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Effectiveness of CT angiography and CT perfusion imaging performed on 16-slice CT scanner in prediction of acute intracranial parenchymal hematoma progression: A retrospective study

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Abstract

Aim: To compare the effectiveness of computed tomography (CT) angiography (CTA), CT Perfusion (CTP) spot signs, and CTP parametric maps obtained from the examinations performed on a 16-slice CT for predicting acute intraparenchymal hematoma (AIPH) progression.

Materials and Methods: Thirty-one patients who presented to the emergency department with acute neurological symptoms and were diagnosed with AIPH on initial head CT examination were included in this study. The patients were administered CTA and CTP within 3 hours of the diagnosis of AIPH and follow-up head CT 24 hours after the first diagnosis. Diagnostic performance of spot signs in CTA and CTP, abnormality presence in CTP parametric maps, and the relationship between them and hematoma progression were investigated.

Results: Sensitivity, specificity, positive predictive, negative predictive and accuracy values in predicting hematoma progression were 85.7%, 95.8%, 95.8%, 85.7%, and 93.5% for CTA spot sign; 71.4%, 95.8%, 83.3%, 92% and 83.9% for CTP spot sign; 14.3%, 87.5%, 100%, 87.5% and 70.9% for all CTP parametric maps, respectively. CTP parametric maps could not be created due to motion artifacts in 19.4% of patients.

Conclusion: The spot sign is a valuable finding that predicts hematoma progression on CTA and CTP examinations performed on a 16-slice CT device. On the other hand, perfusion maps obtained from CTPs are less effective in predicting hematoma progression. Motion artifacts can be seen with a significant frequency in AIPH cases and may prevent the formation of parametric perfusion maps. Limitations of CT equipment and methods should be considered when deciding on the correct method to predict the hematoma progression.

Introduction

Acute intracranial parenchymal hematoma (AIPH) is the type of stroke with the highest mortality and morbidity, seen in 10-30% of patients presenting with stroke and with a mortality rate of 30-50% [1]. AIPH volume, Glasgow Coma Scale score, presence of intraventricular hemorrhage, and age are important predictors of prognosis [2]. In addition, hematoma progression is an independent prognostic marker associated with mortality and morbidity and occurs within the first few hours [3]. Various findings have been described in imaging methods to predict hematoma growth. The main described signs are "Swirl Sign," "Blend Sign," "Hematoma Volume" in non-contrast computed tomography (CT), and "Spot Sign" in CT angiography (CTA) and CT perfusion (CTP) examinations [4-7]. The spot sign has been primarily described for CTA, which is considered as a finding of active bleeding. However, the CTA's primary major constraint for the spot sign is that the examination only includes information about the arterial phase. Capillary and venous phase information is not included in routine CT angiography examinations.

On the other hand, findings of arterial, capillary, and venous phases are obtained in CTP. With this examination, spot signs can be detected in late phases. In addition, "Cerebral Blood Volume" (CBV) and "Cerebral Blood Flow" (CBF) maps obtained from CTP provide informa-

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tion about blood flow. Increased blood flow in and around the hematoma area may be related to progression [8,9]. The main limitation of CTP is the high radiation exposure compared to CTA and the variation of the examination area according to the scanner technology.

In the literature, the effectiveness of CTA and CTP in detecting the spot sign has been compared [7]. However, a 64-slice CT scanner has been used in this comparison. In these systems, which have a very high number of detectors, CTA images are obtained in a few seconds, and the coverage in CTP reaches 4 cm. In contrast, the examination time is longer in 16- and 32-slice scanners and the examination range in CTP varies between 1-2.5 cm. Hence, the effectiveness of CTA and CTP in these systems may vary. Due to the increased duration of CTA, the spot sign may become evident, and the effectiveness of CTP may decrease in the limited examination area.

Our aim was to compare the effectiveness of CTA and CTP spot signs and CTP parametric maps obtained from the examinations performed on a 16-slice CT for predicting hematoma progression.

Materials and Methods

Our study was approved by our institution's Uludag University Clinical Research Ethics Committee, Decision Number: 2016-2/11.

Patients

A search was conducted retrospectively on our Radiology Information System Program (Centricity RiS 4.0, GE Healthcare, Chicago, IL, USA) for the patients went to CT, CTA and CTP examinations on our 16-slice CT device, and diagnosed with AIPH. Thirty-one patients older than 18 years of age who admitted to the emergency department with acute neurological symptoms and were diagnosed with AIPH on initial non-contrast head CT between July 2016 – July 2018 were found and included in this study. The patients were administered CTA and CTP within 3 hours of the diagnosis of AIPH and were followed up with conservative medical treatment only for 24 hours, according to the neurosurgery's decision. Blood urea, creatinine, and glomerular filtration rate (GFR) levels were investigated before CTA and CTP in all patients. All these kidney function parameters were normal before the examinations requiring iodinated contrast media in all patients. Follow-up CT was performed one day after admission for hematoma progression. Exclusion criteria were history of trauma at admission, diagnosis of AIPH with vascular malformation, allergy to contrast material, impaired renal function laboratory parameters, being under 18 years of age, and absence of one or more of the above-mentioned radiological examinations. Informed consent was obtained from all patients included in this study.

Imaging

All examinations were performed on a 16-slice CT scanner (SOMATOM Perspective, Siemens, Erlangen, Germany). Initial head CT was obtained from the lower edge of the C2 vertebra to the vertex in the axial plane from the topogram in the sagittal plane. CTA and CTP examinations were performed within the first 3 hours following hematoma detection. A sagittal new topogram was obtained in the first step for these two examinations. Afterward, non-contrast sections of CTA were taken from the lower edge of the C6 vertebra corpus to the vertex. The bolus tracking method was used to detect the arterial phase. A single axial slice was obtained at the level of the aortic arch. Region-of-interest (ROI) was placed in the aortic lumen, which provides continuous density measurement. Afterward, the same slice was taken periodically at 2-second intervals. Subsequently, 1 ml/kg non-ionic monomer iodinated contrast media (Omnipaque® 300 mg/mL) was administered with an automated injection scanner at a 5 ml/sec rate through a 16-18G intravenous cannula placed in the antecubital venous system. When the density in the vessel's lumen reached 100 HU, contrast-enhanced CTA sections were obtained in the same plane as the non-contrast. Then we paused for ten minutes. Meanwhile, CTP with a 1.6 cm coverage size was planned to pass through the widest part of the hematoma in initial non-contrast CT. After 10 minutes, CTP was started. The contrast media was administered at the same amount and rate as CTA using an automated injection scanner five seconds before the beginning of CTP. Follow-up head CT was performed 24 hours after the first examination and precisely the same as the first examination. Technical parameters of non-contrast CT, CTA, and CTP examinations are given in Table 1.

Interpretation

All images were evaluated together by two observers with 20 and 5 years of experience in neuroradiology. Observers were blind to the study results. The consensus of the observers was accepted as the final decision. In the evaluations, a dedicated image processing program (syngo MultiModality Workplace VE36A, Siemens, Erlangen, Germany) was used for the images obtained on the scanner. Hematoma volumes were measured in the first and control non-contrast CT. A volume increase of more than 33% was considered progression [10]. Localization of hematomas was recorded. The presence of spot sign in the hematoma was evaluated in the source images obtained in CTA and CTP. In all spot sign interpretations, the window width set as 300 Hounsfield units (HU), and the window level 120 HU when evaluating all source images. CTP source images were opened using the program's "CT Perfusion" module. CBV, CBF, and permeability maps were created after determining arterial input function and venous output function, and segmentation of vascular structures. ROIs were placed on the normal side-MCA horizontal segment for arterial input function and superior sagittal sinus or transverse sinus for venous output function. The increase of related parameters within the hematoma was investigated in these maps. Quantitative evaluation was made by the division of the numeric results of perfusion abnormality by contralateral hemispheric normal appearing white matter results. All results have been recorded.

Statistical analysis

The frequency and level of demographic data (age, gender), the frequency of hematoma progression, the presence of spot signs in CTA and CTP, and the presence of

Table 1. Parameters of CT techniques.

	Non-Contrast CT	CTA – Non-Contrast Phase	CTA – Angiography Phase	CTP
kV Size CTDIvol	130	110	110	80
Effective mAs	250	110	110	150
Slice Thickness	0.75 mm	0.75 mm	0.75 mm	2 mm
Matrix	512*512	512*512	512*512	512*512
Coverage Size				1.6 cm
Duration (s)	20	15.12	15.06	40
Number of Phases	1	1	1	40
DLP	910.90 mGy*cm	662.6 mGy*cm	662.6 mGy*cm	731.09 mGy*cm
CTDIvol	52.02 mGy	18.26 mGy	18.26 mGy	380.77 mGy

Table 2. Imaging and follow-up findings of patients.

Patient Number	Location	Hematoma Volume (ml)	CTA Spot Sign	CTP Spot Sign	Progression
1	Basal Ganglia	0.05	Yes	Yes	Yes
2	Basal Ganglia	7.73	No	No	No
3	Lobar	33.48	No	No	No
4	Lobar	57.70	No	No	No
5	Lobar	2.06	Yes	Yes	Yes
6	Basal Ganglia	2.54	No	No	No
7	Basal Ganglia	19.31	Yes	Yes	Yes
8	Deep White Matter (opened to ventricle)	47.93	No	No	No
9	Deep White Matter (not opened to ventricle)	0.03	No	No	No
10	Basal Ganglia	2.24	No	No	No
11	Basal Ganglia	39.18	No	No	No
12	Basal Ganglia	20.90	Yes	Yes	Yes
13	Basal Ganglia	9.84	No	No	No
14	Basal Ganglia	2.54	No	No	No
15	Deep White Matter (opened to ventricle)	124.02	No	No	No
16	Lobar	6.61	No	No	No
17	Basal Ganglia	3.18	No	No	No
18	Basal Ganglia	8.92	No	No	No
19	Lobar	50.92	No	No	No
20	Basal Ganglia	90.45	No	No	No
21	Basal Ganglia	49.97	Yes	Yes	Yes
22	Deep White Matter (opened to ventricle)	52.69	No	No	No
23	Lobar	7.73	No	No	No
24	Basal Ganglia	3.15	No	No	No
25	Basal Ganglia	6.41	No	No	No
26	Cerebellum	6.45	No	No	No
27	Basal Ganglia	35.89	No	No	No
28	Deep White Matter (opened to ventricle)	59.21	No	No	No
29	Basal Ganglia	34.56	No	No	No
30	Basal Ganglia	3.67	No	No	No
31	Cerebellum	1.59	Yes	Yes	Yes

abnormalities in CTP parametric maps were determined. Diagnostic performance of spot sign presence in CTA and CTP and abnormality presence in CTP parametric maps were examined. The relationships between CTA – CTP spot sign presence, abnormality presence in CTP perfusion maps and hematoma progression were investigated using Fisher's exact test. The compatibility of CTA and CTP in terms of the presence of spot signs was evaluated by Cohen's Kappa analysis. Coefficient of agreement (κ) in Kappa analysis less than 0.00 was considered to be discordant, 0.00-0.20 slightly agreeable, 0.21-0.40 mildly agreeable, 0.41-0.60 moderately agreeable, 0.61-0.80 highly agreeable, 0.81-0.99 near-perfect agreeable, 1 perfectly compatible. The level of significance in the evaluations was accepted as p=0.05. All statistical analyses were made in SPSS 23.0 (IBM Corp, Armonk, NY, USA) program.

Results

The mean age was 61.4 ± 15.0 (31 - 91). 67.7% (21/31) cases were male, and 32.3% (10/31) cases were female. Basal ganglia hematoma was detected in 58.1% (18/31)

of patients, lobar hematoma in 19.4% (6/31), deep white matter hematoma not opened to the ventricle in 9.7% (3/31), deep white matter hematoma opened to the ventricle in 6.5% (2/31) and cerebellar hematoma in 6.5% (2/31). In 22.6% (7/31) of patients, hematoma progression was seen. CTA spot sign was observed in 22.6% (7/31) cases, whereas CTP spot sign in 19.4% (6/31). Motion artifact was seen in 19.4% (6/31) of patients, and CBV, CBF, and permeability maps could not be formed in these patients. An increase in CBF, CBV, and permeability was observed in only one of the other cases, and no significant changes were detected in the CBF, CBV, and permeability maps in the other cases (Table 2-3).

Sensitivity, specificity, positive predictive, negative predictive and accuracy values in predicting hematoma progression were 85.7% (6/7), 95.8% (23/24), 95.8% (23/24), 85.7% (6/7), and 93.5% (29/31) for CTA spot sign; 71.4% (5/7), 95.8% (23/24), 83.3% (5/6), 92% (23/25) and 83.9% (26/31) for CTP spot sign; 14.3% (1/7), 87.5% (21/24), 100% (1/1), 87.5% (21/24) and 70.9% (22/31) for CBV, CBF and permeability, respectively. CBF, CBV and permeability maps could not be created due to motion artifacts in each three patients with and without hematoma progression (Table 2-3). There were significant relationships between hematoma progression and CTA spot sign ($p<0.001$), and CTP spot sign ($p=0.03$), but no significant relationship between progression and perfusion parametric map abnormalities ($p>0.05$). The agreement between CTA and CTP for spot sign was high ($\kappa=0.67$, $p<0.001$) (Table 4).

A case example is shown in Figure 1.

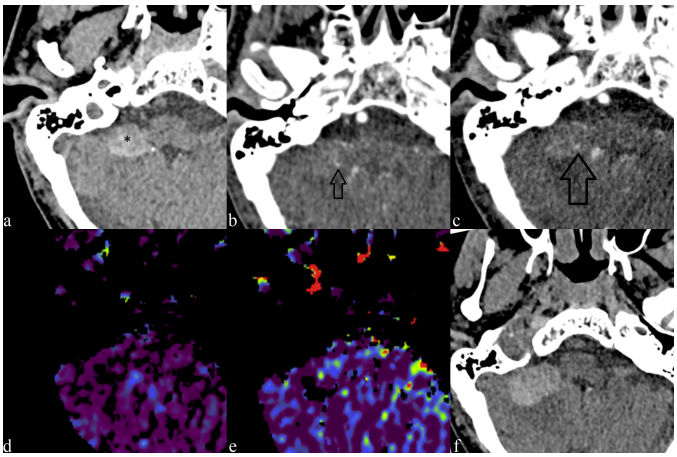

Figure 1. A patient with progressed right cerebellar hematoma. Non-contrast initial CT (a); right cerebellar parenchymal hematoma (*). CTA (b) and CTP (c); spot signs (empty black arrows) in the hematoma. Permeability (d) and CBV (e) maps derived from CTP; no visible change in and around hematoma. Follow-up CT (f); horizontally increased size of hematoma.

Table 3. CTP Findings of patients.

Patient Number	CBV	CBF	Permeability	Motion in CTP
1	Increased	Increased	Increased	No
2	Not Increased	Not Increased	Not Increased	No
3	Not Increased	Not Increased	Not Increased	No
4	Not Known	Not Known	Not Known	Yes
5	Not Increased	Not Increased	Not Increased	No
6	Not Increased	Not Increased	Not Increased	No
7	Not Known	Not Known	Not Known	Yes
8	Not Increased	Not Increased	Not Increased	No
9	Not Increased	Not Increased	Not Increased	No
10	Not Increased	Not Increased	Not Increased	No
11	Not Known	Not Known	Not Known	Yes
12	Not Known	Not Known	Not Known	Yes
13	Not Increased	Not Increased	Not Increased	No
14	Not Increased	Not Increased	Not Increased	No
15	Not Known	Not Known	Not Known	Yes
16	Not Increased	Not Increased	Not Increased	No
17	Not Increased	Not Increased	Not Increased	No
18	Not Increased	Not Increased	Not Increased	No
19	Not Increased	Not Increased	Not Increased	No
20	Not Increased	Not Increased	Not Increased	No
21	Not Increased	Not Increased	Not Increased	No
22	Not Known	Not Known	Not Known	Yes
23	Not Increased	Not Increased	Not Increased	No
24	Not Increased	Not Increased	Not Increased	No
25	Not Increased	Not Increased	Not Increased	No
26	Not Increased	Not Increased	Not Increased	No
27	Not Increased	Not Increased	Not Increased	No
28	Not Increased	Not Increased	Not Increased	No
29	Not Increased	Not Increased	Not Increased	No
30	Not Increased	Not Increased	Not Increased	No
31	Not Increased	Not Increased	Not Increased	No

Discussion

In our study, the CTA spot sign predicted hematoma progression with higher sensitivity and accuracy than the CTP spot sign in a 16-slice CT scanner. Both examinations showed a high level of significant concordance. In addition, motion artifact was observed in CTP in approximately 20% of the cases, and therefore, CBV, CBF, and permeability maps could not be created. These maps showed a lower level of effectiveness relative to the spot sign in detecting hematoma progression.

There are 2 studies comparing the effectiveness of CTA and CTP in the literature [7,11]. In the first study, the sensitivity of the CTP spot sign has been 78%, and the sensitivity of CTA has been 44% [7]. However, a 64-slice CT scanner has been used in the first study. In these systems, the coverage size varies between 3 and 4 cm [12]. The CTP coverage size, which was 1.6 cm in our study, has been 4 cm in the study of Kocuylm et al. [7]. We think that the reason for the higher sensitivity of CTP is that, with the widening of the coverage size, spot signs outside the widest area of the hematoma may be detected. CTA has been performed with a bolus tracking method similar to our study [7]. CTA times in these systems are considerably shorter than the 16-slice CT used in our study [13]. We performed imaging for 15 seconds in the caudocranial direction following the detection of contrast in the aortic arch. Therefore, the cranium was visualized in the last

Table 4. Diagnostic performances of the CTA spot sign, CTP spot sign, and CTP perfusion map abnormality presence for the AIPH progression prediction.

	CTA Spot Sign	CTP Spot Sign	CTP CBV Abnormality	CTP CBF Abnormality	CTP Permeability Abnormality
Sensitivity	85.7% (6/7)	71.4% (5/7)	14.3% (1/7)	14.3% (1/7)	14.3% (1/7)
Specificity	95.8% (23/24)	95.8% (23/24)	87.5% (21/24)	87.5% (21/24)	87.5% (21/24)
PPV	95.8% (23/24)	83.3% (5/6)	100% (1/1)	100% (1/1)	100% (1/1)
NPV	85.7% (6/7)	92% (23/25)	87.5% (21/24)	87.5% (21/24)	87.5% (21/24)
Accuracy	93.5% (29/31)	83.9% (26/31)	70.9% (22/31)	70.9% (22/31)	70.9% (22/31)
P value	<0.001*	0.03*	0.160	0.160	0.160

PPV: Positive Predictive Value, NPV: Negative Predictive Value, *: p<0.05.

half of the examination. We observe that venous sinuses and superficial and deep cerebral veins are also opacified in CTAs in routine clinical practice. The main reasons for the low sensitivity of CTA (44% vs. 85.7%) compared to our study are that the spot sign was lowered because the examination in 64-slice CT only contained information about the arterial phase, and in our method, presumably, we performed imaging in the late arterial phase. In the second study, 16-slice CT has been used, similar to our scanner [11]. However, perfusion imaging has been performed with two 12 mm thick sections in this study. Therefore, an examination has been carried out with a coverage size of 24 mm, which is more than our study. In addition, no information has been given that the images were evaluated in the standard window level and width. Moreover, in case samples, CTA images have been shown with a vascular window setting that was less sensitive to opacification, and CTP images have been presented with higher contrast and narrowed window range, which had increased sensitivity to opacification [11]. Despite this, we evaluated all images in the standard window setting (see Methods – Imaging). In addition, contrast media has been administered at an injection rate of 8 ml/s in CTP and 5 ml/s in CTA [11]. The rate of CTA injection was not specified in the first study, but the amount of contrast media given in CTA and CTP has been different. As the contrast injection rate and amount increase, contrast enhancement becomes evident in CT scans [14]. Hence, spot signs might appear more prominent in CTP in the second study [11]. We aimed to evaluate the effectiveness of CTA and CTP in more standardized ways. For this reason, we applied the exact amount and rate of contrast media in CTA and CTP. We think that our study is technically more standardized and contains more objective findings when compared with these studies.

CTP is an examination method that mainly provides information about cerebral microcirculation, otherwise, blood flow [15]. This technique examines the first pass effect of intravenously administered contrast material at the capillary level. The condition most commonly used CTP is acute ischemic stroke [15]. Its use has increased, especially with interest in spot sign of AIPHs. However, it has been stated in some studies that parametric maps (e.g., CBV, CBF, mean transit time) obtained from perfusion images can predict hematoma progression [8,9]. Our study used CBF, CBV, and permeability maps, especially since they may reflect the increasing enhancement of the spot sign. However, in 19.4% of the cases, we observed motion artifacts that were not expressed in previous studies and that were evident enough to prevent the formation of parametric maps. Some of the AIPH patients have low GCS scores when they come; therefore, they cannot show the necessary cooperation for the examination [16]. Especially, the fact that duration is longer than CTA and non-contrast CT creates a tendency to move. Slight movements can be corrected with motion correction methods at the post-processing stage. Although we applied this technique to the patients in our study, we could not generate parametric patients in 6 patients. The effectiveness of parametric maps was much lower than the CTA and CTP spot signs. We think that CTP should be performed with the primary aim of detecting spot signs in AIPH cases rather than CT perfusion parametric map measurements.

Spot sign is a finding defined for CTA in early studies [17]. It was thought to reflect extravasation within the hematoma. However, after a while, the emergence of spot signs that are not in CTA on post-contrast CT led to the idea that CTA's effectiveness in spot signs is limited because it only carries information about the arterial phase [18]. In order to solve this problem, studies using post-contrast CT, multiphasic CTA, and CTP were conducted [7,19,20]. In studies, the sensitivity of CTA varies between 46-93%, specificity between 50-95%, the sensitivity of CTP between 78-89%, and specificity between 74.5-100% [21]. We think that the main reason for the low efficiency of CTP and the high efficiency of CTA in our study is the difference in the scanner technology we used, examination protocols, and the number of cases compared to other studies.

Our study has some limitations. The main ones are that it is single-centered, and the number of cases is low. Especially the low number of cases with progression may have affected the sensitivity levels. Multicenter studies with more subjects may evaluate the accuracy of our findings more objectively.

Conclusion

In conclusion, the spot sign is a valuable finding that predicts hematoma progression on CTA and CTP examinations performed on a 16-slice CT scanner. The diagnostic efficiency of CTPs with a short coverage size decreases, and CTAs may show the spot sign more clearly due to the prolongation of the scanning period. On the other hand, perfusion maps obtained from CTPs are less effective in predicting hematoma progression. Motion artifacts can be seen with a significant frequency in AIPH cases and may

prevent the formation of parametric maps. Limitations of CT equipment and methods should be considered when deciding on the right method to predict the hematoma progression.

Ethics approval

Our study was approved by our institution's Uludag University Clinical Research Ethics Committee, Decision Number: 2016-2/11.

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