Emerg Radiol (2009) 16:195–201
DOI 10.1007/s10140-008-0785-3

ORIGINAL ARTICLE

Accuracy of CT angiography for the diagnosis of vascular abnormalities causing intraparenchymal hemorrhage in young patients

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Received: 25 October 2008 / Accepted: 8 December 2008 / Published online: 9 January 2009

Abstract The objective of this study is to measure the accuracy of multidetector CT angiography (MD CTA) in the detection of vascular abnormalities in patients ≤40 years with spontaneous intraparenchymal hemorrhage (IPH) presenting to the emergency department. After institutional review board approval, a retrospective study was performed of 43 consecutive patients ≤40 years, who presented to our emergency department with IPH and that were evaluated with MD CTA. MD CTA images were reviewed by a neuroradiologist to determine IPH location, presence of a vascular abnormality, and associated extraparenchymal hemorrhage. Diagnostic accuracy was measured comparing it to the available reference standards, which included conventional catheter angiogram (CCA), surgical macroscopic findings, and pathology results. Medical records were reviewed for risk factors and correlation with final diagnosis. MD CTA demonstrated an accuracy of 97.7%, with a sensitivity of 96.4% (95% CI 0.79–0.99) and a specificity of 100% (95% CI 0.74–0.99) for the detection of vascular abnormalities in young patients with IPH. Additionally, MD CTA had a PPV of 100%, and the NPV 93.8% in this population. Of the 43 patients included in the study, 28 patients (65%) had a causative vascular etiology for the IPH. Among the 28 patients with vascular etiologies for the IPH, 11 had an AVM (39.2%), nine a ruptured aneurysm (32.14%), seven dural venous sinus thrombosis (25%), and one had vasculitis (3.57%). MD CTA is highly accurate in the detection of vascular abnormalities in the setting of IPH, which as a group represents the most frequent etiology of IPH among patients age ≤40 years. MD CTA performed in the Emergency Department provides accurate, rapid and critical presurgical and premedical treatment information in young patients with IPH.

Keywords MD CTA · STROKE · Neuroradiology · Angiography · Young · Accuracy · CTA

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Introduction

Intraparenchymal hemorrhage (IPH) accounts for 10% to 15% of all stroke episodes [1, 2]. In the United States, approximately 37,000 to 52,400 people have an IPH per year [2]. It is known as the most injurious type of stroke causing a 30-day mortality rate of 35% to 52% [1, 3] and with only 38% surviving the first year [2].

Spontaneous IPH has been well described in young patients. Previous reports have shown an incidence of 0.3/100,000 in patients aged ≤35 years [4, 5] and other series have estimated a frequency ranging from 0.7% to 40% in children and young adults with stroke [5, 6]. Vascular abnormalities are, as a group, the most common etiology of IPH in this population, present in up to 40% to 62.5% of cases, based on conventional angiogram series [5, 7–9]. Furthermore, numerous series have also determined an

increase in the likelihood of finding a vascular lesion on conventional angiography in young patients with intraparenchymal hemorrhage compared to older patients, in whom hypertension and cerebral amyloid angiopathy emerge as the most common etiologies [10–12]. Vascular abnormalities in this group include arteriovenous malformation (AVM), arteriovenous fistula (AVF), aneurysms, cavernous malformations, venous thrombosis, vasospasm, and vasculitis [5, 13].

Although conventional catheter angiography (CCA) remains the gold standard for diagnosis of vascular abnormalities in IPH cases [9, 12, 14], its invasive procedural risk and elevated cost favors less invasive, more economical, and safer techniques, as the initial study [9–11].

High-quality computed tomography angiogram (CTA) acquisition became available in the late 1990s, with the advent of multidetector CT scanners, and has become a valuable tool for the diagnosis of aneurysms (Fig. 1) and other vascular abnormalities [1, 9, 15]. Nevertheless, the accuracy and yield of MD CTA for the detection of vascular abnormalities in children and young adults with intraparenchymal hemorrhage has not been well documented in the literature.

Our intent in this study is to evaluate the accuracy and yield of MD CTA in the diagnosis of vascular abnormalities in patients aged ≤40 years who present to the emergency department with spontaneous intraparenchymal hemorrhage compared to reference standards such as catheter conventional angiography (CCA), surgical and pathological findings.

Materials and methods

Patient selection and clinical data

With prior approval of our Hospital's Institutional Review Board, we retrospectively searched through our radiology database identifying all patients age ≤40 years admitted to our Emergency Department, with acute spontaneous IPH who underwent MD CT head angiography during a consecutive 5-year period from 2002 to 2007. We excluded patients with (1) a known intracranial vascular anomaly, (2) a known brain neoplasm, (3) those with imaging findings suggestive of ischemic stroke on admission, and (4) subarachnoid hemorrhage within the Sylvian fissures and/or basal cisterns. Patients with sulcal subarachnoid hemorrhage, less than 2 cm in their major diameter associated with the IPH were included in the study.

Electronic medical records were reviewed by two physicians. The recorded clinical variables included: (1) age, (2) gender, (3) IPH risk factors including hypertension, tobacco, alcohol, and/or cocaine/amphetamine use, coagulopathies, use of oral contraceptives, use of antiplatelet therapy with aspirin and/or clopidogrel, anticoagulation with warfarin or low molecular weight heparin, International Normalized Ratio (INR) and PT/PTT values on admission, (4) reports of imaging studies (MD CTA and CCA), (5) macroscopic surgical findings, (6) pathology reports, and (7) in-hospital and 1-year mortality. Patients were categorized as hypertensive based on documented diagnosis on past medical history and/or known use of antihypertensive medications. Patients were categorized as having altered coagulation if they (1) were receiving antiplatelet therapy, and/or (2) had received excessive anticoagulation, defined as patients receiving warfarin therapy and an international normalized ratio >3.0 at admission [16], or low molecular weight heparin therapy and an activated partial thromboplastin time (aPTT) greater than 80 sec at admission. All patients with a CCA had the exam performed within the initial 48 h after the MD CTA.

Image acquisition

CT angiography was performed on a General Electric 16- or 64-slice helical CT scanner (General Electric Medical Systems, Waukesha, WI, USA) by scanning from the skull base to the vertex using the following parameters: pitch,

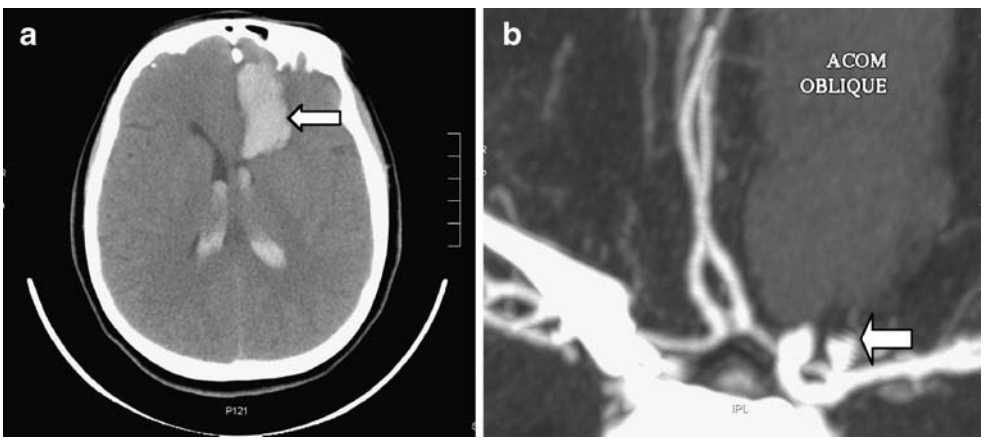

Fig. 1 **a** A 26-year-old female with a left frontal IPH (*arrow*) and IVH extension in a non-enhanced head CT. **b** Coronal MIP reformats from a CTA shows a left supraclinoid ICA aneurysm (*arrow*) with a second adjacent smaller aneurysm

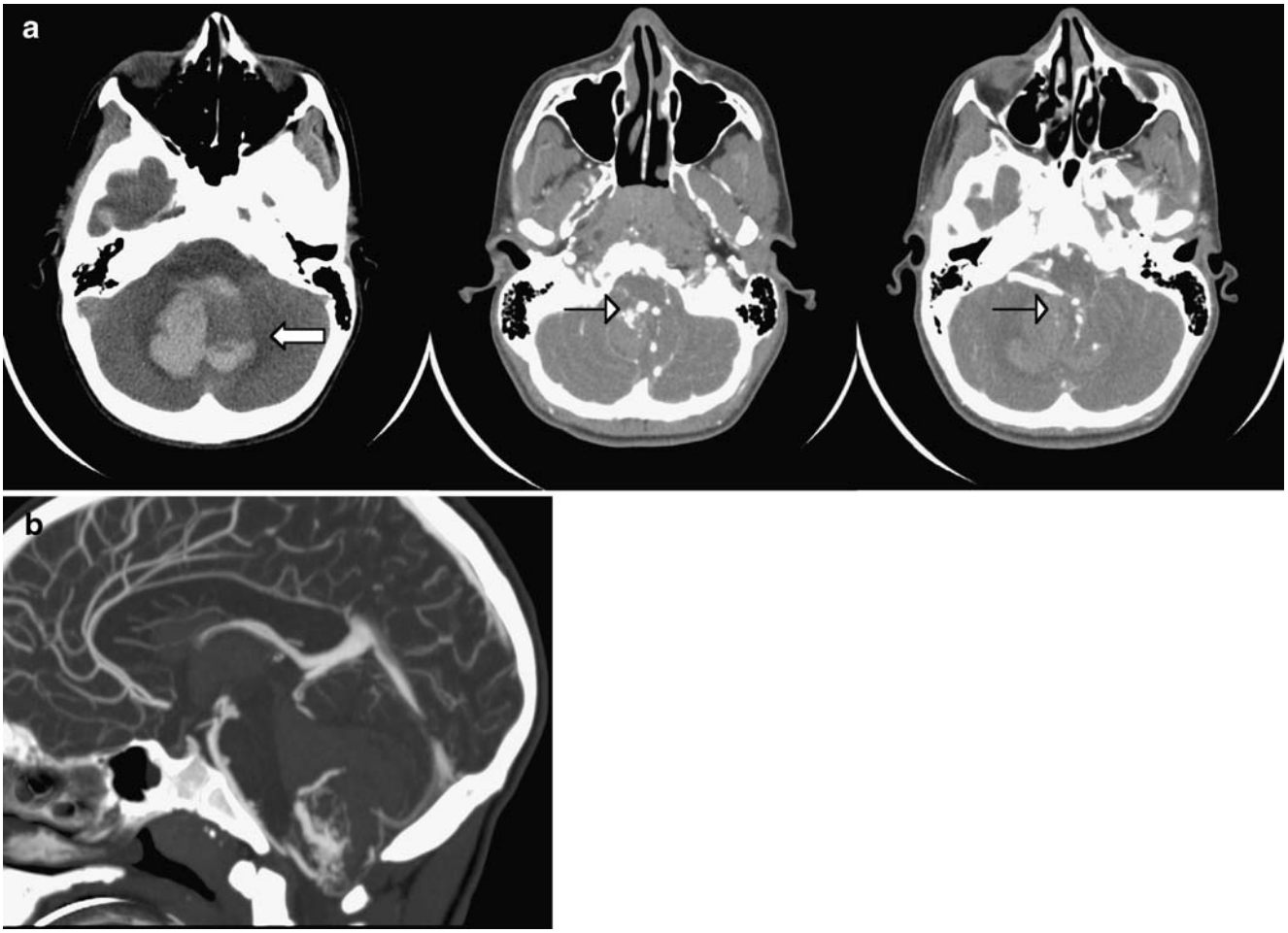

Fig. 2 **a** A 14-year-old male with a large cerebellar IPH (*arrow*) and associated IVH in a nonenhanced CT of the head. Axial source images of a MD-CTA shows a posterior fossa AVM with a nidus (*thin arrow*) involving the right cerebellar tonsil and vermis. **b** Sagittal reformatted MIP image from a MD CTA demonstrating the AVM in the inferior cerebellum

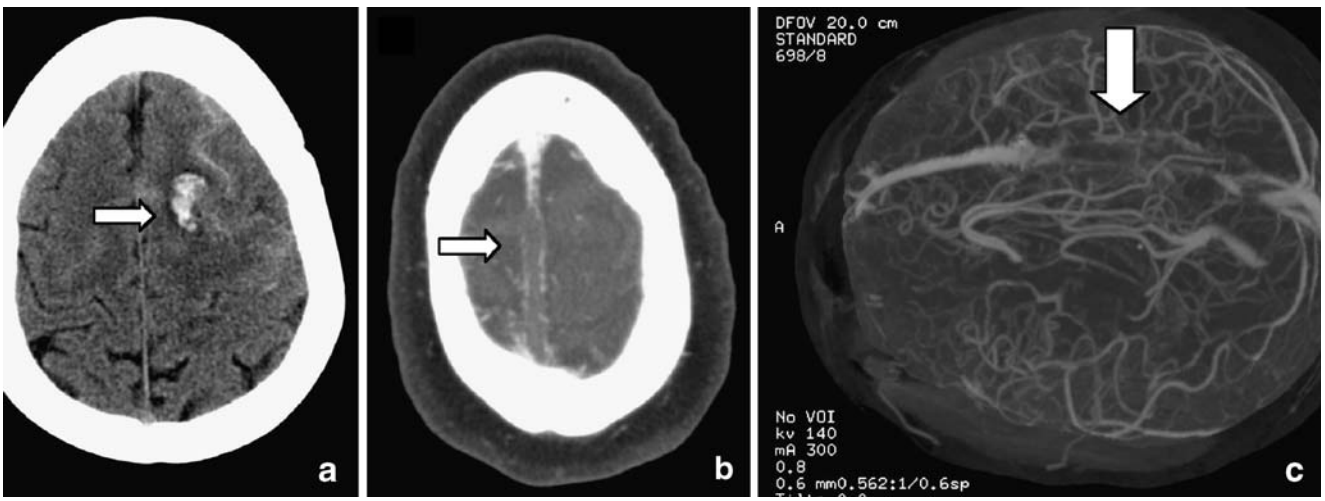

Fig. 3 A 39-year-old female with a history of oral contraceptive use and dehydration. **a** Noncontrast head CT demonstrates a left frontal IPH (*arrow*) with associated sulcal SAH. **b** Axial source images from a CTA demonstrates thrombosis of the mid superior sagittal sinus (*arrow*). **c** Whole brain axial reformatted MIP images, with bone removal shows thrombosis of the mid superior sagittal sinus (*large arrow*), distal left transverse sinus, and left sigmoid sinus extending into the left jugular vein, the later not completely visualized

0.7; collimation, 3 mm; maximal mA, 210 to 250; kVp, 140; field of view, 18 cm; and nonionic contrast material, 90 to 120 mL of Isovue 370 (Medrad, Indianola, PA, USA) administered by power injector at 2 to 3 ml/s into an antecubital vein with either a fixed 25-s delay between the onset of contrast material injection and the start of scanning (the delay was increased to 40 s in patients with atrial fibrillation), or SmartPrep, an automatic contrast-bolus triggering technique (General Electric Medical Systems, Waukesha, WI, USA). 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 3-D laboratory. CCA was performed with previously described standard technique.

Image interpretation

An experienced neuroradiologist evaluated the noncontrast head CT as well as the MD CTA source and maximum intensity projection (MIP) images, blinded to all patient information including clinical condition and imaging reports. The presence of a causative vascular etiology and incidental vascular abnormalities not directly related to the IPH were documented. Anatomical location of the IPH was classified as lobar, basal ganglia/thalamus, infratentorial, and mixed. The presence of concomitant intracranial hemorrhages [intraventricular hemorrhage (IVH), subdural hemorrhage (SDH) and sulcal SAH] was also registered. A second senior neuroradiologist was consulted when there was a discrepancy between the imaging report and the trial reader, in order to achieve a consensus. Positive MD CTAs were defined as those in which a vascular abnormality as the IPH etiology was identified. CCA exams were also reviewed by a neuroradiologist, with knowledge of the MD CTA results.

Statistical analysis

Conventional catheter angiography was considered as the primary gold standard for the diagnosis of a vascular abnormality. When CCA was not available, usually due to the necessity of rapid IPH removal, surgical and pathological findings were considered to be the reference standards in order to determine the accuracy of MD CTA for the identification of vascular abnormalities in spontaneous IPH. The study did not compare the accuracy of MD CTA in detecting secondary objectives such as intranidal aneurysm, feeding, or draining vessels or lesion dimension. Accuracy, sensitivity (SE), specificity (SP), positive and negative predictive values (PPV and NPV), as well as the corresponding 95% confidence intervals were calculated. We applied the Cochran–Mantel–Haenszel Statistics method using the SAS 9.1 version software package (SAS Institute, Cary, NC, USA) to assess the relationship of confirmed vascular abnormalities and a positive MD CTA, controlling for every clinical variable. Results were considered statistically significant if the p value was <0.05.

Results

A total of 80 patients were identified through our database search. A total of 37 patients were excluded from the study secondary to the presence of SAH in the Sylvian fissures/basal cisterns (30), angiographically occult lesions such as cavernous malformations (five), surgical intervention prior to MD CTA imaging (one), and a known brain tumor (one).

Hence, 43 patients were included for complete analysis, of which 20 were male (46.5) and 23 were female (53.5%). The mean age was 28.2 years (range 4–40). The most prevalent IPH risk factors in our patient population were alcohol use (15 cases, 34.8%), tobacco use (13 cases, 30.2%), impaired coagulation (ten cases, 23.3%), altered liver function tests (seven cases, 16.3%), hypertension (six cases, 14%), and cocaine/amphetamine use (six patients, 14%). Controlling for every different condition, the Cochran–Mantel–Haenszel statistical analysis found no direct association of any of the analyzed risk factors with the presence of a vascular abnormality in the reference standard results or in the MD CTA results (Table 1). Seven patients died during their hospital stay (five with and two without vascular etiologies for the IPH). No additional cases of mortality were encountered at 1 year follow-up, representing an overall mortality of (16.3%).

MD CTA results were compared to the reference standards, which were available in all 43 patients. MD CTA demonstrated a causative vascular abnormality in 27 cases, while reference standards, which included conventional catheter angiography (CCA) (20), surgical inspection (29), and pathological examination (24), together demonstrated 28 causative vascular abnormalities. Therefore, of the total

Table 1 IPH risk factors in our patient population

Risk factor	Total		Positive MD CTA	
	N=43		N=27	
	N	Percentage	N	Percentage
Alcohol use	15	34.8	6	22.2
Smoking	13	30.2	7	25.9
Impaired coagulation	10	23.3	5	18.5
Altered liver function tests	7	16.3	1	3.7
HTN	6	14	0	-
Cocaine/amphetamines	6	14	4	14.8
Cancer	5	11.6	1	3.7
Oral contraceptives	4	9.3	3	11.1

Table 2 Diagnostic accuracy of MD CTA in IPH

	Confirmed vascular abnormality	Confirmed nonvascular abnormality	Total
Positive MD CTA	27	0	27
Negative MD CTA	1	15	16
	28	15	43

Sensitivity 96.4% (95% CI 0.79–0.99); specificity, 100% (95% CI 0.74–0.99); PPV 100%; NPV 93.8%; accuracy 97.7%

43 patients included in the study, 28 patients (65%) had a causative vascular etiology for the IPH, and 15 patients (35%) had a nonvascular etiology for the IPH. There was 1 false-negative MD CTA: an AVM that was diagnosed by the presence of dysplastic vessels on pathological examination, which was not identified in a preoperative CCA.

The overall accuracy of MD CTA in the identification of vascular abnormalities as the cause of spontaneous IPH was 97.7%, with a sensitivity of 96.4% (95% CI 0.79–0.99) and a specificity of 100% (95% CI 0.74–0.99). The PPV was calculated to be 100%, and the NPV 93.8%. (Table 2) Among the 28 patients with vascular etiologies for the IPH, 11 had an AVM (39.2%) (Fig. 2), nine a ruptured aneurysm (32.14%), seven dural venous sinus thrombosis (25%) (Fig. 3), and one had vasculitis (3.57%). Of the seven patients with dural venous sinus thrombosis, three patients additionally had MRI with magnetic resonance venography reaching the same diagnosis made with CCA and MD CTA.

A total of 15 patients had nonvascular etiologies for the IPH: six patients had HTN (including two patients with eclampsia), two patients had metastases due to non-small cell lung cancer and spindle cell sarcoma, one patient had a primary brain tumor (anaplastic oligoastrocytoma), two IPHs were attributed to cocaine/ecstasy use, and a definite cause for the IPH could not be determined in four patients (Table 3).

MD CTA identified 27 lobar (62.8%), nine infratentorial (20.9%), and five basal ganglia/thalamic IPHs (11.6) %, as well as two cases with mixed IPH location (4.7%). Nineteen of the 27 lobar hemorrhages (70.4%), seven of the nine infratentorial hemorrhages (77.8%), and one of the two mixed hemorrhages (50%) had a causative vascular abnormality. None of the five basal ganglia hemorrhages had an underlying vascular etiology. Anatomical location of IPH had no statistically significant correlation with the presence of a causative vascular abnormality in this studied population, according to the Cochran–Mantel–Haenszel method.

In the entire group, nine IPHs were associated with IVH (20.9%), four had a coexistent sulcal SAH (11.6%), and three had also a subdural hemorrhage (7.0%). Ten cases of IPH presented with both associated IVH and sulcal SAH (23.3%), and two had the presence of all three subtypes of associated intracranial hemorrhages (4.7%). No direct association was established between the existence of any of the concomitant intracranial hemorrhages and the presence of causative vascular abnormalities on MD CTA.

Discussion

Spontaneous IPH secondary to vascular etiologies is frequent and has a significant impact in the morbidity and mortality among children and young adults [2, 7]. Intraparenchymal rehemorrhage secondary to untreated vascular abnormalities, which may reach an 18% risk per year, further increases morbidity and mortality, highlighting the importance of accurate detection of vascular abnormalities at the initial presentation [17].

In our population of 43 patients, we encountered 28 cases with a vascular etiology as the direct cause of the IPH (65.1%). Our results show a slightly higher prevalence than the 40% to 62.5% prevalence reported by authors in prior CCA studies [5, 7–9]. This is probably related to two separate factors: the younger age (mean of 24.7 years) and lower prevalence of hypertension (14%) in our patient population compared to other studies, both of which have been related to an increased probability of finding a vascular lesion [10–12].

A diagnostic algorithm for the evaluation of children and young adults with IPH has not been well established [18]. While CCA is the gold standard for the detection of vascular abnormalities in all ages, there are significant

Table 3 IPH etiologies on MD CTA

IPH etiologies	Total		Positive MD CTA	
	N=43		*N*=27	
	N	Percentage	*N*	Percentage
Arteriovenous malformation	11	25.6	10	37.0
Aneurysms	9	20.9	9	33.3
Venous Thrombosis	7	16.3	7	25.9
Vasculitis	1	2.3	1	3.7

concerns due to the radiation exposure in younger patients (which may reach 10–12 mSv in some studies), as well procedural complication rates of 0.4% to 4% in children [19]. The concern regarding the radiation exposure from a MD CTA exam in young patients, as mentioned by Brenner [20], is well-founded. However, the radiation dose of a CT of the head and CT angiography of the intracranial vessels reaches 1.7 and 1.9 mSv, respectively [21], which compares favorably to the radiation exposure of CCA. Additional advantages of MD CTA compared to CCA are its availability and fast acquisition, which is particularly useful when there is rapid IPH evacuation, rapid patient transfer, or instauration of anticoagulation is required for patients with venous sinus thrombosis [22]. We detected a false-negative case, which may have been secondary to significant intrahematoma pressure and consequent obliteration of the AVM; hence, we strongly recommend a follow-up MD CTA or CCA once this pressure has decreased.

Although MRA is widely used in young patients with IPH as a result of its advantage of no radiation exposure, data supporting its diagnostic accuracy is minimal and has only been performed in small cohorts of patients. For example, Liu et al. demonstrated that MRA combined with MRV had a diagnostic accuracy of only 66% in a cohort of 38 patients [23]. Recently a study intended to evaluate the incidence of vascular malformation in children with spontaneous intracranial hemorrhage, demonstrated good accuracy of MRI and MRA compared to reference standards; however, these results were based on only seven MRI exams [24].

MD CTA is increasingly being utilized as the initial examination in the evaluation of adult patients with IPH [25]. However, the accuracy of CT angiography has not been well studied in younger patients, particularly in the diagnosis of vascular abnormalities resulting in IPH. Our study demonstrates that MD CTA is highly accurate (97.7%) in the identification of vascular abnormalities as the etiology of spontaneous IPH in patients ≤40 years, demonstrating a sensitivity of 96.4% and specificity of 100% compared to catheter angiography, surgical, and pathological findings.

Our study's limitations are its retrospective nature and small sample size. These likely account for the lack of statistical correlation between anatomical IPH location and associated simultaneous extraparenchymal hemorrhage with the presence of a causative vascular abnormality in our study population, which differs from the previously reported increased predictive values of lobar location and concomitant extraparenchymal hemorrhage for the presence of vascular abnormalities in patients with IPH [5, 13, 14]. Hence, future studies among young patients with larger samples should be conducted. Ideally, the CCA should have been performed immediately after the MD CTA for appropriateness in comparison; however, the patients' health conditions did not always permit this timing.

Finally, our results illustrate that the existence of an IPH risk factor in this age group did not preclude the presence of an underlying vascular abnormality, confirming that the presence of any of these conditions should not hinder further investigation for a vascular abnormality as the etiology for the IPH. These results contrast with older patients with basal ganglia hemorrhage and/or known hypertension, which have much lower prevalences of vascular malformations.

Conclusion

Our results demonstrate that MD CTA is highly accurate in the detection of vascular abnormalities in the setting of IPH, which are the most frequent etiologies of IPH among patients age ≤40 years. MD CTA performed in the Emergency Department provides accurate, rapid, and critical presurgical information in young patients with IPH.

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