patients, which is lower than reported in previous conventional angiography studies, which ranged from 27.5 to 52.5%. This is likely due to the older mean age in our patient population (65 years), compared with...
male sex, age, known HTN, and impaired coagulation were independent risk factors for IPH. The sensitivity of the NCCT for the prediction of an underlying vascular abnormality was lower in patients aged 71–94 years (98%), but the specificity was similar in all age groups (99%).

The diagnostic yield of MDCTA in different age groups is shown in Table 4. The positive predictive value of CTA was 5.7% in patients aged 46–70 years and 2.3% in those aged 71–94 years. These findings suggest that MDCTA is a useful screening examination for patients aged 46–70 years but may have limited utility in older patients.

Table 5 summarizes the independent clinical and radiologic predictors of a higher yield of MDCTA in IPH. Age less than 46 years, female sex, history of stroke, and absence of IVH were significantly associated with a higher diagnostic yield of MDCTA. These findings suggest that younger patients with a history of stroke and absence of IVH are more likely to benefit from MDCTA evaluation.

In conclusion, the diagnostic yield of MDCTA in patients with IPH is age-related, with higher sensitivity in younger patients. Age, sex, history of stroke, and absence of IVH are important clinical predictors of a higher diagnostic yield of MDCTA.

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Thus, only 65 patients in this group had neither clinical nor MR imaging findings to explain the IPH (16.3%).

We identified patients with clinical and radiologic characteristics that predict a higher yield of MDCTA for the presence of an underlying vascular etiology for the IPH (Table 5). Our results are similar to those of most prior conventional angiography studies, in which yields of 50%–89% in patients younger than 40–50 years,7-9,10,15 significant differences in the yield of conventional angiography for different IPH locations,7-15 increased prevalence of aneurysms in women,16 and lower angiographic yields in patients with hypertension and/or impaired coagulation are reported.7,8,11,14,15 Given the relatively lower sensitivity of MDCTA for the detection of small vascular lesions, patients with these clinical and radiologic characteristics who have a negative initial CTA should undergo conventional angiography to exclude a small vascular lesion as the IPH etiology.

Evidence of amyloid angiopathy was demonstrated in 27% of patients with lobar IPH and no vascular etiology who underwent either subsequent MR imaging and/or pathologic examination, with a mean age of 76 years. These results are similar to those reported in prior studies, in which cerebral amyloid angiopathy has been associated with 20%–75% of lobar IPHs in older patients.22,25-27 In addition, hemorrhagic cavernous malformations and brain tumors were found, on average, in patients 21 and 6 years younger than the average patient in our study, respectively—though these were distributed over a broad age range. Hence, if the initial CTA examination is negative, a contrast-enhanced MR imaging examination with a gradient-echo susceptibility sequence should be performed to evaluate for amyloid angiopathy and brain tumors in older patients, and for cavernous malformations and brain tumors in younger patients.

The limitations of our study are its retrospective nature, the inclusion of only patients who presented with IPH and were evaluated with MDCTA (patients who, on clinical grounds, may have been deemed less likely to harbor an underlying vascular etiology for the IPH may not have undergone MDCTA), and the presence of a selection bias in the performance of gold standard examinations following MDCTA (these were performed with higher frequency in patients with positive CTAs compared to patients with negative CTAs). Thus, the overall diagnostic yield and sensitivity of MDCTA in adult patients with spontaneous IPH may be lower than the results reported in this study.

**Conclusions**

MDCTA is an accurate diagnostic technique for the evaluation of adult patients presenting to the emergency department with spontaneous IPH, demonstrating a vascular etiology in 14.6% of patients. MDCTA has high diagnostic yields in patients with the following: 1) a high probability NCCT (84%); 2) age younger than 46 years (47%), particularly young women (63%); 3) lobar (20%) or infratentorial (16%) IPH location, especially in lobar IPH involving either the parietal (30%) or temporal (29%) lobes and lobar IPH with associated IVH (25%); 4) female sex (18%); or 5) neither known hypertension nor impaired coagulation at presentation (33%). Given these
findings, we recommend that MDCTA be performed in all patients within these subgroups. For cases of deep gray matter IPH and patients with other clinical characteristics, the decision to perform MDCTA should be based on the clinical assessment.

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