Computed tomography angiography: improving diagnostic yield and cost effectiveness in the initial evaluation of spontaneous nonsubarachnoid intracerebral hemorrhage

Clinical article

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Object. Computed tomography angiography (CTA) is increasingly used as a screening tool in the investigation of spontaneous intracerebral hemorrhage (ICH). However, CTA carries additional costs and risks, necessitating its judicious use. The authors hypothesized that subsets of patients with nontraumatic, nonsubarachnoid ICH are unlikely to benefit from CTA as part of the diagnostic workup and that particular patient risk factors may be used to increase the yield of CTA in the detection of vascular sources.

Methods. The authors performed a retrospective analysis of 1376 patients admitted to Dartmouth-Hitchcock Medical Center with ICH over an 8-year period. Patients with subarachnoid hemorrhage, hemorrhagic conversion of ischemic infarcts, trauma, and known prior malignancy were excluded from the analysis, resulting in 257 patients for final analysis. Records were reviewed for medical risk factors, hemorrhage location, and correlation of CTA findings with final diagnosis. Multiple logistic regression analysis was used to investigate the combined effects of baseline variables of interest. Model selection was conducted using the stepwise method with p = 0.10 as the significance level for variable entry and p = 0.05 the significance level for variable retention.

Results. Computed tomography angiography studies detected vascular pathology in 34 patients (13.2%). Patient characteristics that were associated with a significantly higher likelihood of identifying a structural vascular lesion as the source of hemorrhage included patient age younger than 65 years (OR = 16.36, p = 0.0039), female sex (OR = 14.9, p = 0.0126), nonsmokers (OR = 103.8, p = 0.0008), patients with intraventricular hemorrhage (OR = 9.42, p = 0.0379), and patients without hypertension (OR = 515.78, p < 0.0001). Patients who were older than 65 years of age, with a history of hypertension, and hemorrhage located in the cerebellum or basal ganglia were never found to have an identified structural source of hemorrhage on CTA.

Conclusions. Patient characteristics and risk factors are important considerations when ordering diagnostic tests in the workup of nonsubarachnoid, nontraumatic spontaneous ICH. Although CTA is an accurate diagnostic examination, it can usually be omitted in the workup of patients with the described characteristics. The use of this algorithm has the potential to increase the yield, and thus the safety and cost effectiveness, of this diagnostic tool.

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Key Words • computed tomography angiography • diagnostic yield • intracerebral hemorrhage • arteriovenous malformation • vascular disorders

Abbreviations used in this paper: AVM = arteriovenous malformation; CTA = computed tomography angiography; DSA = digital subtraction angiography; ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage.
as a screening tool. It is less invasive, can be performed rapidly, and has a lower stroke risk than DSA.\(^6\)\(^\text{13}\) On the other hand, CTA exposes patients to additional radiation, as well as risks including contrast-induced nephropathy, allergic reactions, and even death.\(^4\) Therefore, it is important to optimize the screening yield of CTA in isolated ICH. In addition, in the current setting of rationalization of health care costs, improving the yield and cost effectiveness of this diagnostic tool could decrease unnecessary expenses in patients with ICH, without compromising their health outcomes.

In the current study, we attempted to identify patients who do not benefit from CTA as part of an initial screening and quantify risk factors that could be used to increase the yield of CTA in the detection of vascular sources in patients with nontraumatic, nonsubarachnoid ICH.

**Methods**

**Study Population**

Radiological, diagnosis-related group, and operative procedure codes were used to identify patients admitted to Dartmouth-Hitchcock Medical Center between January 1, 2000, and September 1, 2008, with the diagnosis of ICH. Exclusion criteria included patients with SAH, antecedent history of trauma, hemorrhagic conversion of infarct, or hemorrhage in the setting of a known brain tumor. The patients were selected by 2 independent investigators, and in case of disagreement, a third investigator was used.

**Outcome Variables**

For those meeting inclusion criteria, medical records were reviewed and the following parameters were collected: age, sex, location of hemorrhage, presence of the following conditions (hypertension, hypercholesterolemia, diabetes mellitus, atrial fibrillation, coronary artery disease, cerebrovascular disease), smoking history, and impaired coagulation. Patients were considered hypertensive if they had a history of hypertension on medical records or were taking antihypertensive medications at the time of presentation. Patients were classified as having impaired coagulation at presentation if they were receiving daily aspirin or antiplatelet agents, had a platelet count of less than 50,000 cells per cubic millimeter of blood, were receiving anticoagulation therapy using warfarin and had an international normalized ratio greater than 2.0, or were receiving anticoagulation therapy using heparin and had an activated partial thromboplastin time of more than 80 seconds. Positive CTA was defined as a study in which an underlying vascular origin for the ICH was identified. These results were correlated with the results of conventional angiography, MRI, and pathology when available.

**Imaging Specifications**

Computed tomography and CTA were performed on 16- or 64-section helical CT scanners (Lightspeed or Lightspeed VCT, GE Healthcare). Noncontrast head CT was performed using axial acquisition with image sets produced at 5 mm and 1.5 mm. Computed tomography angiography was performed with helical acquisition of 0.625-mm slice thickness and spacing, at 120 kV, and a 20-cm FOV. During the intravenous injection of 65–110 ml of nonionic contrast material at 4–5 ml/sec, images were acquired from the foramen magnum to the cranial vertex. Scan delay was determined using a timing bolus. Image processing consisted of standard axial, coronal, and sagittal multiplanar volume-reformatted images and 3D volume-rendered reconstructions using an Advantage Workstation with Volume Viewer software (GE Healthcare). Physicians interpreting the 3D images could manipulate them.

**Statistical Analysis**

Chi-square tests were used to investigate the association of categorical baseline variables of interest with CTA. Logistic regression was used to investigate the combined effects of baseline variables of interest. Model selection was performed using the stepwise method as implemented in SAS, with a significance level of p = 0.10 for variable entry and p = 0.05 for variable retention.

**Results**

**Demographics**

From January 1, 2000, to September 1, 2008, 1,376 patients at our institution underwent head CT that demonstrated ICH. Of those patients, 514 underwent further investigation using CTA. Two hundred fifty-seven patients were excluded from the analysis based on the predefined exclusion criteria: SAH (219 patients), antecedent history of trauma (23 patients), hemorrhagic conversion of an infarct (5 patients), or hemorrhage in the setting of a known brain tumor (10 patients). Two hundred fifty-seven patients remained for analysis, with a mean age of 66.1 years (range 9–93 years); 51% of the patients were men.

**Negative CTA for Source of Hemorrhage**

Two hundred twenty-three patients had a negative CT angiogram in the initial evaluation of the cause of ICH (Table 1). These patients had a mean age of 67.9 years (range 30–93 years) and 52% were men. Sixty-eight patients had basal ganglia, thalamic, or brainstem hemorrhages, 121 had lobar hemorrhages, and 25 had a cerebellar hemorrhage. Fifty-two of the patients had impaired coagulation. Five patients had hemorrhages in newly diagnosed brain tumors. Sixteen of the patients with a negative vascular source of hemorrhage had an incidental aneurysm discovered on their CTA that was not a source of the ICH. One patient had negative CTA, but was investigated further using DSA given his young age (less than 45 years old), and was found to have an AVM. Two of the CTA-negative patients (younger than 45 years old) had negative DSA and were found to have a cavernous malformation on MRI.

**Positive CTA**

Thirty-four patients had a positive CTA finding (Table 1). These patients had a mean age of 54.1 years (range 9–82 years) and 44% were men. Of the 34 patients with a positive CTA, 9 had parietal AVMs (Fig. 1), 3 had frontal AVMs, 3 had cerebellar AVMs, 2 had temporal AVMs,
2 had brainstem AVMs, 1 had a basal ganglia AVM, 3 had dural arteriovenous fistulas, 2 had Moyamoya disease (Fig. 2), 5 had ruptured middle cerebral artery aneurysms, 2 had ruptured anterior communicating artery aneurysms, 1 had a ruptured posterior communicating artery aneurysm, and 1 had a superior sagittal sinus thrombosis. With the exception of those patients with aneurysms and sinus thrombosis, all patients underwent DSA before eventual operative intervention.

**Baseline Characteristics**

Patients with a negative CTA were older (p < 0.001) and had a significantly higher incidence of hypertension (p < 0.001), hypercholesterolemia (p < 0.001), heart disease (p < 0.001), smoking history (p < 0.001), and impaired coagulation (p = 0.036; Table 1). Isolated temporal lobe hemorrhage was significantly higher in patients with a positive CT angiogram (p < 0.001).

**Multivariate Logistic Regression Analysis**

Patients who were found to have a structural cause of hemorrhage on CTA had the following significant characteristics: younger than 65 years old (OR = 16.36, p =

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**TABLE 1: Baseline characteristics of patients who underwent CTA**

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Negative CTA (n = 223)</th>
<th>Positive CTA (n = 34)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean age ± SD</td>
<td>67.9 ± 14.4</td>
<td>54.1 ± 16.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>age &gt;65 yrs</td>
<td>155 (70)</td>
<td>5 (15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>male</td>
<td>116 (52)</td>
<td>15 (44)</td>
<td>0.50</td>
</tr>
<tr>
<td>hypercholesterolemia</td>
<td>108 (48)</td>
<td>1 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>atrial fibrillation</td>
<td>35 (16)</td>
<td>1 (3)</td>
<td>0.083</td>
</tr>
<tr>
<td>smoking history</td>
<td>132 (59)</td>
<td>1 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>heart disease</td>
<td>95 (43)</td>
<td>1 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>29 (13)</td>
<td>1 (3)</td>
<td>0.16</td>
</tr>
<tr>
<td>cerebrovascular disease</td>
<td>26 (12)</td>
<td>1 (3)</td>
<td>0.21</td>
</tr>
<tr>
<td>temporal lobe hemorrhage</td>
<td>4 (2)</td>
<td>7 (21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>lobar nontemporal hemorrhage</td>
<td>117 (52)</td>
<td>14 (41)</td>
<td>0.30</td>
</tr>
<tr>
<td>cerebellar hemorrhage</td>
<td>25 (11)</td>
<td>2 (6)</td>
<td>0.52</td>
</tr>
<tr>
<td>subdural hematoma</td>
<td>3 (1)</td>
<td>1 (3)</td>
<td>0.97</td>
</tr>
<tr>
<td>basal ganglia hemorrhage</td>
<td>58 (26)</td>
<td>6 (18)</td>
<td>0.40</td>
</tr>
<tr>
<td>intraventricular hemorrhage</td>
<td>93 (42)</td>
<td>15 (44)</td>
<td>0.94</td>
</tr>
<tr>
<td>brainstem hemorrhage</td>
<td>10 (4)</td>
<td>1 (3)</td>
<td>0.97</td>
</tr>
<tr>
<td>anticoagulation</td>
<td>52 (23)</td>
<td>2 (6)</td>
<td>0.036</td>
</tr>
<tr>
<td>hypertension</td>
<td>208 (93)</td>
<td>2 (6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* All values given as number of patients (%) unless otherwise indicated.

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**Fig. 1.** Axial images obtained in a 58-year-old woman presenting with progressively severe headache and depressed mental status. **Left:** Noncontrast head CT scan demonstrating extensive (4 x 4 x 7 cm) left temporoparietal ICH with intraventricular extension. **Right:** Computed tomography angiogram demonstrating a 5 x 4 x 4-cm AVM in the left parietal and temporal lobes supplied by the left posterior cerebral, anterior cerebral artery, and middle cerebral artery branches, and mainly draining in the superior sagittal sinus.

**Fig. 2.** Axial images obtained in a 57-year-old woman who presented after having been found unresponsive by her husband at home. **Left:** Noncontrast head CT scan demonstrating left ICH extending into the left temporal role and the lateral ventricles. **Right:** Computed tomography angiogram demonstrating nonopacification of the distal supraclinoid segments of the internal carotid arteries and M1 segments of the middle cerebral arteries bilaterally, with numerous lenticulostriate collateral vessels consistent with Moyamoya disease.
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IH, this strategy is both cost-intensive and exposes
given the low likelihood of discovering vascular lesions
would benefit from its use.7,11,14,16,19,21,22
of acute spontaneous ICH, several investigators have at-
35%–52% 30-day mortality rate,3,10 with only 38% of pa-
tients surviving the first year.18 When a vascular lesion
is the cause of the ICH, its identification is imperative to
prevent further morbidity and death from recurrent hem-
orrhage.1,3,9,17,18 Prior reports have recommended that all
patients with ICH undergo a further workup for vascular
pathology, with at least 1 screening study.8,15 However,
given the low likelihood of discovering vascular lesions in
ICH, this strategy is both cost-intensive and exposes patients to risks of radiation, contrast-induced renal injury, and death.
To improve the yield of angiography in the workup
of acute spontaneous ICH, several investigators have at-
ttempted to identify high-risk patient populations that
would benefit from its use.7,11,14,16,19,21,22 Younger age (<
40–50 years),7,19,22 absence of hypertension,16,21,22 presence
of associated SAH or intracranial hemorrhage,7,11,14,16
and temporal or frontal lobe location7,14 have all been
identified as features that increase the chance of finding
a vascular source through DSA. In addition, criteria have
been developed to stratify ICH patients as low or high
risk for a vascular lesion based on findings on noncon-
trast head CT.5 However, Halpin et al.8 found vascular
causes of ICH using conventional angiography in 24% of
patients deemed unlikely to have positive findings based
on the head CT criteria. Specifically, 13% of hypertensive
patients, 18% of patients with posterior fossa hemorrhage,
and 31% of patients with basal ganglia hemorrhage were
found to have a vascular cause for their ICH. In addition,
Matsumoto et al.15 found coexisting aneurysms in 21% of
women and 9% of men presenting with hypertensive ICH.
Both of these groups have advocated the universal use of
DSA as an initial screening tool in all patients presenting
with spontaneous ICH.
At many institutions, CTA has largely replaced DSA as
the first diagnostic test in the workup of spontaneous
ICH,4 given its efficiency and lower complication risk.
In an attempt to investigate the diagnostic accuracy of
CTA, Delgado Almamoz et al.7 performed a retrospec-
tive analysis of their data on ICH, with the use of CTA
as the initial screening tool. Their results confirmed the
high sensitivity and specificity of CTA in identifying vas-
cular lesions, and they also demonstrated that younger
age, lobar or infratentorial hemorrhage, female sex, and
no history of hypertension or impaired coagulation are
more prevalent in patients with positive CTA. They then
devised a secondary ICH score combining these param-
eters and the already established noncontrast head CT
criteria;4 there was a higher percentage of vascular origin
among patients with higher scores. Further investigation
on which combination of parameters produces the high-
est and lowest risk would help determine which patients
should undergo CTA as part of the diagnostic workup.
More importantly, such an analysis may provide clarity
on which patients can be safely managed without the ad-
dition of CTA. Furthermore, the quantitative contribution
of each parameter to the probability of a positive CT an-
giogram has not been investigated.
In the current study, we attempted to identify groups
of patients that would not benefit from CTA as part of the
diagnostic workup and to individually quantify risk fac-
tors that could increase the yield of CTA in the detection
of vascular sources in patients with nontraumatic nonsub-
arachnoid ICH. In agreement with the current literature,
we identified a vascular origin in 13.2% of the patients
with spontaneous ICH who underwent CTA. Multivari-
ate regression analysis identified factors that were signifi-
cantly associated with positive CTA. Specifically, patients
younger than 65 years old, female patients, nonsmokers,
patients with intracranial hemorrhage, and patients
without hypertension were respectively 16.36, 14.9, 103.8, 9.42, and 515.78 times more likely to have a positive CT angiogram than the patients without these risk factors. It appears, therefore, that preexisting hypertension is the most significant factor for developing ICH in patients with-
out a structural vascular cause. Interestingly, smoking also
appears to have a major effect on spontaneous ICH.
Further subgroup analysis demonstrated that patients
older than 65 years of age, who had preexisting hyperten-
sion, and location of hemorrhage in the basal ganglia or

TABLE 2: Multivariate logistic regression results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wald χ²</th>
<th>p Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>intercept</td>
<td>19.34</td>
<td>&lt;0.0001</td>
<td>none</td>
</tr>
<tr>
<td>age (&lt;65 yrs vs &gt;65 yrs)</td>
<td>8.33</td>
<td>0.0039</td>
<td>16.36 (2.45 to 109.26)</td>
</tr>
<tr>
<td>sex (female vs male)</td>
<td>6.22</td>
<td>0.0126</td>
<td>14.90 (1.79 to 124.46)</td>
</tr>
<tr>
<td>smoking (nonsmoker vs smoker)</td>
<td>11.36</td>
<td>0.0008</td>
<td>103.80 (6.98 to &gt;999.999)</td>
</tr>
<tr>
<td>intracranial hemorrhage (yes vs no)</td>
<td>4.31</td>
<td>0.0379</td>
<td>9.42 (1.13 to 78.36)</td>
</tr>
<tr>
<td>hypertension (no vs yes)</td>
<td>18.61</td>
<td>&lt;0.0001</td>
<td>515.78 (30.21 to &gt;999.999)</td>
</tr>
</tbody>
</table>

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cerebellum were never found to have a positive CT angiogram (68 patients). Patients with these demographics may be managed safely without obtaining CTA in the workup. Because these older patients are more likely to have worse renal function, eliminating CTA for screening in these patients may significantly reduce renal complications. In addition, all patients younger than 45 years of age without hypertension, smoking history, and impaired coagulation had a structural cause of hemorrhage found on further workup (34 patients). Most were identified on CTA, but 1 patient was found to have an AVM on subsequent DSA, and 2 patients had cavernous malformations discovered on MRI. All of these patients eventually required DSA for diagnosis or treatment planning; thus CTA may be safely eliminated from the diagnostic workup of patients with these characteristics as well.

For patients who present with spontaneous ICH (without SAH, history of trauma, or malignancy) in the emergency room and belong in the first group (older than 65 years of age, with preexisting hypertension, and location of hemorrhage in the basal ganglia or cerebellum), the clinician should have an extremely high threshold to perform CTA. Young patients who belong in the second group (younger than 45 years of age without hypertension, smoking history, and impaired coagulation) should all undergo an angiographic study for further investigation. Given that all those patients in our study eventually underwent a conventional angiogram for further lesion characterization or treatment (and in 1 case for definitive diagnosis given the negative CTA), the use of DSA could be considered as a first-line screening tool for this subgroup of patients, to avoid the additional radiation and contrast exposure. If DSA is negative, MRI should be performed to investigate the possibility of a cavernous malformation or newly diagnosed tumor. In the rest of the patients (155 patients in the current series) no definitive conclusion can be drawn about the necessity of an initial angiographic study, and therefore the decision needs to be tailored based on the clinical scenario and the presence of the aforementioned risk factors.

The present study has several limitations. The results are affected by its retrospective nature, because we included patients who presented with ICH and underwent CTA. The results are affected by a selection bias, because patients who were believed clinically to have a low possibility of ICH did not undergo CTA. In addition, the patients who underwent further testing after negative CTA were selected based on the clinician’s judgment, and therefore the true sensitivity of CTA cannot be derived.

Conclusions

For patients with acute ICH, several criteria should factor into the decision of whether to perform CTA. The most significant of these factors is hypertension. Patients older than 65, with hypertension, and location of hemorrhage in the basal ganglia or cerebellum have an extremely low likelihood of a vascular lesion and can be safely managed without CTA. Patients younger than 45 years, without risk factors of smoking or anticoagulation, have a very high likelihood of a structural vascular lesion. These patients may best be managed using DSA as the first diagnostic study, because DSA will eventually be required for most of these patients. Patients who do not fit into these groups can safely and effectively be screened with CTA as part of the diagnostic workup.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Bekelis. Acquisition of data: Bekelis, Desai, Gibson, Gologorsky, Eskey. Analysis and interpretation of data: Bekelis, Desai, Eskey. Drafting the article: Bekelis. Critically revising the article: Erkmen, Desai, Eskey. Statistical analysis: Bekelis, Zhao. Study supervision: Erkmen, Eskey.

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