COMPARATIVE STUDY OF CHRONIC LOWER LIMB ULCERS USING MULTIPLE IMAGING MODALITIES

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The purpose of this study is to assess the usefulness of non invasive imaging in patient of lower limb ulcer and determine the severity and extent of lower extremity arterial disease in these patients. The present study is based on 30 patients with complaint of non healing ulcer of lower limb of more than 6 weeks duration. The patients were subjected to plain radiographs and color flow imaging and MR angiography. The patients were categorized according to age and grade of ulcer was determined with Wagner's criteria. The limited number of cases 30 in the present study and MRA non contrast enhanced at 0.2 T is major limitations of this study. However in view of observed evidence plain radiographs and color Doppler evaluation plays an indispensable role in imaging and evaluating patients with chronic non healing ulcer. MRA can be tailored especially in poor patients which are economically constrained. It gives crucial information regarding favorable parameters like vascularity, degree of stenosis and extent of disease.

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1. Introduction

Vascular ulcers are a common cause of surgical consultation. These vascular ulcers are more common in diabetics. For vascular surgeons, only painful extremities and swollen legs are more likely to trigger a consultation. The great majority of vascular ulcers are chronic and/or recurrent. They cause a considerable amount of morbidity among patients with peripheral vascular disease, including work incapacity. The burden placed on the patient and the health care system due to the care of chronic vascular ulcers is significant. Additionally, these non healing ulcers place the patient at much higher risk for lower extremity amputation. Chronic leg ulcers typically manifest as arterial, neurotrophic or venous ulcers. They are distinct with regard to their location, appearance, bleeding, and associated pain and findings [1-3].

Normal wound healing process can't be accelerated, though it's course might be altered by a few physical, physiological and pathological factors. Various imaging techniques have been tried at times to evaluate a healing wound. But it has been slowly realized that imaging is unlikely to play a primary role in this field. Still, looking into the useful information imaging provides, at times a short review is made.

The present study is an effort to evaluate the role of non invasive imaging modalities in patient presenting with chronic non-healing (> 6 weeks duration) lower limb ulcers, and to demonstrate the usefulness of these modalities individually and in comparison to other imaging modalities used. Lower limb ulcers will be categorized, and severity of ischemia will be assessed. Pertinent physiologic abnormality like plaques, thickening of arteries, thrombus, venous incompetence will be identified.

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2. Material and methods

The present study is based on 30 patients in Sir Sunderlal Hospital, who were referred to Department of Radiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi with complaint of non healing ulcer of lower limb of more than 6 weeks duration.

1. Plain radiographs
2. Duplex scanning with color flow imaging
3. MR angiography (selected cases)

Plain Radiographs

The patients were subjected to plain radiographs with GE (Elpro) 300 M.A. - LL at setting of 40-50 Kv and 8-10 mAs. Radio graphs obtained for leg and foot in anteroposterior (AP), oblique and lateral projections. The radiographs were examined for vascular calcifications, osteomyelitis, bone destruction, deformities, complications and soft tissue abnormality.

Duplex Scanning with color flow imaging

The examination begins with the patient lying supine on the couch. In decubitus position, the adductor canal is scanned, popliteal artery to bifurcation, and scanning of posterior tibial and peroneal arteries is completed. In supine position the anterior tibial arteries are scanned. Further in this position the dorsalis pedis artery is traced and also the plantar arteries. The posterior tibial artery is usually the easier of the two branches of tibio peroneal trunk to locate. It can be located by placing the transducer in a longitudinal position on the medial aspect of mid calf area behind the tibia and then followed up down the calf. Peroneal artery runs more deeply down the calf than the posterior tibial artery closer to the posterior aspect of tibia and interosseous membrane. It can be examined either by a posteriomedial or antero lateral approach. Anterior tibial artery is examined from an anterolateral approach. The anterior tibial artery lies on the membrane and can be located using color flow in either longitudinal or transverse plane. The dorsalis pedis may be examined in front of the ankle joint before it passes deep to the metatarsals.

We used GE Logic 400; 5-10 MHz linear array transducer depending upon the need and build of the patients.

The following points were observed and noted,

1 Vascular calcification, thickening of arteries, presence of plaques
2. Spectral waveforms were obtained
3 Presence of collaterals
4. Vascularization at ulcer area
5. Bone destruction
6. Soft tissue morphology (eg. cellulitis)
7. Venous reflux, varicosities, valve incompetence
8. Any other findings

MR angiography

MR angiography (selected patients) one third patients (11) were scanned with 0.2 Tests GE-SIGNA profile-I 7.70 version permanent magnet system with dedicated body coils installed in our department. Lower limb vessels were visualized using FSPGR sequences in contiguous axial planes with TR/40 and TE/12. No contrast enhancement was used. In few cases gradient echo sequences (GRE) were obtained to characterize bony features.

A note was made of following features

1) Subjective caliber of vessels
2) Presence of stenosis
3) Varicosities or venous malformations
4) Soft tissue abnormalities

The patients were categorized according to etiology and age and duration of ulcer were noted. A special note was made of grade of ulcer in patients presenting with diabetic foot ulcer. All patients were subjected to plain radiographs and Duplex scanning with Color flow imaging. Eleven patients were additionally subjected to Magnetic Resonance Imaging (MRI). A comparison of findings between Doppler indices and findings of MRI were contemplated.

Statistical Analysis

The data obtained in this study were analyzed with SPSS 11.5 Software for mean, standard deviation and Pearson's chi square test. *P* value <0.05 was considered to be statistically significant.

3. Results

A prospective study of 30 patients who presented with complaint of non-healing lower limb ulcers (> 6 weeks duration) was taken up for plain radiographs and Duplex study evaluation. Eleven patients were subjected to MRI examination. The number of male patients was 24 and female was 6. The mean age of the patients are 54.43 ±15.35 in years

The age distribution revealed maximum incidence of non healing ulcer in the fourth and fifth decades (43.3%) followed by sixth and seventh decade (40%). The youngest patient was 22 years old and oldest being 82 years of age.

Patients who presented with ulcers of lower limbs including foot ulcers of more than 6 weeks duration were subsequently subjected to non invasive imaging modalities including MRI where possible. The mean duration of ulcers was 17.50 ± 11.00 months.

Table 1. Duration of ulcers (in months) with respect to specific etiology.

Etiology	Age Group					Total
	< 6	6-12	12-18	18-24	> 24	
Buerger's Disease	0	0	0	0	1	1
Squamous cell Carcinoma	0	0	0	0	1	1
Diabetic ulcer	3	6	4	3	3	19
Leprotic ulcer	0	3	1	1	0	5
Varicose ulcer	1	1	0	1	0	3
Venous malformation	0	0	0	0	1	1
Total	4 13.3%	10 33.3%	5 16.7%	5 16.7%	6 20.0%	30 100%

However, other cases of varicose ulcer, squamous cell carcinoma, Buerger's disease and venous malformation did not show arterial calcification. Here it must be pointed out that Duplex scanning was able to pick up arterial calcification in extra 5 cases of diabetic foot ulcer as calcified plaques and focal calcification and 2 cases of leprotic foot ulcer, hence as compared to plain radiographs. Doppler proved to be more sensitive in picking up calcified plaques and focal calcification. Majority of patients with diabetic foot ulcer (52.63%) and leprotic ulcer (60%) had positive plain radiograph findings.

Doppler Study Evaluation

Doppler study proved to be the most useful modality in terms of holistic information regarding lower limb ulcers. It was very useful in picking up arterial stenoses, pre and post stenotic waveform changes and abnormal spectral waveform. It was also useful in assessing vascularity in the region of ulcer area as well as formation of collaterals. Calcifications, arterial or dystrophic, focal plaques were identified. Changes like subcutaneous thickening, bony destruction, venous congestion and neo angiogenesis were noted.

Thus, conventional B scan with Doppler (duplex scanning) complemented with colour flow imaging was 100% sensitive in depicting changes according to different etiologies. For example in case of Buerger's disease arterial stenosis as well as bony destruction was demonstrated. In case of diabetic ulcer, vascularity, ischemia, stenosis, subcutaneous thickening, cellulitis was shown. Congenital venous malformation showed abnormal venous channels. Varicose ulcers showed tortuous varicosities and features of venous stasis and incompetent valves. Direct measurement of a stenosis is often not possible in the lower limb and severity of stenosis must then be estimated from indirect parameters. The changes in peak systolic velocity (PSV) have been put forward for assessment of stenosis. Various criteria have been put forward for assessment of lower limb arterial stenosis, Cossman *et al* method has been applied in this study [4].

Table 2. Doppler indices verses peak systolic velocity in various etiological groups.

Etiology	**Peak Systolic Velocity**				**Total**
	0	**1.5-2**	**2-4**	**>4**	
Buerger's	0	0	0	1	1
Carcinoma	1	0	0	0	1
Diabetic	0	4	9	6	19
Leprotic	5	0	0	0	5
Varicose	3	0	0	0	3
Venous malformation	1	0	0	0	1
Total	10 (33.3)	4 (13.3)	9 (30.0)	7 (23.3)	30 (100.0)

Majority of patients belong to diabetic foot ulcer hence the grade of ulcer (Wagner *et al*) was compared with severity of stenosis (Cossman *et al*) [4, 5].

Table 3: Diabetic Foot Ulcer grade compared with peak systolic velocity (N=19).

Count	Peak Systolic Velocity			Total
	>4	1.5-2.0	2.0-4.0	
Grade II	0	3	4	7
Grade III	3	1	5	9
Grade IV	3	0	0	3
Total	6	4	9	19

MRI observations were possible in eleven cases out of thirty in this study. Out of which, 5 were of diabetic foot ulcer, 2 patients of leprotic ulcer, one of Buerger's disease and one each of varicose ulcer, squamous cell carcinoma and congenital venous malformation.

Table 4: MRI observation compared with Doppler.

Etiology	**MRI Vs Doppler**	
DF Ulcer	+	+
DF Ulcer	+	+
DF Ulcer	+	+
DF Ulcer	-	+
DF Ulcer	-	+
Leprotic ulcer	+	+
Leprotic ulcer	+	+
Buerger's	+	+
Varicose	+	+
SCC	+	+
CV malformation	+	+

MRI observations were not very useful in picking up early arterial stenosis, or collaterals, as compared to Doppler. However, in gross cases like varicose ulcer, malignant ulcer, venous malformations, Buerger's disease the abnormalities were beautifully depicted. Severe stenosis and gross ischemic changes were shown by MR study. Out of five cases of diabetic foot ulcer which showed positive findings on duplex study, only three cases showed discernible changes on MRI. Hence MR study proved to be 60% sensitive compared to Doppler in cases of diabetic foot ulcer.
Five cases of diabetic foot ulcer were subjected to MR angiography and compared with corresponding Doppler study and ulcer grade.

Table 5: MR correlation with severity of stenosis (Doppler) and Ulcer grade in diabetic foot ulcer.

Sr.No.	**% Stenosis**	**Grade**	**MRA**
1	50-75%	III	Positive
2	0-49	II	Negative
3	> 75	III	Positive
4	50-75	II	Positive
5	0-49	III	Negative

4. Discussion

In this study (n=30) majority of cases were of diabetic foot ulcer (n=19; 63.33%) followed by leprosy (n=5; 16.67%) and venous ulcers secondary to varicose veins (n=3; 10%). The Western data suggest that most common cause of a leg ulcer is venous disease (range 37-76%) [6-9].

Lower limb ulcer were significantly higher in older population i.e. fourth - fifth decade (43.33%) followed by sixth and seventh decade (40%). This is because there appears to be a clear association between age and chronic leg ulceration. Different studies suggest that the prevalence of leg ulceration progressively increases with increasing age [8-10].

Arterial wall calcification develops in the middle layer of the vessel wall and is otherwise known as medial calcinosis or Monckeberg's Sclerosis causing stiffening of the vessel wall. Leskinen *et al*. found that both asymptomatic peripheral vascular disease and medial arterial calcification were common in patients with chronic renal failure, a sequelae of diabetes [11]. McDermott *et al.* found that 13% of peripheral arterial disease (PAD) goes unrecognized in general medicine practice because of the high prevalence of asymptomatic disease other than intermittent claudication [12]. It is important to note that 25% of patients with intermittent

claudication will go on to develop critical lower extremity ischemia manifested by rest pain within 5 years of onset of claudication [11].

In this study majority of patients were of diabetic foot ulcers (n=19), out of these 52.63% had positive plain radiographs findings (which included osteomyelitis, neuropathic foot and vascular calcification). Yuh and Baraniewski *et al.* reported a sensitivity and specificity of 75% each [13]. The study also showed that 57.89% of diabetic foot ulcer had gross arterial calcification, this suggest lower extremity arterial disease in these patients.

In university group diabetes program (UGDP) 16.1% patients reported as having arterial calcification [14]. In a study by Young, Adams *et al.* medial arterial calcification was reported to be significantly higher in neuropathic diabetic patients with history of foot ulceration [15]. Others cases like venous insufficiency (varicose ulcers), Buerger's disease congenital venous malformation and squamous cell carcinoma did not show plain radio graph findings. Three patients had neuropathic foot due to leprosy (60%).

Duplex scanning was positive in all patients, giving vital information like degree of stenosis, abnormal waveform, luminal narrowing and plaques, collaterals, neovascularization, varicosities, and abnormal venous channels. Thus conventional B scan with Doppler (Duplex scanning) with color flow imaging was 100% sensitive in demonstrating these abnormalities. It also showed that with increasing severity of disease the frequency and number of collaterals increased. With duplex scanning it is possible to examine flow patterns in a precisely defined area within the vessel lumen. Triplex scanners make the identification of arterial stenosis even easier and reduce the scanning time. Duplex ultrasonography has a sensitivity of 80% and a specificity of 90-100% for detecting femoral and popliteal disease compared with angiography, but it is less reliable for assessing the severity of stenosis in the tibial and peroneal arteries [16]. Fry *et al.* conducted a prospective study to determine whether duplex ultrasound is diagnostically equivalent to arteriography in diagnosis of extremity vascular trauma [17]. They prospectively evaluated first 50 patients comparing Doppler findings with angiography and or operative findings and found that duplex scanning had 100% sensitivity and 100% specificity when compared with arteriography and or operative findings. In the subsequent 175 patients only duplex ultrasonography was done. It detected 18 injuries, 17 of which were confirmed on arteriograms and or surgery.

Classification of ulcerations can facilitate a logical approach to treatment and aid in the prediction of outcome. The most widely accepted classification system for diabetic foot ulcers and lesions is the Wagner ulcer classification system [5], which is based on the depth of penetration, the presence of osteomyelitis or gangrene, and the extent of tissue necrosis. In our study out of 19 patients of diabetic foot ulcer 47.37% presented with Grade III ulcer, 15.79% presented with Grade IV and 36.84% with Grade II ulcer. It was also found that on comparing the ulcer grade of nineteen patients with corresponding peak systolic velocity, it has a statistically significant relation (p <0.05).

All patients irrespective of etiology were subjected to Duplex scanning with or without color flow imaging. Using criteria of Cossman *et al.* [4] severity of stenosis (%) and peak systolic velocity (PSV) was assessed p value <0.05. Peak systolic velocity varied according to etiology. In 19 patients of diabetic foot ulcer, 21.05% had stenosis in order of (0-49%), 31.50%in range of 50-75% and 47.37% had stenosis > 75%. Lone patient of Buerger's disease had advanced disease and had stenosis of > 75%. Three patients presented with ulcers secondary to venous insufficiency (varicose veins). All of them had incompetent valves within the perforating veins connecting the superficial to deep venous system in the leg. In patients with venous incompetence pressure remains high during exertion. High venous pressure is associated with capillary proliferation and increased permeability of large molecules into the skin.

Eleven patients were subjected to magnetic resonance (MR) study in which patients of diabetic foot ulcer (n=5), varicose ulcer, Buerger's disease and congenital venous malforamtion were put to magnetic resonance angiography (MRA). In this study MR angiography proved to be only 60% sensitive when compared to Doppler studies. A comparison was made to evaluate sensitivity of MRA in patients of diabetic foot ulcer with severity of ulcer (Grade) and corresponding stenosis, assessed by Doppler. Out of 5 patients three had Grade III ulcer and two of which showed abnormal MRA (66.67%). Two patients presented with Grade II ulcer and 1 of which showed (50%) abnormal MRA. In comparing MR angiography of five patients with ulcer

grade $p > 0.05$ i.e. no statistical significance was noted within the two variables. On comparing MR angiography with peak systolic velocity the $p > 0.05$ means no statistical significance was noted.

Magnetic resonance angiography (MRA) can also be useful when evaluating lower extremity arterial disease. Carpenter *et al.* found that MRI was 94% accurate in evaluating lower extremely vessels when compared to conventional angiography or surgery [18]. They also found that MRA detected all run off vessels when compared to conventional angiography and in fact was more sensitive than conventional arteriography for visualizing both run off vessels and arterial stenosis.

However, in our study only 11 patients were subject to MR examination, at 0.2% Tesla magnetic field without CE MRA. The modality was able to pick up gross cases but unable to match color flow duplex scanning in other parameters like collaterals, early arterial stenosis, flow abnormalities and neo angiogenesis. In a multicenter trial evaluating MRA and contrast angiography, it was found that both are approximately equivalent in diagnostic accuracy [19]. In another study by Sommerville, Jenkins *et al*. 3D MRA had a sensitivity of 72% and specificity of 90% in differentiating high grade (> 50%) versus low grade (< 50%) stenosis [20].

5. Conclusion

Chronic leg ulcer continued to be a major cause of morbidity in metabolic diseases like diabetes, atherosclerosis, venous insufficiency, malignancy and other peripheral vascular disease. The disease process starts much early, many years before patients become aware of their disability and contributes significantly in loss of human resource during their productive period in terms of economy and growth of a nation. Newer non invasive imaging techniques play an important role in predicting the diagnosis and proper intervention at right time rehabilitation can change the outcome of disease. Duplex scanning and magnetic resonance angiography are two important techniques which can pick the nature of pathology with 100% sensitivity where as MRI can pick up these lesion with 94% accuracy. Combing the two techniques can result in higher degree of specificity (90%) and sensitivity of 72% in differentiating the high grade of stenosis. Higher resolution of MRI (1.2 and 4.6 tesla) can pick up lesion at the beginning with higher specificity and sensitivity.

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