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

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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 (10.3%), 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.[2,3,5] 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 content, ulceration is a major pathologic process in the development of unstable plaques.[8,9] 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.[9–11] 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

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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 Brillancei CT (Philips) was used to scan from aortic arch to top of the outer auricle. Scanning parameters were as follows: tube voltage 120 kV, tube current 120 mA, width of the detector 128 mm × 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 (370 mgI/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 1 mm; 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 categorical 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.

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.

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 555 (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 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%)
P	>.05	

AmF = amaurosis fugax, TIA = transient ischemic attack.

Table 3

Contribution of plaque ulceration to the occurrence of ischemic stroke.

	Ischemic stroke	
Plaque	Yes	No
Ulcerated	20 (28.99%)	49 (71.01%)
Nonulcerated	69 (12.43%)	486 (87.57%)
	$P<.05$	OR=2.875

OR=odds ratio.

in 20 (20.2%) out of the 99 cases. Total 77 patients had carotid arterial plaques on the contralateral side of cerebral infarction, and 13 of them (16.9%) were ulcerated plaques. There was no significant difference between the 2 groups ($P=.576$).

4. Discussion

In this study, we quantified and characterized atherosclerotic carotid plaque with 256-MSCTA, and evaluated the association of plaque morphology and incidence of cerebral symptoms. We found that incidence of ulcerated plaque was higher in the patients with ischemic stroke than that in the patients with TIA or AmF, although there was no significant difference in the plaque ulceration between the groups. In addition, incidence of ischemic stroke was higher in the patients with ulcerated plaques compared with the patients without plaque ulceration. Majority of ischemic stroke occurred on the same side with the carotid arterial plaque.

Atherosclerosis is characterized by the deposition of extracellular lipids followed by migration of proinflammatory cells into the intimal layer of the arterial walls as well as the proliferation and migration of local smooth muscle cells.[13–15] The lipoprotein-driven atherosclerosis further leads to plaque formation at specific sites of the arterial wall through intimal inflammation, necrosis, fibrosis, and calcification. Although atherosclerosis can affect arterial walls in whole cardiovascular system, plaque is often focally distributed in the coronary tree and carotid arteries.[16,17] While some plaques regress and become less likely to result in clinical events, some plaques transform into advanced lesions with large lipid necrotic cores and thin fibrous caps, which can be ruptured to cause clinical events.[13,18–20] Therefore, prediction of a rupture before the event is a major diagnostic challenge. In this regard, the use of medical imaging to predict future cardiovascular or cerebrovascular event has been extensively investigated.[9–11,21,22] The present study demonstrated that 256-MSCTA could assess atherosclerotic carotid plaque surface morphology. It showed that plaque ulceration was associated with cerebral infarction and that ulcerated and irregular plaques were more frequently encountered in the patients with TIA or cerebral infarction.

Table 4

Comparison of ulcerated plaques on cerebral infarction side carotid arteries or contralateral arteries.

	Plaques	
Carotid arterial plaque	Ulcerated	Nonulcerated
Symptom side	20 (20.20%)	69 (77.53%)
Contralateral	13 (16.88%)	64 (83.12%)
P	>.05	

Advantage of the 256-MSCTA is fast scanning with less radiation and much clear image. In the present study, therefore, we used 256-MSCTA with 0.5 seconds rotating speed, 8 cm width detector, which allowed us to complete CTA scanning of carotid artery within 6 seconds and significant reduction of radiation exposure. The image-processing platform of the 256-MSCTA also allowed us to reconstruct the arteries 3-dimensionally (3D) and thus, a better quality and clearer 3D images of ulcerated plaques were obtained. Using this advanced equipment, we found that 69 out of 624 patients (11.05%) had ulcerated plaques, which was similar to the report by de Weert et al.[12] Of the 69 ulcerated plaques, 20 (28.98%) had ipsilateral symptoms of cerebral infarction, which was significantly higher than the 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

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References

[1] Li Q, Wu H, Yue W, et al. Prevalence of stroke and vascular risk factors in China: a nationwide community-based study. Sci Rep 2017;7:6402.
[2] Caplan LR. Diagnosis and treatment of ischemic stroke. JAMA 1991;266:2413–8.

[3] Warlow C, Sudlow C, Dennis M, et al. Stroke. Lancet 2003;362: 1211–24.
[4] Wang H, Pan Y, Meng X, et al. Validation of the mSOAR and SOAR scores to predict early mortality in Chinese acute stroke patients. PLoS One 2017;12:e0180444.
[5] Chen Z, Jiang B, Ru X, et al. Mortality of stroke and its subtypes in China: results from a nationwide population-based survey. Neuroepidemiology 2017;48:95–102.
[6] Stoll G, Jander S, Sitzer M, et al. Unstable carotid stenosis - an inflammatory disease? [in German]. Nervenarzt 2000;71:955–62.
[7] Hartkamp NS, Petersen ET, Chappell MA, et al. Relationship between haemodynamic impairment and collateral blood flow in carotid artery disease. J Cereb Blood Flow Metab 2017;271678X17724027.
[8] Flumignan CDQ, Flumignan RLG, Navarro TP. Extracranial carotid stenosis: evidence based review. Rev Col Bras Cir 2017;44:293–301.
[9] Rafailidis V, Chryssogonidis I, Tegos T, et al. Imaging of the ulcerated carotid atherosclerotic plaque: a review of the literature. Insights Imaging 2017;8:213–25.
[10] Dolega-Kozierowski B, Klimeczek P, Lis M, et al. An evaluation of dual source computed tomography used with the de Weert classification to detect vulnerable plaque, using IVUS virtual histology as a standard of reference. Adv Clin Exp Med 2017;26:123–8.
[11] Wang PQ, Wang Y, Zhang GB, et al. Study on the carotid atherosclerotic plaque of patients suffering from ischemic cerebrovascular disease by 64 slices CT. Eur Rev Med Pharmacol Sci 2015;19:3480–5.
[12] de Weert TT, Cretier S, Groen HC, et al. Atherosclerotic plaque surface morphology in the carotid bifurcation assessed with multidetector computed tomography angiography. Stroke 2009;40:1334–40.
[13] Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. Nature 2011;473:317–25.
[14] Meschia JF, Klaas JP, Brown RDJr, et al. Evaluation and management of atherosclerotic carotid stenosis. Mayo Clin Proc 2017;92:1144–57.
[15] Katsiki N, Mantzoros C, Mikhailidis DP. Adiponectin, lipids and atherosclerosis. Curr Opin Lipidol 2017;28:347–54.
[16] Kubo T, Maehara A, Mintz GS, et al. The dynamic nature of coronary artery lesion morphology assessed by serial virtual histology intravascular ultrasound tissue characterization. J Am Coll Cardiol 2010;55: 1590–7.
[17] Coolen BF, Calcagno C, van Ooij P, et al. Vessel wall characterization using quantitative MRI: what's in a number? MAGMA 2018;31: 201–22.
[18] Raber L, Taniwaki M, Zaugg S, et al. Effect of high-intensity statin therapy on atherosclerosis in non-infarct-related coronary arteries (IBIS-4): a serial intravascular ultrasonography study. Eur Heart J 2015;36:490–500.
[19] Pedrigi RM, de Silva R, Bovens SM, et al. Thin-cap fibroatheroma rupture is associated with a fine interplay of shear and wall stress. Arterioscler Thromb Vasc Biol 2014;34:2224–31.
[20] Calcagno C, Fayad ZA, Raggi P. Plaque microvascularization and permeability: key players in atherogenesis and plaque rupture. Atherosclerosis 2017;263:320–1.
[21] Stone GW, Maehara A, Lansky AJ, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med 2011;364:226–35.
[22] Cheng JM, Garcia-Garcia HM, de Boer SP, et al. In vivo detection of high-risk coronary plaques by radiofrequency intravascular ultrasound and cardiovascular outcome: results of the ATHEROREMO-IVUS study. Eur Heart J 2014;35:639–47.
[23] Fisher M, Paganini-Hill A, Martin A, et al. Carotid plaque pathology: thrombosis, ulceration, and stroke pathogenesis. Stroke 2005;36:253–7.
[24] Rothwell PM, Gibson R, Warlow CP. Interrelation between plaque surface morphology and degree of stenosis on carotid angiograms and the risk of ischemic stroke in patients with symptomatic carotid stenosis. On behalf of the European Carotid Surgery Trialists' Collaborative Group. Stroke 2000;31:615–21.