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ORIGINAL RESEARCH

Comparison of Doppler Ultrasound and Contrast Enhanced Magnetic Resonance Angiography against Digital Subtraction angiography in diagnosis of peripheral arterial occlusive disorder

[1]Dr. Sibi Eranki, [2]Dr. Deepak Chandra Reddy, [3]Dr. Anoop Kumar Nair, [4]Dr. Abhishek Mishra

[1]Classified Specialist, Radiology, Military Hospital Golconda, Hyderabad, Telangana, India
[2]Sr Advisor Radiology, Military Hospital Ambala, Haryana, India
[3]Graded Specialist, Radiology, INHS Patanjali, Karwar, Karnataka, India
[4]Classified Specialist, Radiology, Command Hospital, Udhampur, Jammu and Kashmir, India

Corresponding author
Dr. Abhishek Mishra
Classified Specialist, Radiology, Command Hospital, Udhampur, Jammu and Kashmir, India
Email: zoom.honey@gmail.com

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Abstract

Background: Peripheral arterial occlusive disease (PAOD) is acute or chronic occlusive arterial disease of the lower extremities, most often caused due to atherosclerosis. More than 70% of patients of PAOD of lower limbs are asymptomatic and this is the reason for requiring imaging modalities which are both sensitive and specific in diagnosing and staging the disease

Aim: This study has undertaken the comparison of the imaging modalities, doppler ultrasound (DUS) and contrast enhanced magnetic resonance angiography (CEMRA) against digital subtraction angiography (DSA), which is till now the accepted modality for diagnosis of PAOD.

Methods and Materials: Patients admitted as cases of critical limb ischaemia of lower limbs were taken up in the study. The imaging work-up for these patients included doppler ultrasound, CEMRA and DSA. Imaging was done from the infrarenal aorta and included arteries till the level of the ankle. For comparison purposes, arteries distal to and including the common iliac arteries were selected (9 arteries) and each artery was further divided into 3 segments (proximal, middle and distal thirds) for the purpose of the study.

Results: A total of 872 segments where DSA and doppler sonography could be compared and 866 segments where DSA and CEMRA could be compared. For a given grade on DSA, over-grading was done by doppler ultrasound in 78 segments and in 35 segments on CEMRA. Under-grading of the stenosis was done in 70 segments on doppler ultrasound and in 84 segments on CEMRA. There was a large overlap (both over and underdiagnosis) in the Grade 1 and Grade 2 stenosis in both modalities, however, presence and absence of stenosis was more accurately diagnosed on both modalities, when compared with DSA.

Conclusion: The findings of this study indicate that CEMRA is an accurate non-invasive modality for the detection and grading of PAOD, wherever the necessary equipment and expertise are available. Doppler ultrasound can be used for screening of the disease as well as for tailoring further diagnostic (DSA) and therapeutic procedures.

Keywords: Doppler Ultrasound, Contrast Enhanced Magnetic Resonance Angiography, Digital Subtraction angiography, Peripheral arterial occlusive disease

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Introduction

Atherosclerosis is the leading cause of death and disability in the developed world and the rates are increasing in developing countries as well due to the changing lifestyles[1]. Arterial occlusive diseases resulting from atherosclerosis are a varied group of both acute and chronic clinical conditions resulting from the atherothrombotic occlusion of the arterial system. Coronary heart disease, stroke and lower limb ischaemia are the prime clinical forms of arterial occlusive disease. Of these Peripheral Arterial Occlusive Disease (PAOD) has a prevalence in the range of 3% to 10%, increasing to 15% to 20% in persons over 70 years in several epidemiologic studies.[2,3,4] Also, the incidence of arterial disease is very high amongst asian Indians.[3] Sedentary life style, unhealthy cooking and eating habits and lack of exercise and smoking unmask the risk of atherosclerotic disease in Indians[5,6,7].

More than 70% of patients of PAOD of lower limbs are asymptomatic[8, 9] and this is the reason for requiring imaging modalities which are both sensitive and specific in diagnosing the disease. Vasculogenic claudication is the most common symptom with which patients of PAOD present[10]. Diligent history taking with emphasis to identify risk factors like smoking, sedentary habits and other co-morbid conditions like hypertension, diabetes mellitus and dyslipidemia is important.

This study has undertaken the comparison of the imaging modalities, doppler ultrasound and (CEMRA) against DSA which is till now the accepted modality for diagnosis of PAOD.

Methods and Materials

Study Design: Prospective comparative study.

Place of study: The study was carried out at two tertiary referral centers with a large out-patient load.

Sample population

All patients of peripheral vascular disease being evaluated on outpatient or inpatient basis during study period were included in the study if fulfilling the inclusion criteria and willing to take part in the study.

Inclusion criteria

a) Patients having symptoms of vascular claudication and/or rest pain or have tissue loss with or without pre-gangrene or gangrene and satisfying the diagnostic criterion for critical limb ischaemia (CLI).
b) Patients giving informed consent for inclusion in the study.

Exclusion criteria

a) Patients with contraindications for magnetic resonance imaging or use of iodinated contrast media.
b) Patients who are diagnosed as acute limb ischaemia on the initial imaging modality and requiring immediate surgical intervention.
c) Patients with prior endovascular/graft treatment for the disease with alteration in the native vascular anatomy.

Patient selection

The patients were initially referred from the surgical outpatient department for doppler evaluation. The initial inclusion criterion was to confirm presence of vascular claudication and

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then to assess for critical limb ischaemia. If the patient has any of the symptoms/signs of CLI (rest pain, tissue loss, pre-gangrenous or gangrenous changes in the limb), the patient was included as a possible case for the study. Written informed consent for the whole procedure was taken from the patients to participate in the study.

Clinical evaluation and further investigations

General information, symptomatology and clinical criteria for inclusion in the study were noted for all cases including brief clinical history and presence of other co-morbid conditions (history of smoking, diabetes, hypertension, coronary or cerebral arterial disease, renal insufficiency, dyslipidemias and nephrotoxic drugs) was also noted.

Following the doppler evaluation, in concurrence with the treating surgeon, an appointment for MRI and DSA are given to the patient. Serum creatinine and blood urea levels were evaluated for all patients before the DSA and CEMRA examinations. A cut-off of 45mg% for blood urea and 1.4 mg% for serum creatinine were set, patients with values higher than this were not taken up for the post-contrast examinations and were not included in the study.

Both CEMRA and DSA were performed within 7 days of the doppler examination in all the cases finalized for the study. The sequence of the examinations depended on the availability of table time in MRA unit and the DSA unit. However, in most circumstances, the CEMRA preceded DSA. This enabled the interventional radiologist to perform angioplasties after the diagnostic study in a single sitting.

Imaging

The imaging work-up for the patients included Doppler ultrasound, digital subtraction angiography and contrast enhanced MR angiography. Imaging was done from the infrarenal aorta and included arteries till the level of the ankle. For comparison purposes, arteries distal to and including the Common iliac arteries were selected.

The arterial segments which were evaluated were - common iliac artery (CIA), external iliac artery (EIA), common femoral artery (CFA), superficial femoral artery (SFA), deep femoral artery (DFA) or profunda femoris, popliteal artery (PA), anterior tibial artery (ATA), posterior tibial artery (PTA) and deep peroneal artery (DPA). These arteries were further divided into three arbitrary segments into proximal, middle and distal thirds for ease of assessment. Thus, in each case, a total of 27 segments were evaluated on each imaging modality and compared.

The grading of the stenosis was done as follows in all imaging modalities:

a) Grade 0 – normal vessel
b) Grade 1 - < 50% stenosis
c) Grade 2 – 50 to 99% stenosis
d) Grade 3 – 100% stenosis or complete occlusion

The doppler ultrasound examinations were performed on Logiq P5 premium (GE Healthcare, Chicago, IL, USA), CEMRA was performed on a 1.5 Tesla machine (MagnetomSymphony, Siemens Healthcare, Erlangen, Germany) and DSA was done at interventional center of the institution (Philips Integris Angiography Suit, Philips Medical Systems, Best, The Netherlands).

Sample Size

Assuming a 30% prevalence of stenotic lesions for each segment (as noted in previous studies), for significance level (α) of 5% and a power (β) set to 95%, the sample size was calculated to 385. The total number of segments assessed were more than the required sample size in both limbs of the study.

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Statistical Analysis

All the tabulations were done on microsoft excel sheet and the statistical formulae were keyed into the individual Excel sheets. The relevant statistical parameters were calculated using twoway contingency tables and online SSP calculator (www.socscistatistics.com/tests/chisquare2/default2.aspx).

Results

General Attributes

In our study, the number of cases included was 34 (all males) with an average age of 55 years. All patients were current or reformed smokers or consumed tobacco in one form or the other.

Vessel segments

Of the 34 cases, one case had a below knee amputation and one had an above-knee amputation. These arterial segments were therefore not available for interpretation during the current study. One patient had complete occlusion of the distal CFA and SFA over a long segment and contrast angiography was not possible in this case. One case had significant venous contamination of the distal vessels on the CEMRA with uninterpretable images and they were excluded from inclusion in the statistical analysis. For the final tabulation and comparison, there were a total of 872 segments where DSA and doppler sonography could be compared and 866 segments where DSA and CEMRA could be compared

Normal and diseased segments

Of the total segments, Grade 0 was given to 609 segments on DSA, 634 segments on CEMRA and 605 segments on doppler ultrasound. Eighty-one segments were given a grade 1 on DSA while, CEMRA and doppler ultrasound had 92 and 83 segments in this grade. Grade 2 was given to 43 segments on DSA, 26 segments on CEMRA and 40 segments on doppler ultrasound. There were 139 segments graded as 3 on DSA, 114 on CEMRA and 144 on doppler Ultrasound.

Statistical analysis

For the entire arterial tree, compared with DSA, the sensitivity, specificity and accuracy of Doppler ultrasound were 70.4%, 87.7% and 83.0%. This meant a positive predictive value of 68% (95% CI = 62 to 73%) and a negative predictive value of 88.8% (95%CI = 86.1 to 91%). For the same region, the sensitivity, specificity and accuracy of CEMRA were 66.1%, 94.3% and 86.0%, respectively, with a positive predictive value of 82% (95% CI = 76 to 87%) and a negative predictive value of 87.4% (95%CI = 84.7 to 90%). If only presence or absence of stenosis (or occlusion) was considered, doppler ultrasound had a sensitivity, specificity and accuracy of 81.7%, 91.5% and 88.5% with a positive predictive value of 80% (95% CI = 75 to 84%) and a negative predictive value of 92.0%(95%CI – 89.7 to 94%). Similarly, for CEMRA, the sensitivity, specificity and accuracy were 80.2%, 95.7% and 91.1% with a positive predictive value of 88.7% (95% CI = 84 to 92%) and a negative predictive value of 92.0%(95%CI – 89.7 to 94%). Chi-Square calculation with a 4 x 3 contingency table and a significance level of .05 results in a p-value of .123 implying the result is not statistically significant at $p < .05$.

Table 1: Grade-wise distribution for doppler ultrasound Vs DSA and CEMRA

	DSA	CEMRA	DUS
Grade 0	609 (617.42) [0.11]	634 (613.17) [0.71]	605 (617.42) [0.25]
Grade 1	81 (85.53) [0.24]	92 (84.94) [0.59]	83 (85.53) [0.07]

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Grade 2	43 (36.42) [1.19]	26 (36.17) [2.86]	40 (36.42) [0.35]
Grade 3	139 (132.64) [0.31]	114 (131.72) [2.39]	144 (132.64) [0.97]
Column Totals	872	866	872

Case 1: Fifty-seven years old male patient with claudication pain in right gluteal region and in right lower limb.

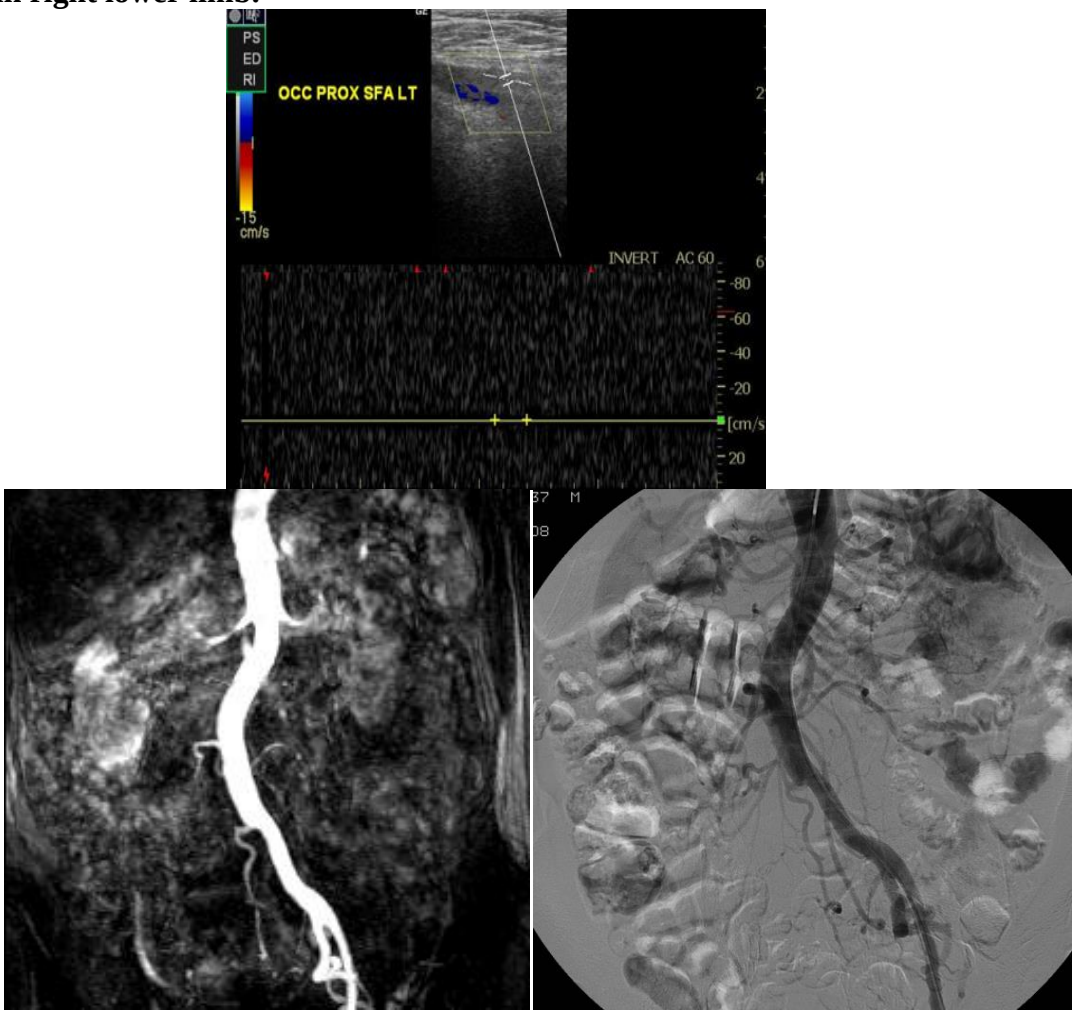

Fig 1a: Doppler ultrasound image at the right common iliac artery revealing complete occlusion of the vessel with no flow signal seen. Fig 1 b and c are the corresponding CEMRA and DSA images showing complete occlusion of the right common iliac artery (black solid arrow) at the origin with normal course and caliber of the left common and external iliac arteries.

Case 2: Forty-five years old male patient with claudication and pregangrenous changes in left lower limb. Clinically, all pulses distal to proximal SFA were not palpable.

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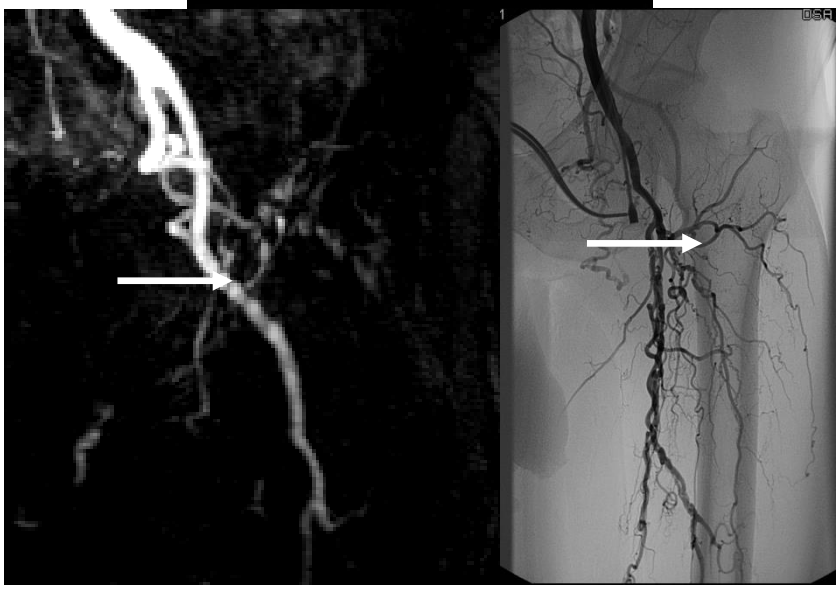

Fig 2 b. **c.**

Fig 2 a: Colour Doppler image showing a normal caliber CFA with complete occlusion of the SFA on the left side. The flow in the profunda femoris (labeled DFA) is present.
The CEMRA (Fig 2 b) as well as the DSA (Fig 2 c) for the thigh region show normal course and caliber of the common femoral and the profunda femoris arteries and complete occlusion of the left superficial femoral artery (solid white arrow).

Case 3: Twenty-seven year old with claudication in left calf.

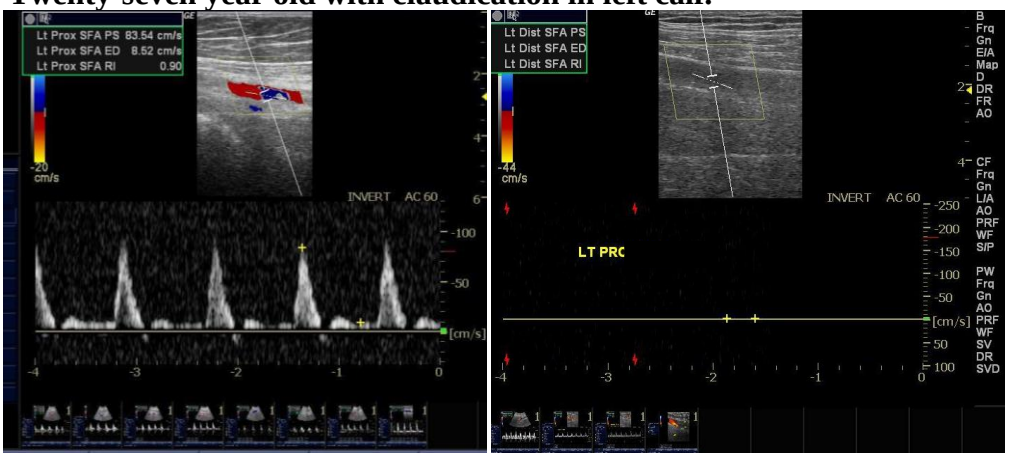

Fig 3 a. **3 b.**

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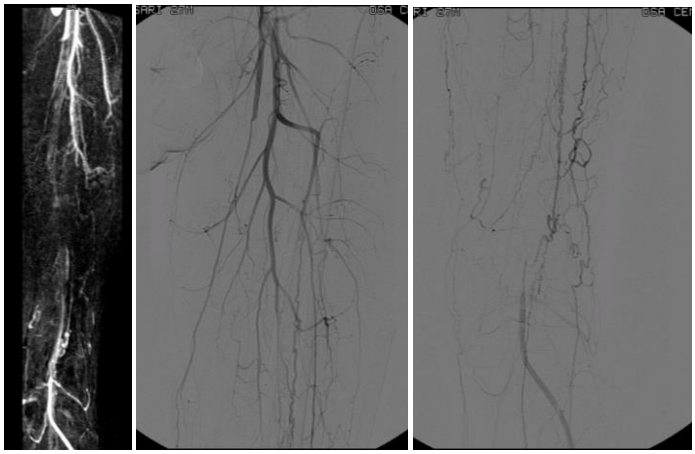

Fig 3 c. d. e.

Fig 3: The doppler ultrasound images for the left thigh region show normal triphasic waves in the proximal SFA (Fig 3 a) and complete occlusion of the left distal SFA (Fig 3 b). The corresponding CEMRA (Fig 3 c) and DSA (Fig 3 d and e) also show the same findings. Also noted is reformation of the distal SFA from collateral vessels arising from the left DFA.

Discussion

In many hospitals all over the world, doppler ultrasound and CEMRA are now used as non-invasive or minimally invasive alternatives to diagnostic intra-arterial DSA for the detection and grading of PAOD and for treatment planning. These modalities are desirable because they might avoid diagnostic intra-arterial DSA, a more expensive procedure that is associated with possible local or systemic complications. [10] However, both duplex US and MR angiography have limitations, and only a few studies have been done comparing accuracy of duplex US versus contrast-enhanced MR angiography for the detection PAOD.[11]

If revascularization is being considered, most centers use DUS as the initial imaging modality, which is sometimes followed by digital subtraction angiography (DSA) (90). Only a few centers use CEMRA angiography as the initial imaging modality for detecting stenoses in patients with PAOD.[12]

Marianne de Vries and Rody Ouwendijk, et al in their Multicenter Randomized Trial on the clinical and cost comparisons between DUS and Contrast Enhanced MR Angiography found that replacing DUS with contrast-enhanced MR angiography for the initial imaging work-up of patients with PAOD reduces the need for additional imaging and has higher therapeutic confidence, although diagnostic costs are higher.[13] In addition to avoiding radiation exposure and use of intravenous nephrotoxic agents, Rolf W. Huegli and Markus Aschwanden et al have observed that the 3 dimensional vascular delineation of the arterial tree and the bone and soft tissue contrast are much better in case of MR angiography than DUS. The main limitation according to this study was artifacts in the MR angiography produced by venous contamination which could be as high as 12% of total imaging.[14]

In a meta-analysis of CEMRA and colour doppler ultrasound, Karen Visser and Myriam Hunink (2000) found that the pooled sensitivity of CEMRA (97.5%) was higher than that of duplex US (87.6%) with similar pooled specificities (CEMRA = 96.2% and DUS = 92.7%). They found that gadolinium enhanced MRA had better discriminatory power than DUS and is highly sensitive and specific method, as compared to peripheral angiography for the work-up of peripheral vascular diseases.[15]

Compared with all the above-mentioned studies, the present study had some critical differences. Instead of considering the whole of the arterial segment for evaluation, three arbitrary divisions were made within the same artery. This resulted in evaluation of a much

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larger number of arterial segments per patient/case for better comparison of the imaging modalities.

In the present study, both DUS and CEMRA have good negative predictive values (duplex ultrasound = 89% and CEMRA = 87%) and these imaging techniques can be used as screening modalities. Although higher negative predictive values are required for any screening modality, the radiologist can take help from clinical evaluation of the case and absence of significant disease can be ruled out by these modalities in a large number of cases. The results of the present study corroborate the findings of the meta-analysis performed by Visser and Hunink, in which CEMRA was found to have greater discriminatory power over duplex US in the work-up of patients with PAOD.[15] The sensitivity and specificity of CEMRA was high in the iliac region with accurate identification of all the grade 2 or grade 3 stenosis in the current study as compared with DSA and definitely more than Duplex ultrasound. The overall lower sensitivity of CEMRA (and particularly the distal vessels) could be attributable to two causes, venous contamination (most commonly the paired calf veins) and inappropriate timing of the contrast study after administration of gadolinium contrast.

In view of the results of the current study, the use of CEMRA as a primary imaging work-up examination for PAOD in hospitals that have the necessary expertise and equipment is justified. In the event that contrast-enhanced MR angiography reveals equivocal findings, targeted DUS of lesions of questionable severity can then be performed before proceeding to intraarterial DSA or directly visualized during DSA. In this context, it should be mentioned that not every patient is a suitable candidate for contrast-enhanced MR angiography because of various contraindications. DUS, though is less sensitive than DSA and CEMRA, has low running costs, safety profile and possibility to repeat the examination any number of times. In the Indian scenario, where cost is a major consideration in choosing appropriate diagnostic modality, DUS will have greater role than CEMRA in the current clinical practice.

Conclusion

In conclusion, the findings of this study indicate that CEMRA is highly accurate for the detection and grading of PAOD, given that the necessary equipment and expertise are available. Doppler ultrasound can be used for screening of the disease as well as for tailoring further diagnostic (CEMRA or DSA) and therapeutic procedures. Due to higher negative predictive value and the potential capability to yield inflow and outflow information, we believe that CEMRA will have an increasingly important role in the diagnostic work-up of suspected PAOD.

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