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FULL PAPER

Differentiation of chronic total occlusion and subtotal occlusion of the femoropopliteal artery—role of retrograde flow sign and collateral circulation on CT angiography images

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Objective: To study the value of a retrograde flow sign and the collateral circulation on CT angiography (CTA) for the differential diagnosis of chronic total occlusion from subtotal occlusion of the femoropopliteal artery (FPA).
Methods: 50 patients with obstruction of the FPA underwent CTA and digital subtraction angiography examinations of the lower limbs. The frequency of a retrograde flow sign and collateral circulation on CTA in chronic total and subtotal occlusion was noted and analyzed, with the results of digital subtraction angiography as a standard to judge total or subtotal occlusion. The decreasing CT value from the distal to proximal direction on CTA suggests the existence of retrograde flow.
Results: There were significant differences in the occurrence rates of a retrograde flow sign on CTA in the chronic total and subtotal obstruction groups (X^2 = 13.1, p < 0.05), as well as a collateral circulation sign (X^2 = 13.5, p < 0.05). Employing both the retrograde flow sign and the collateral circulation sign to diagnose chronic total obstruction of the FPA had a sensitivity of 92.3% and specificity of 89.8%.
Conclusion: The retrograde flow sign combined with a collateral circulation sign is of great clinical value for differentiation of chronic total stenosis from severe stenosis (subtotal occlusion) of the FPA.
Advances in knowledge: A retrograde flow sign combined with a collateral circulation sign is of great clinical value to differentiate between chronic total stenosis and severe stenosis (subtotal occlusion) of the FPA.

INTRODUCTION

Lower limb arteriosclerosis obliterans can cause chronic occlusion of the lower limb arteries, which can progress to gangrene and eventual death,[1] rendering treatment of this disease extremely necessary. The treatment of chronic total occlusions is quite different from that of subtotal occlusions of the femoropopliteal artery (FPA), as recanalization by interventional therapy of the former is often technically difficult and associated with a poor prognosis;[2] thus, differentiation between these two lesions is clinically important. Although this goal can be achieved by digital subtraction angiography (DSA) of the lower limb arteries, the invasiveness and expense of DSA inhibits its use as a first choice modality.[3] Initially, we attempted to distinguish the two on CT angiography (CTA) by observing the filling of contrast medium in the area of the lesion and distal portion of the obstruction, but failed due to two reasons. First, both chronic total and subtotal blocking of the FPA can prevent filling of contrast medium in the area of the lesion on CTA. Second, the portion of the artery distal to the occlusive lesion can be filled with blood because of the tiny blood flow passing through and collateral circulation bypassing the occlusive regions in chronic subtotal and total occlusions, respectively.[4] Despite this, for most cases of chronic total occlusion we found an interesting phenomenon: in a section of the arterial lumen distal and close to the obstructive lesion, the CT values decreased from the distal to proximal part of the lumen, which was opposite to normal blood flow in the FPA (referred to as a retrograde flow sign). We hypothesized that a retrograde flow sign is caused by collateral blood flow from the proximal to the distal end of the lesion in chronic total occlusion and then retrograde filling in the proximal direction. If this hypothesis is true, this sign together with the collateral vessels displayed on CTA strongly suggests total chronic occlusion rather than subtotal occlusion of the artery. The purpose of this study was to test this hypothesis.

METHODS AND MATERIALS

Patients

From January 2014 to October 2015, 140 cases of femoral and/or popliteal artery obstruction diagnosed in our hospital by CTA and DSA examinations before surgery were retrospectively reviewed. However, only a total of 50 patients were included in this study after eliminating those cases that met the following exclusion criteria: presence of supra-inguinal arterial lesions, multiple arterial lesions of the lower limbs, artery length from the distal end of the occlusion to the end of popliteal artery of less than 1.25 cm (three points were measured at 0.625 cm intervals) and a history of bypass surgery or stent implantation. The final study cohort included 35 males and 15 females with a mean age of 67.3 ± 7.8 years (age range, 31–85 years). The study protocol was approved by the Ethics Committee of our hospital and written informed consent was obtained from all 50 patients.

CT angiography examination

CTA was performed using a 128-slice CT scanner (Discovery CT750HD; GE Healthcare, Milwaukee, WI). Patients were scanned craniocaudally in the supine and foot first position. Non-ionic contrast medium (iohexol, 350 mgI ml^{-1}) was injected via the medial cubital vein with a power injector (Ulrich Medical, Ulm, Germany) at a flow rate of 4–5 ml s^{-1} for a total volume of 80–100 ml. Immediately thereafter, 50 ml of saline was infused at the same rate. The collimator width was 0.6 × 64.0 mm with a pitch of 0.85, reconstruction thickness and interval of 0.625 mm, voltage of 120 kV and current intelligent control (auto mA). The scanning of the whole lower limb artery was triggered automatically at 10 s after the attenuation threshold of the abdominal aorta reached 100 HU.

Digital subtraction angiography of the lower limb arteries

Within 2 weeks after a CTA examination, all patients underwent DSA examinations using a digital flat-panel angiography system (Innova 2100-IQ DSA; GE Healthcare). The best puncture site of the femoral artery was chosen based on the CTA images. Non-ionic contrast medium (iopromide, 300 mgI ml^{-1}) was injected with a power injector (Ulrich Medical) at a flow rate of 15 ml s^{-1} to show the bilateral common and external iliac arteries and lower limb arteries. For severe arterial stenosis, a catheter (5 Fr C2 Cobra) was placed in the proximal end of the stenosis and 6 ml of contrast agent was injected at a rate of 6 ml s^{-1} to display the lumen at and after the stenosis.

Image post-processing and measurement

DSA images were used for differential diagnosis of total from subtotal occlusion of the FPA. Total occlusion of the FPA was defined as interruption of lumen continuity and disappearance of anterograde blood flow. Subtotal occlusion was defined as severe stenosis of more than 99%, but with some tenuous anterograde blood flow. The collateral circulation vessels were defined as a direct communication between two ends of an occlusion via small collateral vessels.

The degree of arterial stenosis was calculated using the following formula: Severity of stenosis = (normal vessel diameter at the proximal end of the stenosis – vascular diameter at the stenosis)/normal vessel diameter at the proximal end of the stenosis ×100%.

Raw CT scan data were transmitted to an off-line workstation and reconstructed using the maximum intensity projection (MIP), volume rendering and multiplanar reconstruction techniques. Collateral circulation vessels were observed on MIP, volume rendering, multiplanar reconstruction and axial images. Calcification of bone and the arterial walls were erased from images using a subtraction technique with three-dimensional software.

The CT values of the lumen at three points were directly measured on axial images with a region of interest with an area of 2 mm^2 from the distal end of the occlusion to the end of the popliteal artery at an interval of 6.25 mm (10 scanning planes) with 10 HU or more considered a significant gradient of CT values. Calcification of the arterial wall was avoided when measuring CT values by using the CT value of the region of interest distal and close to the calcification. The decreasing CT values from the distal to proximal direction on CTA axial images suggested the existence of retrograde flow or a retrograde flow sign. Simultaneously, CT values of the contralateral FPA at the same levels of the pathologic measurement side were measured on axial CTA images and marked on MIP images for normalization and to exclude the effects of various factors slice by slice.

All CTA measurements and analyses were performed by two senior radiologists with more than 10 years of experience in vascular imaging and both were blinded to the DSA results. DSA images were analyzed by two interventional radiologists with more than 8 years of experience. The two senior radiologists consulted with each other if disagreement existed, as did the interventional radiologists.

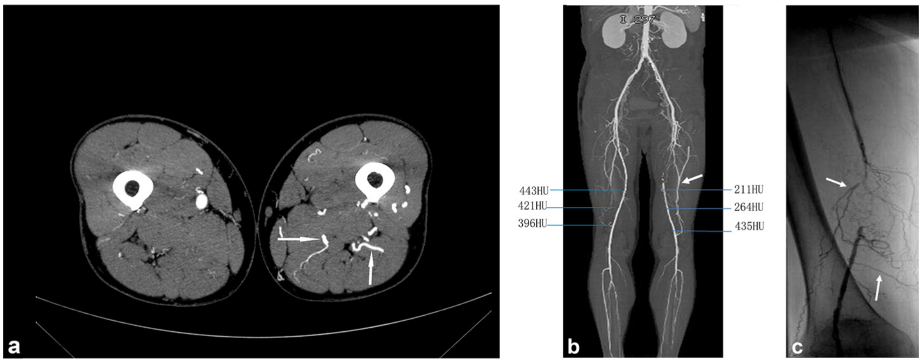
Statistical analysis

The chi-square test was used for all statistical analyses with SPSS software [v. 17.0; IBM Corp. (formerly SPSS Inc.)]. Two-sided probability (p) values less than 0.05 were considered statistically significant.

RESULTS

A total of 50 occlusive lesions were detected in 50 patients (Figures 1a–2c). DSA of the lower limb arteries confirmed chronic total occlusion in 26 cases and subtotal occlusion in 24 cases (Figures 1c and 2c). There was significant difference in the number of retrograde flow signs on CTA images between the chronic total occlusion group and the subtotal occlusion group [76.9% (20/26) *vs* 20.8% (5/24) cases, respectively, X^2 = 13.1, $p < 0.05$; Figure 1b]. Also, there was a significant difference in collateral circulation on CTA images between the two groups [80.8% (21/26) *vs* 29.2% (7/24), respectively, X^2 = 13.5, $p < 0.05$; Figure 1b]. Employing a retrograde flow sign to diagnose chronic total occlusion of the FPA had a sensitivity of 76.9% and specificity of 79.2%. Employing a collateral circulation sign to

Figure 1. (a) A 65-year-old male with total occlusion of left femoral artery. Axial CT angiography image showed no filling of contrast medium in the area of the occlusive lesion of the left femoral artery, but remarkable collateral circulation vessels can be seen (arrow). (b) The same patient as in (a). CT angiography showed an occlusive lesion of the left femoral artery and decreasing CT values from the distal to proximal direction (retrograde flow sign) in the lumen after the occlusion accompanied by collateral circulation vessels (arrow). The CT values were directly measured on axial images and labelled on the maximum intensity projection image. (c) The same patient as in (a, b). Digital subtraction angiography confirmed total occlusion lesion of the left femoral artery and surrounding collateral circulation (arrows).



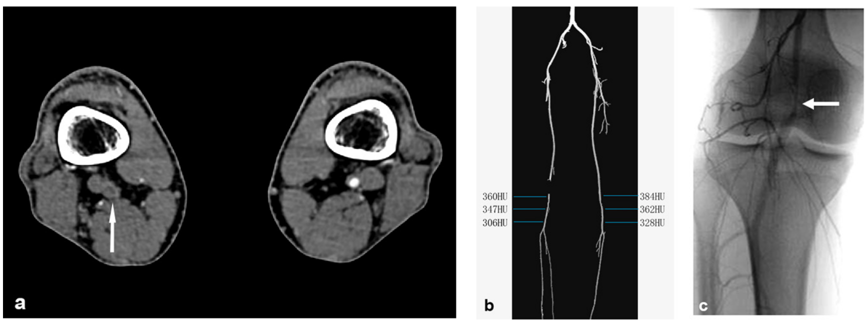
diagnose chronic total occlusion of the FPA had a sensitivity of 80.8% and specificity of 70.8%. There were no significant differences in sensitivity and specificity between the two signs (X^2 = 0.115 and 0.444, respectively, $p > 0.05$). Employing a retrograde flow sign together with a collateral circulation sign to diagnose chronic total occlusion of the FPA had a sensitivity of 92.3%, which was higher than the sensitivity obtained by using one of the two signs alone (X^2 = 8.59 and 5.18, respectively, $p < 0.05$) and specificity of 89.8%, which was also higher than the specificity obtained by using one of the two signs alone (X^2 = 4.62 and 11.5, respectively, $p < 0.05$).

DISCUSSION

Occlusion of a lower limb artery is most commonly seen in the FPA, which may be related to the anatomical and blood flow characteristics of these arteries.[5] At the distal end of FPA occlusion lesions, a retrograde flow sign (decreasing CT values from the distal to proximal direction on CTA axial images) is due to retrograde filling with contrast medium in the lumen of the artery. Retrograde collateral circulation causes the vessels distal to the occlusion site to be the first filled with contrast agent, and then the flow is reversed to the proximal side, causing a higher CT value in the distal than the proximal lumen at a distance below the occlusion.[6] In this article, we studied the value of retrograde flow sign and the collateral circulation on CTA for the differential diagnosis of chronic total occlusion from subtotal occlusion of the FPA. No similar study was found in the literature.

A retrograde flow sign was observed in 76.9% (20/26) of cases with total occlusion in this study, strongly suggesting chronic total occlusion. Even so, another six cases of total occlusion did not show this sign, but rather displayed anterograde flow. The reason for this exception may be that the collateral vessels directly connected the two ends of the occlusion site like a bridge, causing anterograde blood flow similar to a normal artery, instead of retrograde blood flow.[7] A second reason is the relative late phase of acquisition in which all segments distal to the occlusion have been filled by retrograde flow. So, the lack of a retrograde sign is

Figure 2. (a) A 58-year-old male with subtotal occlusion of the right femoral artery. An axial CT angiography image showing no filling of contrast medium in the area of the occlusive lesion (arrow) and no remarkable collateral circulation vessels are shown. (b) The same patient as in (a). CT angiography showed an occlusive lesion of the right femoral artery and decreasing CT values from the proximal to distal direction (anterograde flow) in the lumen after the occlusion without obvious collateral circulation. The CT values were directly measured on axial images and labelled on the maximum intensity projection image. (c) The same patient as in (a, b). Digital subtraction angiography confirmed subtotal occlusion of the right femoral artery with a thin narrow lumen (arrow) passing through the lesion area.



insufficient to exclude the existence of chronic total occlusion. However, the appearance of this sign strongly suggests the existence of retrograde collateral blood. The retrograde flow sign is useful with high specificity for the diagnosis of total FPA occlusion and for differential diagnosis from subtotal occlusion.

FPA chronic total occlusion can cause collateral vessels to open in order to ensure blood supply to the limb distal to the occlusion.[8] But, with subtotal occlusion, there remains a small amount of anterograde blood flow to supply the distal limb, thus collateral circulation is less likely to form or it is too small to be seen on CTA (Figure 2a–c).[9] Therefore, the collateral vessels on CTA images can be used to indicate total occlusion. In the present study, a collateral circulation sign along with a retrograde flow sign were employed to diagnose chronic total obstruction, which had a sensitivity of 92.3% and specificity of 89.8%.

In the subtotal occlusion group, 20.8% (5/24) of patients also showed a retrograde flow sign. Two reasons may be responsible for this. One is that some of these lesions were actually totally occluded at the time of CTA showing a retrograde flow sign, but were recanalized partially at the time of the DSA examination within 2 weeks afterward. Another simpler explanation for this is that the critical stenosis is haemodynamically significant enough such that blood reaches the peripheral vessel quicker via the collateral route than via the stenosis.

There were some shortcomings to this study that should be addressed. First, it was not possible to directly display the direction of blood flow on CTA images,[10] so decreasing or increasing CT values were used to judge the flow direction indirectly.[11] Second, the small sample size in this study may have influenced the accuracy of the results to some extent. Therefore, future studies with larger cohorts are needed to confirm the significance of a retrograde flow sign and collateral circulation sign.

CONCLUSION

A retrograde flow sign combined with a collateral circulation sign is of great clinical value for differentiation between chronic total stenosis and severe stenosis (subtotal occlusion) of the FPA.

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