Angiography with the 256-multislice spiral computed tomography and its application in evaluating atherosclerotic plaque and cerebral ischemia

Pei-Pei Sun, MMa, Ping-Yong Feng, BMb,*, Qiang Wang, BMb, Shan-Shan Shen, MMc

Abstract
Ulceration of carotid arterial plaque is associated with cerebral events. Detection of ulcerated plaques will benefit patient from stroke and other ischemic events. The aim of this study was to evaluate morphology of atherosclerotic plaques in the carotid arteries and to assess its clinical impact in predicting cerebral events.

A total of 386 patients were examined with 256-multislice spiral computed tomographic angiography (MSCTA). It was found that 356 of the 386 patients had cerebral ischemic symptoms. Specifically, 35 patients had amaurosis fugax (AmF), 178 had transient ischemic attack (TIA), and 143 had ischemic stroke. Abnormal images were found in 658 carotid arteries by MSCTA. Of the 658 abnormal images of carotid arteries, besides the 34 cases of carotid arterial occlusion, 624 cases were atherosclerotic plaques. Of the 624 plaques, 394 (63.2%) were smooth surface plaques, 161 (25.8%) were irregular surface plaques, and 69 (11.1%) were ulcerated plaques. Incidence of ulcerated plaque was higher in the ischemic stroke patients (13.1%) compared with that in the TIA group (10.9%), AmF group (6.6%), or symptom-free group (9.4%) although it was not statistically significant (P = .288). However, there was significant difference in the incidence of ischemic stroke between the ulcerated (20/69, 28.9%) and nonulcerated groups (69/555, 12.4%, P < .05, odds ratio = 2.875).

These findings suggested that 256-MSCTA is an advanced imaging tool to determine not only arterial stenosis but also morphologic assessment of atherosclerotic plaques, which will benefit the patients by predicting the cerebral events in advance.

Abbreviations: AmF = amaurosis fugax, MSCTA = multislice computerized tomographic angiography, OR = odds ratio, TIA = transient ischemic attack.

Keywords: angiography, atherosclerotic plaques, cerebral ischemia, 256-multislice spiral computed tomographic angiography

1. Introduction
Prevalence of stroke is increasing by 8.7% annually in China.[1] Mortality of stroke is approximately 30% and the rest 70% survivors suffer from paralysis.[2–4] It has been reported that approximately 20% to 30% stroke is associated with carotid arterial atherosclerosis or stenosis.[2–5] Recently, it is considered that unstable atherosclerotic plaque of carotid arteries is one of the major risk factors for the development of acute cerebral event.[6–8] Therefore, evaluation on the plaque stability in the carotid arteries may serve as a predicting factor for cerebral events in clinic.

Stability of the atherosclerotic plaques largely depends on the morphology and structure of the plaques. In this context, ulceration is a major pathologic process in the development of unstable plaques.[6–9] Ulcerated plaques possess unique morphology and can be detected with noninvasive imaging scanning. In this regard, multislice computerized tomographic angiography (MSCTA) has been used to determine carotid arterial stenosis and morphology of the atherosclerotic plaques, especially, ulcerated plaques.[6–11] However, nonuniformity in atherosclerosis distribution within an individual may cause difficulty in predicting plaque behavior from conventional CTA imaging alone. The present study was, therefore, designed to evaluate morphologic features of the atherosclerotic plaques in carotid arteries using the advanced 256-MSCTA, and to assess the association of ulcerated plaque and cerebral events.

2. Materials and methods

2.1. Patients
Total 386 patients, who were examined with 256-MSCTA from December 2011 through November 2012, were enrolled into this study. Of them, 258 (66.8%) were males and 128 (33.2%) were females aged from 37 to 87 years old with an average of 61.15. This study was approved by The Institutional Review Board of Ethics Committee of Second Hospital of Hebei Medical
University. All participants received written and oral information prior to giving written consent, and the study was performed in accordance with the Helsinki II declaration.

2.2. Equipment, parameters, and scanning method
Philips Brilliance CT (Philips) was used to scan from aortic arch to top of the outer auricle. Scanning parameters were as follows: tube voltage 120kV, tube current 120 mA, width of the detector 128 mm x 0.625 mm, slice thickness 0.9 mm, distance between slices 0.45 mm, collimation 0.625 mm, FOV 180 mm, spiral distance 0.938, spinning speed of the tube 0.5 s/rot. The nonionic contrast iodine (370mgI/mL) was injected through elbow vein at a speed of 4 to 5 mL/s, total 40 to 50 mL followed by injection of 30 mL normal saline. Scan delay time was triggered by computerized program and region of interest was placed at aortic arch with triggering threshold of 200 HU.

2.3. Image process and analysis
To identify atherosclerotic alteration, abnormal image was searched on axial images followed by being processed on the Portal workstation with various techniques including maximum intensity projection, volume rendering, curved planar reformation, multiple planar reformation, and advanced vessel analysis. Images were blindly analyzed by 2 experienced neuroradiologists to evaluate morphology of the atherosclerotic plaque and its location. The 2 neuroradiologists were allowed to discuss when they had discrepancy.

2.4. Evaluating criteria
1. Criteria for evaluating morphology of the atherosclerotic plaque:
   Scanned images were analyzed following the categories and evaluation criteria proposed by de Weert et al.[12] that is, smooth, irregular, and ulcerated plaque. Plaques were classified as ulcerated if extension of contrast material was present beyond the vascular lumen into the surrounding plaque over 1mm; plaques were classified as irregular if the plaque surface morphology showed irregularities without any sign of ulceration; if the plaques were not ulcerated or irregular, they were classified as smooth.[12]

2. Criteria for evaluating clinical symptoms: Clinical symptoms were classified as no symptoms, amaurosis fugax (AmF), transient ischemic attack (TIA), and cerebral infarction (or ischemic stroke). AmF was defined as a sudden, focal neurologic deficit that was confined to the eye and originated from vascular cause. AmF often occurred in 1 eye and could last few seconds, minutes, or even 1 hour. TIA was defined as a sudden, focal neurologic deficit that lasted less than 24 hours. Cerebral infarction (ischemic stroke) was defined as a sudden, focal neurologic deficit that lasted longer than 24 hours.

2.5. Statistical analysis
Data were analyzed with SPSS 13.0 statistical analysis software. Association between plaque morphology and vascular stenosis or brain ischemic status was analyzed. Difference between categorial data was analyzed with a Pearson Chi-squared or Fisher Chi-squared test, and $P < .05$ was considered as significant. The association between the presence of ulcerated plaque and clinical symptoms was evaluated and odds ratio (OR) $> 1$ was considered as significant association.

3. Results
3.1. General patients’ characteristics
The MSCTA images of the 386 patients were evaluated and it was found that 356 patients had cerebral ischemic symptoms. Specifically, 35 patients had AmF, 178 patients had TIA, and 143 patients had ischemic stroke.

Abnormal images were found in 658 carotid arteries. Of them, occlusion was found in 34 carotid arteries and atherosclerotic plaques were found in 624 carotid arteries. Of the 624 plaques, 394 (63.2%) were smooth surface plaques, 161 (25.8%) were irregular surface plaques, and 69 (11.1%) were ulcerated plaques. Surface of the smooth plaques was flat and smooth in surface and relatively stable. In contrast, the surface of irregular or ulcerated plaques was not smooth or even broken, and often had intra-plaque bleeding and reduced fibrotic tissue.

3.2. Association between plaque morphology and clinical manifestation
As shown in Table 1, incidence of ulcerated plaque was higher in the ischemic stroke patients (13.1%) compared with that in the TIA group (10.3%), AmF group (6.6%), or symptom-free group (9.4%). However, there was no significant difference in the incidence of ulcerated plaque between the groups with different clinical manifestation ($P = .288$, Table 2).

We found that 20 of 69 (28.9%) patients, who had ulcerated plaques, showed ischemic stroke. In contrast, 69 of 535 (12.4%) patients, who had nonulcerated plaques, showed ischemic stroke. There was significant difference in the incidence of ischemic stroke between the ulcerated and nonulcerated groups ($P < .05$, OR $=2.875$, Table 3).

Next, side of the carotid arterial plaque occurrence and cerebral infarction was analyzed. As shown in Table 4, out of 143 patients who had cerebral infarction, 99 (69.2%) patients had cerebral infarction on the same side of carotid arterial plaque. Furthermore, complete occlusion of carotid arteries was found in 10 (10.1%) out of the 99 cases, and ulcerated plaques was found

| Table 1 |
|---|
| Percentage of various morphologic plaques by symptoms. |
| Plaque morphology | Smooth | Irregular | Ulcerated | Percent of ulcerated plaques |
| No symptoms | 23 | 6 | 3 | 9.37 |
| AmF | 33 | 24 | 4 | 6.55 |
| TIA | 164 | 72 | 27 | 10.26 |
| Ischemic stroke | 174 | 59 | 35 | 13.06 |

AmF= amaurosis fugax, TIA = transient ischemic attack.

| Table 2 |
|---|
| Comparison of ulcerated and nonulcerated plaques in the patients with symptoms. |
| Plaques | Ulcerated | Nonulcerated |
| No symptoms | 3 (9.37%) | 29 (90.63%) |
| AmF | 4 (6.55%) | 57 (93.44%) |
| TIA | 27 (10.27%) | 236 (89.73%) |
| Ischemic stroke | 35 (13.06%) | 233 (86.94%) |

AmF = amaurosis fugax, TIA = transient ischemic attack.
often focally distributed in the coronary tree and carotid affect arterial walls in whole cardiovascular system, plaque is necrosis, speci-tein-driven atherosclerosis further leads to plaque formation at extensively investigated.[9]

future cardiovascular or cerebrovascular event has been challenge. In this regard, the use of medical imaging to predict prediction of a rupture before the event is a major diagnostic patients with TIA or cerebral infarction.

irregular plaques were more frequently encountered in the associated with cerebral infarction and that ulcerated and plaque surface morphology. It showed that plaque ulceration was incidence of cerebral infarction in the patient with nonulcerated plaques (69/555, 12.43%), suggesting cerebral infarction may be associated with plaque ulceration.

This study also demonstrated that incidence of cerebral event was higher in the ipsilateral side of plaque ulceration (22.47%) than that in the contralateral side of plaque ulceration (16.88%), although it was not statistically different. Similarly, Fisher et al.[23] reported that incidence of plaque ulceration in either side of carotid arteries was not different, although patients with cerebral infarction symptoms had higher incidence of plaque ulceration in the carotid arteries compared with that of patients without symptoms. Rothwell et al.[24] reported that plaque ulceration might exist on the contralateral carotid artery if cerebral symptoms and ulcerated plaque were found on the ipsilateral side. These findings indicated that systemic risk factors might contribute to the formation of unstable plaque.

There were limitations in the present study. First, the number of cases enrolled into this study was small. This limited number of studies might contribute to the controversy of the findings that the ulcerated plaques were lesser in AmF condition (6.55%) as compared with that in symptom-free group (9.37%), although it was not statistically different. Second, while the images of atherosclerotic plaques were classified as smooth surface plaques, irregular surface plaques, and ulcerated plaques under MSCTA, these features of the plaques were not confirmed through angiographic or pathologic methods.

Taken together, 256-MSCTA was applied in the present study to assess the morphology of carotid arterial plaques in 386 patients. Plaque ulceration was found in 11.05% of the carotid arteries, and 20.20% of the carotid artery plaque ulceration was on the ipsilateral side of cerebral symptoms, while 16.88% carotid artery plaque ulceration was on the contralateral side of cerebral event. These findings suggested that 256-MSCTA is an advanced imaging tool to determine not only arterial occlusion but also morphologic assessment of atherosclerotic plaques, which will benefit the patients by predicting the cerebral events in advance.

### Author contributions

Conceptualization: Ping-Yong Feng.
Data curation: Qiang Wang, Shan-Shan Shen.
Formal analysis: Qiang Wang, Shan-Shan Shen.
Writing – original draft: Pei-Pei Sun.

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### Table 3

| Plaque                  | Ischemic stroke |
|------------------------|-----------------|
|                         | Yes             | No              |
| Ularated               | 20 (28.99%)     | 49 (71.01%)     |
| Nonulcerated           | 69 (12.43%)     | 486 (87.57%)    |

OR = odds ratio.

### Table 4

| Carotid arterial plaque | Ulcerated | Nonulcerated |
|-------------------------|-----------|--------------|
| Symptom side            | 20 (20.20%) | 69 (77.53%)  |
| Contralateral           | 13 (16.88%) | 64 (83.12%)  |

P < .05
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