The Egyptian Journal of Radiology and Nuclear Medicine (2013) **44**, 231–236

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

www.elsevier.com/locate/ejrnm
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ORIGINAL ARTICLE

Assessment of the distal runoff in patients with long standing diabetes mellitus and lower limb ischemia: MDCTA versus DSA

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Received 18 December 2012; accepted 19 February 2013
Available online 27 March 2013

KEYWORDS
DM;
Lower limb;
Ischemia;
CT;
Angiography

Abstract *Objective:* The purpose of our study was to evaluate the diagnostic accuracy of multidetector computed tomography angiography (MDCTA) in comparison with digital subtraction angiography (DSA) in patients with long standing diabetes mellitus and chronic lower limb ischemia.
Subjects and methods: One hundred patients with long standing DM and chronic limb ischemia underwent both CT angiography and DSA. The distal runoff of each lower limb was divided into 13 arterial segments. The status of each segment was graded as: 1, (normal or less than 10% stenosis); 2, (10–49% stenosis); 3, (50–99% stenosis); 4, occlusion. The effect of calcification on the diagnostic accuracy of CT angiography was evaluated. CTA findings were compared with DSA findings for each arterial segment. The sensitivity and specificity of CT angiography were determined using DSA as the gold standard.
Results: A total of 100 patients were included (mean age, 58 years; 70% men). The sensitivity and specificity of CT angiography were significantly affected by the degree of vessel wall calcification, and increase the need for additional imaging.
Conclusion: Vessel wall calcifications decrease the diagnostic accuracy of CT angiography in patients with long standing DM and peripheral arterial disease.

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Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

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1. Introduction

By the age of 60, approximately 3–6% of men have intermittent claudication related to lower extremity arterial occlusive disease (1).

About 20% of men and women with intermittent claudication have diabetes compared with 6% of those without intermittent claudication (2).

Atherosclerosis is the most common form of chronic peripheral vascular disease (1).

For patients with advanced occlusive disease, surgical treatment or angioplasty is a viable therapeutic strategy. The accurate vascular anatomic mapping of the sites and severity of disease is essential when planning such procedures.

The "gold standard", Digital Subtraction Angiography (DSA), is now more often used with therapeutic interventions rather than purely diagnostic studies. Catheter-based angiography is being replaced by computerized tomographic angiography (CTA) and magnetic resonance angiography (MRA) for carotid, renal, and peripheral vascular diagnostic examinations (3).

Computed tomographic (CT) angiography is increasingly used for diagnostic imaging in patients with peripheral arterial disease. The use of multi-detector row technology has resulted in shorter acquisition time, increased volume coverage, lower dose of contrast medium, and improved spatial resolution for assessing small arterial branches (3,4).

Many studies have shown an association between diabetes mellitus and the development of peripheral arterial disease (PAD). Overall, intermittent claudication is about twice as common among diabetic patients than among non-diabetic patients. PAD in patients with diabetes is more aggressive compared to non-diabetics. This is contributed to sensory neuropathy and decreased resistance to infection (5).

In one geographically defined population, almost 25% of patients undergoing lower extremity revascularization were diabetic (6).

The purpose of this study was to evaluate MDCT angiography with thin collimation compared with digital subtraction angiography (DSA) in the assessment of the distal runoff in patients with long standing DM in whom extensive mural calcification is expected to hinder accurate evaluation of distal run-off on CT angiography.

2. Patients and methods

2.1. Study design and patient selection

Permission to perform this prospective study was granted in the radiology and vascular surgery departments and the ethics committee of our institute. The study was carried out as a part of the vascular diagnostic workup for these patients.

Evolution of the idea has occurred at our radiology department meeting during discussion of MDCT Angiographic and DSA images of a case with long standing DM suffering from peripheral LL ischemia with excessive vessel wall calcifications at the infra-popliteal segment 1.

From January 2011 to September 2012, 100 consecutive patients were eligible for inclusion if they reported to have long standing DM and lower extremity ischemic manifestation (Table 1). Referral was based on medical history, physical examination as well as ABI measurements, vascular risk factors are given in Table 2. A careful history taking and examination were done to distinguish intermittent claudication from nonvascular causes that may mimic claudication (pseudoclaudication), especially in those patients in whom peripheral neuropathy is also frequent. An abnormal ABI (0.9 or less) was sufficient to make the diagnosis in a clinically appropriate setting.

Exclusion criteria were history of renal insufficiency and severe adverse reactions to iodinated contrast material.

The arterial tree of each lower limb was divided into 13 segments, these were the tibioperoneal trunk, ATA (proximal, middle and distal), PTA (proximal, middle and distal), peroneal artery (proximal, middle and distal), dorsalis pedis artery, medial and lateral planter arches. The following four-point scale was used to assign a grade of stenotic or occlusive disease. Grade 1 indicated (normal or < 10% luminal narrowing). Grade 2 indicated (10–49% luminal narrowing). Grade 3 indicated (50–99% luminal narrowing). Grade 4 indicated arterial occlusion. When two or more stenotic luminal lesions were detected in the same vessel segment, the most severe lesion was used for assignment of a grade. Planter arches and dorsalis pedis arteries were assessed only for patency or occlusions. Image quality was considered diagnostic if all diagnostic information were adequately obtained, non diagnostic if diagnostic information could not be obtained due to inadequate vessel opacification or haziness of the segment.

Patients were classified according to the degree of calcifications into four types, type I those with grade 0 with no or little vessel wall calcifications or diagnostic difficulty, type II with grade 1 calcification in whom calcifications affect less than 50% of the wall, type III with grade II calcifications which affect more than 50% of the vessel walls, type IV patients with grade III calcifications which circumferentially affect the vessel wall.

For image evaluation we reviewed the axial source images, together with the Multiplanner Reformats (MPR), Maximum Intensity Projections (MIP) as well as the Volume Rendering images (VR). All images were evaluated without knowledge of further work-up findings.

Table 1 Clinical presentation of lower extremity arterial disease in 100 patients.

Presentation	No.	%
Claudication [Rutherford grade I]	65	60
Rest pain [Rutherford grade II]	23	16
Tissue loss [Rutherford grades II and III]	12	15

Table 2 Vascular risk factors in the 100 patients.

Risk factor	No.	%
Diabetes mellitus	100	100
Hypertension	52	52
Cardiac	60	60
Hyperlipidemia	68	68
Smoking	45	45
Multiple risk factors	48	48

2.2. MDCT angiography

All MDCT angiography were done on 16 MDCT scanner (GE Bright speed, Milwaukee, Wisconsin, USA). Data were acquired craniocaudally with the following parameters: section thickness of (0.6 mm), with helical scan mode, table Pitch (0984:1 and 1.75:1, respectively), table movement (39.7 and 17, respectively), each patient received 120 mL of contrast material (Omnipaque 350, GE Healthcare Inc., Princeton, NJ) injected via the inserted canula at a rate of 5 ml/sec. using a compatible pump injector (Stellant D CT injector, MEDRAD). The acquired images were transferred to a nearby workstation for evaluation and computer post processing (advantage workstation, AW) with available software that allows the generation of MIP, MPR and 3D VR images.

2.3. Digital subtraction angiography

All MDCT angiography studies were done prior to the DSA with the maximum time between CTA and DSA being 23 days (average 10 days).

None of our patients exhibited changes in symptoms during the interval between the two examinations.

Digital subtraction angiography was performed using 4-French pigtail catheter using a right common femoral artery approach ($n = 65$) and a left common femoral artery approach ($n = 35$). Undiluted contrast material (Omnipaque 350, GE Healthcare Inc., Princeton, NJ) was used with an average contrast dose of 175 mL (range, 130–260 mL). In all cases, we obtained the posteroanterior view of the lower abdomen and the entire range of the lower extremities using the stepping-table digital subtraction angiography technique. All digital subtraction angiographic findings were evaluated on the films by the angiographer. Table 3 shows the pathological findings in all assessable segments.

3. Results

There were 100 patients, 70 men and 30 women with a mean age of 58 years (range 49–75), clinical presentation was lower extremity arterial diseases of variable degrees. Three patients had above knee amputation. All patients had diabetes mellitus.

The distal runoff of each limb was divided into 13 segments, this resulted in a total number of 2561 arterial segments covered by MDCTA including the assessable and non assessable segments. Of these 2561 segments, 136 (5.3%) segments were considered non assessable either due to timing problems, patient motion or metallic arthrodesis of the knee (causing blooming artifacts resulting in difficulty to assess arterial patency or degree of stenosis). Thus, the total number of arterial segments on MDCTA available for analysis was 2425 segments including the DP and planter arches.

The distribution of the non assessable segments on MDCTA was as follows: unilateral ATA in 10 patients (= 30 seg.), unilateral TPT in 18 patients (= 18 seg.), unilateral PTA in 8 patients (24 seg.), unilateral Peroneal artery in 4 patients (12 seg.), DP in 16 patients (10 bilateral = 20 seg. and 6 unilateral = 12 seg.), plantar arches in 8 patients (4 bilateral = 16 seg. and 2 unilateral = 4 seg.). Total = 136 segments.

Complete agreement between MDCTA and DSA was recorded in 1547 of 1929 segments (80%) Table 4. 382 (20%) lesions were interpreted discordantly Table 5. Of these the degree of stenosis was overestimated in MDCTA in 207 segments (10.7%). There were 175 segments (9.2%) in whom the degree of stenosis was underestimated on MDCTA.

Of the 1929 segments examined for stenosis and occlusions, we had 287 segments with grade 0 calcifications (14.88%), 296 segments with grade I calcifications (15.35%), 568 segments with grade II calcifications (29.45%) and 778 segments with grade III calcifications (40.33%). We calculated sensitivity, specificity, PPV and NPV for MDCT angiography in grading the abnormal segments (segments with stenosis and occlusions) using DSA as our gold standard.

For the runoff station and after analyzing the effect of calcification on the diagnostic performance of MDCT for grade 0 calcifications, sensitivity, specificity, PPV and NPV were 90%, 86%, 77.3% and 90%, respectively. For grade 1 calcifications, sensitivity, specificity, PPV and NPV were 88.1%, 77%, 80.4% and 74.1%, respectively. For grade 2 calcifications, sensitivity, specificity, PPV and NPV were 78.6%, 74%, 67.8% and 70% respectively. For grade 3 calcifications, sensitivity, specificity,

Table 3 Stenotic and occluded segments as detected by CTA and DSA.

	0 and < 10% (1)		10–49% (2)		50–99% (3)		Occlusion (4)	
	DSA	CTA	DSA	CTA	DSA	CTA	DSA	CTA
TPT	33	31	39	22		50	55	63
PTA prox.	36	42	36	45		52	58	
PTA mid.	32	26	41	30		78		5
PTA dist.	39	44	43	55		79	65	1
ATA prox.	31	29	41	26		50	55	
ATA mid.	34	28	39	23		82		
ATA dist	36	39	35	42		86		
Pero. prox	35	34	37	42		72		
Peroneal mid.	30	35	39	45		76		
Peroneal dist.	31	39	37	46		80		
DP	Patent				Occluded			
	DSA		CTA		DSA		CTA	
	95		85		47		57	
Planter arches	Patent				Occluded			
	DSA		CTA		DSA		CTA	
	200		180		154		174	

Table 4 Comparison of CT angiography with digital subtraction angiography using the four score of stenosis (not including the DP or the planter arches) = 1929 segment (because these evaluated only for patency and occlusion only).

Degree of stenosis	Degree of stenosis by CAT	Degree of stenosis by DSA
Normal or less than 10% stenosis	355 (17.88)	337/1929 (17.47%)
10–49% stenosis	368 (19.6)	387/1929 (20.6%)
50–99% stenosis	717 (36.65)	655/1929 (33.95%)
Occlusion	489 (25.88)	550/1929 (28.58%)

Table 5 Over and under graded pathology as detected by MDCT compared with DSA.

Degree of stenosis	Under graded on CTA	Over graded on CTA
Normal or less than 10% stenosis	17	27
10–49% stenosis	59	58
50–99% stenosis	34	89
Occlusion	65	33

Table 6 Effect of calcifications on the sensitivity and specificity of CTA.

	Grade 0 (%)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)
Sensitivity	90	88.1	78.6	71.4
Sensitivity	90	88.1	78.6	71.4
Specificity	86	77	74	67.3
+PPV	77.3	80.4	67.8	59
−PPV	90	74.1	70	66.2

PPV and NPV were 71.3%, 67.3%, 59% and 66.2%, respectively. Table 6 shows the effect of calcifications on the sensitivity, specificity, +ve PPv and −ve PPV.

4. Discussion

Diabetic patients are four times more likely than the general population to develop peripheral artery disease (7). Previous studies have shown high rates of foot ulcers and lower extremity amputations in PAD patients with diabetes as well as faster rates of PAD progression in patients with diabetes compared with patients without diabetes (8).

Digital subtraction angiography (DSA) is still used as the benchmark for peripheral artery disease evaluation. It provides high resolution imaging of the entire lower limb vascular tree and allows percutaneous vascular intervention at the same sitting.

Computed tomographic (CT) angiography is increasingly used for minimally invasive imaging of various vascular territories. The introduction of multi-detector row CT scanners has substantially improved CT angiography. It requires only venous vascular access and is an outpatient examination with a minimal risk. MDCT is now widely available and easily tolerated by most of the patients. It offers volume coverage, with decreased dose of contrast medium, decreased acquisition time and this is important in ill and emergency patients and in children, and improved spatial resolution for the assessment of smaller arterial branches, including the aortoiliac and lower extremity arteries.

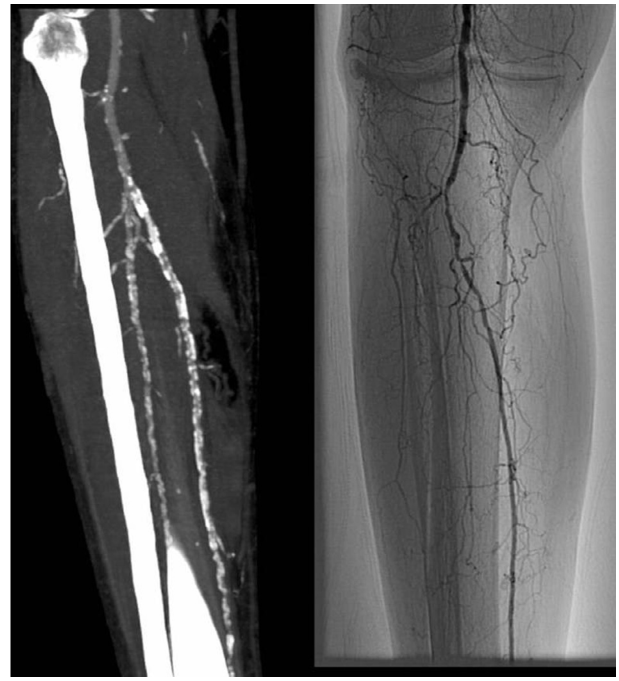

Fig. 1 A 65 year old male with right toe color changes. Coronal MPR image (a), shows heavy calcification (grade III) affecting the walls of the PTA (short arrows) and peroneal artery (arrowhead) with difficulty in judging the degree of pathology. DSA (b) shows complete occlusion of the peroneal artery and sever atherosclerotic changes of the PTA.

A disadvantage of MDCTA over DSA is the presence of heavy arterial wall calcifications, as the vessels often cannot be adequately evaluated due to partial volume and 'blooming' artifacts which typically lead to overestimation of the degree of stenosis. This applies particularly to the small caliber vessels below the level of the knee, and as estimated in the literature (9).

Color Doppler ultrasonography which is considered the initial imaging modality in patients with suspected peripheral arterial disease has its own drawbacks, it is operator dependent, grading the degree of stenosis can be problematic especially in obese patients or patients with calcified arteries. In addition, duplex US does not provide a road map equivalent to that obtained with conventional DSA, MR or CT angiography.

MR angiography (MRA) is a valuable technique in the assessment of arteries of the pelvis and lower limbs. This technique is non-invasive and requires no ionizing radiation. Access to MR remains limited and a significant minority of patients do not tolerate MRI.

We used the thinnest collimation possible for CTA because the diagnostic accuracy of stenosis grading (particularly for small vessels) is best with the thinnest section width.

In our study we focused on the distal runoff in diabetic patients because these vessels can represent a diagnostic dilemma because of their small caliber in addition to the frequent and heavy calcifications that can be found in these patients with long standing diabetes. Those types of patients were a matter of argument between us as radiologists and the vascular surgeons regarding the value of MDCT in examining the runoff of that type of patients, and whether to proceed directly to DSA especially if angioplasty is anticipated or to proceed to another non invasive procedure such as Doppler or MRA. From our experience, Doppler can have a damped role in such patients with extensive vessel wall calcifications. Not all patients can tolerate MRA.

Romano M. 2004 (10) evaluated twenty-two patients with peripheral arterial diseases and reported a sensitivity and specificity of 93% and 95%, respectively with an overall diagnostic accuracy of 94%, our results were inferior to their results, this is in our opinion attributed to the smaller sample in their study, also they estimated the overall sensitivity, specificity and accuracy, however in our study we calculated the sensitivity, specificity and accuracy for the distal runoff only and these are excepted to have inferior Figs. 1–3.

Arterial wall calcifications can be a serious problem in the visualization of the real lumen. Ouwendijk R. 2005 (11), found a significant change in diagnostic accuracy and interobserver agreement in arterial segments with calcifications than in segments without calcifications and that, in these cases, patients could not be treated without undergoing DSA for accurate evaluation.

In our study CT overestimated the degree of stenosis and occlusions in 207 segments, most of them were in segments affected by grade II and III calcifications and in high grade lesions (50–99%), and this resulted in a significant drop in the sensitivity and specificity of CT. Also CT angiography under graded 65 occluded segments and this can be explained by

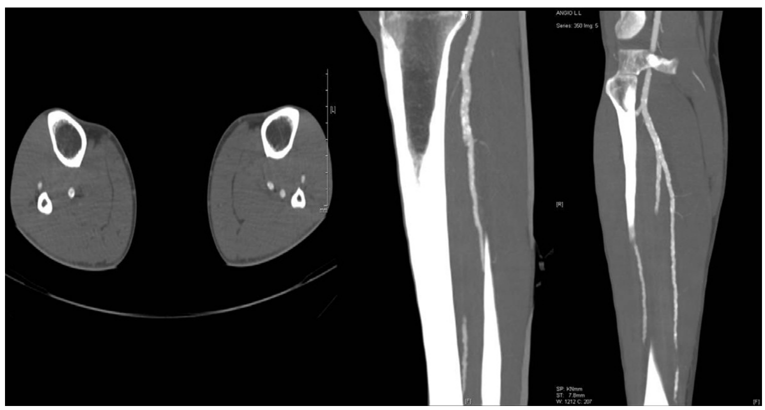

Fig. 2 A 52 year diabetic male patient with claudication pain. Axial (a), Coronal (b) and sagittal (c) MPR images show grade 2 and 3 calcifications affecting the tibioperoneal trunk (short arrows), PTA and peroneal arteries (arrowheads), with that degree of calcification, although the vessel is patent, it is not easy to grade the degree of stenosis with accuracy and whether it is hemodynamically significant or not.

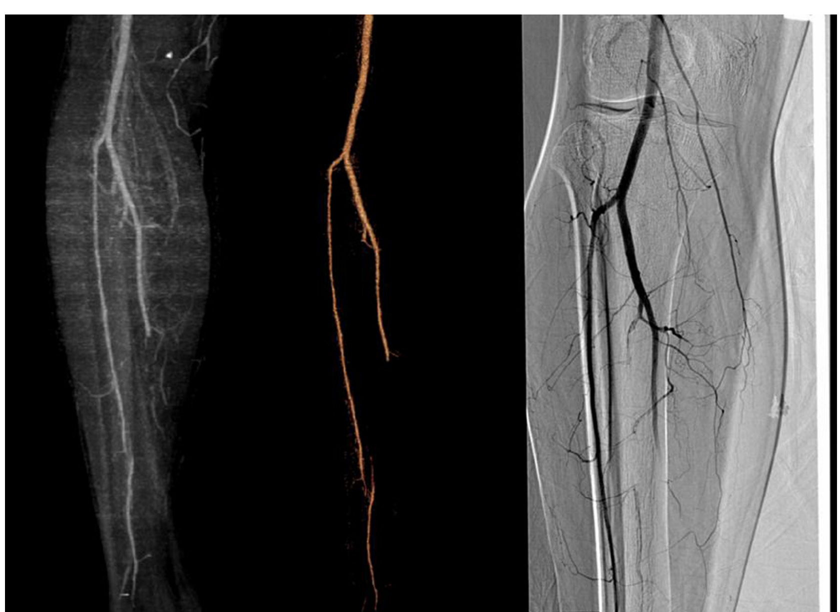

Fig. 3 A 58 year old patient with cold limb. Coronal VR images revealed grade 0 wall calcification with occluded proximal to two thirds of the peroneal artery (arrowhead) and the middle and distal thirds of the PTA (short arrow), DSA image (b) confirms the same findings.

the fact that these segments were assigned a grade III pathology (most of them were graded as subtotally occluded) but these were in fact diagnosed as completely occluded in DSA.

Hideki Ota. AJR 2004 (12), evaluated the effect of mural calcifications on the diagnostic performance of MDCT angiography, they stated that there is a significant negative effect in specificity and accuracy of MDCT, they reported a sensitivity of 95%, specificity of 89.7% and accuracy of 84.2%. In our study we found that calcifications affecting less than the whole circumference of the arterial wall did not significantly affect the accuracy of CT angiography in assessing the runoff vessels, however severe circumferential wall calcifications especially when continuous and in along segment can significantly affect the accuracy of CTA even with the use of "calcium removal software" that was available on our workstation.

Based on the results obtained in our series, it appears that CTA did not obtain sufficient data upon which surgical or intervention decision can be based in patients with heavy runoff calcifications. So in elderly patients and patients with long standing DM with lower extremity arterial diseases, MR angiography can be a good non invasive alternative imaging tool. Recent studies suggest the superiority of contrast-enhanced MR angiography over DSA for the identification of patent arterial segments in runoff vessels of the foot in both diabetic and nondiabetic patients (13).

Our study may have limitations such as the possibility of contrast induced nephropathy especially in diabetic patients, this proved more liable to occur in patients with high baseline renal function, these were excluded from our study, also careful monitoring of the renal function during the study was done by an experienced nephrologist and follow up renal function revealed no changes in the baseline renal function.

To the best of our knowledge, no similar studies are present in the literature evaluating the role of MDCT angiography in patients with lower limb ischemia and long standing DM.

5. Conclusion

The results of our study demonstrated that MDCT angiography found a significant change in diagnostic accuracy in arterial segments with calcifications than in segments without calcifications.

Author's contribution

All authors have approved the article and actively contributed in the work.

Ehab Ali Abd-ElGawad: image revision, data collection.

Mohamed A. Ibraheem: image revision, statistical analysis.

Laila Adel M. Samy: data collection, statistical analysis, final editing.

Ahmed M. Atyia: a vascular surgeon for patient assessment for imaging indication.

Mahmoud Ragab: a nephrologist for patient assessment before and after the procedure.

Funding statement

No disclosure of funding received for this work from any organization.

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