Research Square

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High-Freq uency U lt ras onography in the Evaluation of Cutaneous C hanges in Chron ic Venous Dise ase: C orrel ati on wit h CEA P C linical Classification

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Research Article

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Abstract

Background

Chronic venous disease (CVD) is a common vascular disorder characterized by venous hypertension resulting from valvular incompetence or venous obstruction. Progressive disease leads to structural skin and subcutaneous tissue changes that may not be fully appreciated on clinical examination alone. High-frequency ultrasonography offers a non-invasive method for evaluating these microstructural alterations.

Objective

To assess cutaneous and subcutaneous changes detected by high-frequency ultrasonography in patients with CVD and to determine their association with the Clinical-Etiological-Anatomical-Pathophysiological (CEAP) classification.

Methods

This prospective cross-sectional study included 100 patients with CVD who underwent clinical evaluation and duplex Doppler ultrasonography. Clinical severity was graded using the CEAP classification. High-frequency ultrasonography (6–15 MHz) was performed to assess dermal edema, skin and subcutaneous tissue thickness, dermo-hypodermal junction integrity, inflammatory infiltration, and anechoic lacunae. Associations between ultrasonographic findings and CEAP clinical class were analyzed using the chi-square test.

Results

The mean age of the study population was 47.56 ± 9.92 years, and CEAP class C2 was the most frequent presentation (43%). Great saphenous vein diameter ≥ 5 mm, saphenofemoral junction incompetence, and perforator incompetence were significantly associated with higher CEAP classes ($p < 0.05$). High-frequency ultrasonography demonstrated progressive dermal edema, increased cutaneous and subcutaneous thickness, loss of dermo-hypodermal junction definition, inflammatory infiltration, and anechoic lacunae with increasing disease severity. All ultrasonographic parameters showed significant correlation with CEAP clinical classification ($p < 0.05$).

Conclusions

High-frequency ultrasonography is a valuable non-invasive imaging modality for assessing cutaneous changes in CVD. Ultrasonographic skin alterations correlate significantly with CEAP clinical severity and may provide additional information for disease stratification and management.

Introduction

Chronic venous disease (CVD) is a progressive vascular disorder characterized by venous hypertension resulting from valvular incompetence, venous reflux, or obstruction of the lower extremity veins [1]. Persistent venous hypertension leads to structural and functional alterations in the venous wall and surrounding tissues, producing a wide spectrum of clinical manifestations ranging from asymptomatic varicose veins to advanced skin changes and venous ulceration [2].

Cutaneous manifestations of CVD include hyperpigmentation, venous eczema, lipodermatosclerosis, atrophie blanche, and venous ulcers. These dermatological changes significantly impair quality of life and are associated with recurrent infections, delayed wound healing, and increased healthcare burden [3]. The severity of CVD is commonly classified using the Clinical-Etiology-Anatomy-Pathophysiology (CEAP) system, which provides a standardized clinical grading framework [4]. Although CEAP classification is valuable for clinical staging, it primarily relies on visible and symptomatic findings and may not detect early or subclinical microstructural skin alterations.

Duplex ultrasonography is the imaging modality of choice for evaluating venous hemodynamics in CVD [5]. In addition to assessing reflux and venous diameter, high-frequency ultrasonography enables detailed visualization of skin layers, including the epidermis, dermis, and subcutaneous tissue. It allows objective measurement of cutaneous and subcutaneous thickness and identification of pathological features such as dermal edema, inflammatory infiltration, fibrosis, and disruption of the dermo-hypodermal junction [6].

Previous studies have demonstrated that high-frequency ultrasound can detect early dermal edema and inflammatory changes even in clinically normal-appearing limbs [7]. Such findings suggest that ultrasound may provide additional diagnostic information beyond routine clinical assessment and assist in early severity stratification. However, limited data are available regarding the correlation between detailed skin ultrasound findings and CEAP clinical classification, particularly in the Indian population.

Therefore, the present study was undertaken to evaluate skin changes in patients with CVD using high-frequency ultrasonography and to correlate these findings with CEAP clinical class. By integrating clinical assessment with duplex and skin ultrasound parameters, this study aims to determine the utility of ultrasonography as a comprehensive tool for evaluating cutaneous involvement in CVD.

Materials and methods

Study design and setting

This prospective cross-sectional study was conducted in the Department of Radiodiagnosis at SRM Medical College Hospital and Research Centre, SRM Nagar, Kattankulathur, Tamil Nadu, India, from March 2024 to September 2024. Ethical clearance was obtained from the Institutional Ethics Committee

(Approval No.: SRMIEC-ST0224-1016; dated 07/03/2024). Written informed consent was obtained from all participants prior to enrollment.

Study population

A total of 100 patients diagnosed with CVD and referred for Doppler ultrasound examination were included in the study using a convenient sampling technique. The inclusion criteria are patients clinically diagnosed with CVD; patients referred for lower limb venous doppler examination; age ≥ 18 years. The exclusion criteria are pregnant women; patients with arterial occlusive disease; patients with peripheral edema due to cardiac, renal, or systemic causes; patients with dermatological disorders affecting the lower limbs; patients with deep venous thrombosis.

Clinical assessment

All patients were clinically evaluated and classified according to the CEAP classification system. Only the clinical component (C1-C6) was considered for correlation analysis.

Ultrasound examination

All ultrasound examinations were performed using a GE Logiq P9 ultrasound machine equipped with a high-frequency linear probe (6–15 MHz).

Venous doppler evaluation

Routine duplex Doppler study of the lower limbs was performed to assess: Great saphenous vein (GSV) diameter; SFJ competence; Saphenopopliteal junction competence; Presence of perforator incompetence; Venous reflux. A GSV diameter ≥ 5 mm was considered dilated.

Skin ultrasound assessment

High-frequency ultrasonography was used to evaluate skin morphology at the medial aspect of the leg (upper and lower third) and mid-thigh region. If visible skin lesions were present, scanning was performed over the lesion, adjacent apparently normal skin, and the homologous site of the contralateral limb for comparison. In patients without visible lesions, symmetrical sites in both limbs were examined. The following parameters were assessed: 1. Cutaneous layer thickness - Measured as the distance between the epidermal entrance echo and the dermo-hypodermal junction (DHJ). Thickness was considered increased if greater than the corresponding contralateral or normal skin region. 2. Subcutaneous layer thickness-

Measured as the distance between the dermo-hypodermal junction and the underlying muscular fascia. Increased thickness was defined relative to the contralateral limb or normal reference site. 3. Dermo-hypodermal junction (DHJ)- Assessed for preservation or loss of normal interface. 4. Dermal edema- Identified as diffuse hypoechogenicity within the dermis. 5. Inflammatory infiltration- Assessed based on increased echogenicity of dermal or subcutaneous layers. 6. Anechoic lacunae- Presence of hypoechoic or anechoic areas within subcutaneous tissue suggestive of interstitial fluid accumulation.

Statistical analysis

Data were entered into microsoft excel and analyzed using SPSS software version 26. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as frequency and percentage. The association between CEAP clinical class and ultrasound findings (GSV diameter ≥ 5 mm, SFJ incompetence, perforator incompetence, dermal edema, cutaneous thickening, subcutaneous thickening, loss of DHJ, inflammatory infiltration, and anechoic lacunae) was assessed using the chi-square (χ^2) test. A p-value < 0.05 was considered statistically significant.

Results

A total of 100 patients with CVD were included in the study. The mean age of the study population was 47.56 ± 9.92 years. The majority of patients belonged to the 40-59 years age group (60%) (Table 1). There was a slight female predominance, with females accounting for 53% of cases (Table 2).

CEAP clinical classification

Based on CEAP clinical classification, C2 was the most common presentation (43%), followed by C3 (16%). Advanced stages (C4-C6) constituted 41% of cases. Active venous ulcers (C6) were present in 8% of patients (Table 3).

Venous hemodynamic findings

Duplex Doppler evaluation demonstrated:

- Great saphenous vein (GSV) diameter ≥ 5 mm in 63% of patients
- Saphenofemoral junction (SFJ) incompetence in 62%
- Perforator vein incompetence in 86%

A statistically significant association was observed between CEAP clinical class and GSV diameter ≥ 5 mm, SFJ incompetence, and perforator incompetence (p < 0.05) (Table 3).

Skin ultrasound findings

High-frequency ultrasonography revealed distinct cutaneous and subcutaneous alterations across CEAP classes (Table 4).

Dermal edema

Dermal edema was observed in patients belonging to CEAP classes C2, C3, C4a, C4b, and C6. The association between dermal edema and CEAP class was statistically significant ($\chi^2 = 22.35$; $p < 0.05$) (Table 5). Representative ultrasound findings are shown in Figure 1.

Cutaneous layer thickening

Increased cutaneous thickness was noted in CEAP classes C2, C4a, C4b, and C5. A significant association was observed between cutaneous thickening and CEAP clinical class ($\chi^2 = 49.32$; $p < 0.05$) (Table 5).

Subcutaneous layer thickening

Subcutaneous layer thickening was identified in CEAP classes C3, C4a, C4b, C5, and C6. The association between subcutaneous thickening and CEAP class was statistically significant ($\chi^2 = 35.02$; $p < 0.05$) (Table 5).

Anechoic lacunae

Anechoic lacunae were most frequently observed in CEAP class C3 and were also present in C6 patients. The association with CEAP class was statistically significant ($\chi^2 = 33.93$; $p < 0.05$) (Table 5). Ultrasound depiction of anechoic lacunae is illustrated in Figure 2.

Dermo-hypodermal junction (DHJ)

Loss of the dermo-hypodermal junction was predominantly noted in CEAP classes C4a, C4b, and C5. A strong association was found between DHJ loss and CEAP clinical class ($\chi^2 = 80.37$; $p < 0.05$) (Table 5). Representative imaging is shown in Figure 3.

Inflammatory infiltration

Increased echogenicity suggestive of inflammatory infiltration was observed in CEAP classes C2, C4a, C4b, C5, and C6. This finding demonstrated a statistically significant association with CEAP clinical class ($\chi^2 = 28.34$; $p < 0.05$) (Table 5).

Discussion

CVD is a progressive disorder characterized by venous hypertension and valvular incompetence leading to structural alterations in the skin and subcutaneous tissues.[1] The present study evaluated the role of high-frequency ultrasonography in detecting cutaneous changes and correlated these findings with CEAP clinical classification.

Demographic characteristics

The mean age of participants in this study was 47.56 ± 9.92 years, with the majority belonging to the 40–59-year age group. This finding is consistent with previous studies reporting a higher prevalence of CVD in middle-aged individuals due to cumulative venous hypertension and progressive valvular dysfunction [8,9]. A slight female predominance (53%) was observed, which aligns with earlier reports suggesting hormonal influences, pregnancy-related venous dilation, and occupational factors as contributing mechanisms [10-12]. However, the near-equal gender distribution highlights that CVD significantly affects both sexes.

Venous hemodynamics and CEAP correlation

In the present study, GSV diameter ≥ 5 mm was observed in 63% of patients and showed a significant association with CEAP class. Previous studies have demonstrated that increasing GSV diameter correlates with disease severity and pathological reflux [9, 13]. Similarly, saphenofemoral junction (SFJ) incompetence was identified in 62% of patients, comparable to reported prevalence ranging between 58% and 70% in clinically significant CVD [14]. Deep axial reflux involving the SFJ has been recognized as a major contributor to advanced skin changes and ulcer formation [4].

Perforator vein incompetence was present in 86% of patients and showed a statistically significant association with higher CEAP classes. Prior literature indicates that incompetent perforators are more frequently observed in advanced CVD and are associated with localized venous hypertension and microcirculatory damage [6, 15]. The hemodynamic findings in this study support the established relationship between venous reflux patterns and clinical severity.

Skin ultrasound findings

High-frequency ultrasonography enabled detailed assessment of dermal and subcutaneous alterations across CEAP classes [Table 6]. Dermal edema was observed in CEAP classes C2 to C6 and demonstrated significant correlation with clinical severity. Dermal edema has been described as one of the earliest ultrasonographic manifestations of CVD, reflecting increased capillary permeability and interstitial fluid accumulation [6, 16]. Its presence even in clinically less advanced stages suggests that microstructural changes may precede overt skin manifestations.

Cutaneous layer thickening was identified predominantly in C2, C4, and C5 stages, while subcutaneous thickening was more frequent in C3 to C6. These findings are consistent with previous reports describing progressive fibrosis and lipodermatosclerosis in advanced disease [7, 17]. Quantitative elastography studies have further demonstrated increased skin stiffness corresponding to fibrotic transformation in CVD [18]. Anechoic lacunae were most frequently detected in C3 and C6 classes. Similar hypoechoic interstitial spaces have been reported as markers of venous edema and inflammatory exudation [19]. The presence of such lacunae reflects ongoing fluid accumulation within the subcutaneous tissue. Loss of the DHJ was predominantly observed in C4 and C5 classes. Disruption of normal layer differentiation has been associated with advanced fibrosis and lipodermatosclerosis in previous ultrasonographic studies [20]. This finding may indicate irreversible structural damage in advanced stages.

Increased echogenicity suggestive of inflammatory infiltration was observed in multiple CEAP classes, particularly advanced stages. Chronic inflammation is recognized as a central mechanism in the pathogenesis of venous skin changes and ulcer formation [11, 19]. The significant association between inflammatory infiltration and CEAP class in this study reinforces its clinical relevance.

Clinical implications

The present study demonstrates that high-frequency skin ultrasonography provides objective evidence of microstructural alterations that correlate significantly with CEAP clinical class. By integrating duplex hemodynamic parameters with skin morphology assessment, ultrasound offers a comprehensive, non-invasive approach for severity stratification. Early detection of dermal edema and inflammatory changes may facilitate timely intervention and potentially prevent progression to advanced fibrotic stages.

Limitations

The present study has certain limitations. It was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. The cross-sectional design does not permit assessment of longitudinal disease progression or response to treatment. Ultrasonographic evaluation is operator-dependent, and interobserver variability was not assessed in this study. Additionally, histopathological correlation of skin changes was not performed. Larger multicenter prospective studies with long-term follow-up are required to validate these findings and establish standardized ultrasound criteria for routine clinical practice.

Conclusion

High-frequency ultrasonography is a valuable, non-invasive imaging modality for evaluating cutaneous and subcutaneous alterations in CVD. The study demonstrates a statistically significant correlation between skin ultrasound findings such as dermal edema, cutaneous and subcutaneous thickening, loss of dermo-hypodermal junction, inflammatory infiltration, and anechoic lacunae and CEAP clinical class. Skin ultrasonography enables objective assessment of microstructural changes that may not be evident on routine clinical examination. Integration of detailed skin ultrasound with conventional duplex evaluation may enhance disease severity stratification and assist in clinical decision-making. Further large-scale longitudinal studies are warranted to establish its role as a routine diagnostic and monitoring tool in CVD.

Abbreviations

CVD – Chronic Venous Disease

CEAP – Clinical-Etiological-Anatomical-Pathophysiological Classification

GSV – Great Saphenous Vein

SFJ – Saphenofemoral Junction

DHJ – Dermo-Hypodermal Junction

SD – Standard Deviation

SPSS – Statistical Package for the Social Sciences

MHz – Megahertz

Declarations

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was conducted in accordance with ethical standards and was approved by the Institutional Ethics Committee (Approval No.: SRMIEC-ST0224-1016; dated 07/03/2024). Written informed consent was obtained from all the participants.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Written consent for Publication

The authors confirm that this manuscript has not been published previously and is not under consideration for publication elsewhere.

Availability of data and material

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable. The study did not involve the development of custom code. Data analysis was performed using IBM SPSS Statistics version 26.

Authors' Contributions

Pabbisetty Sushma: Conceptualization, methodology, data collection, formal analysis, and manuscript drafting.

Jaya Selin Praveena Joseph: Study design, supervision, data interpretation, and critical revision of the manuscript.

Senthil kumar Aiyappan: Correspondence, overall supervision, manuscript review, and final approval of the submitted version.

All authors read and approved the final manuscript.

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Tables

Table 1. Age-Wise Distribution of Study Participants (n = 100)

Age group (years)	Number of patients/legs (n=100)	Percentage (%)
19-29	7	7%
30-39	20	20%
40-49	28	28%
50-59	32	32%
≥ 60	13	13%
Mean ± SD	47.56 ± 9.92	

Table 2. Gender -wise distribution of study participants (n = 100)

Sex	Number (n)	Percentage (%)
Male	47	47%
Female	53	53%

Table 3. Correlation between CEAP clinical class and SFJ, Perforator incompetence and great saphenous vein (GSV) diameter (n = 100)

CEAP Class	SFJ competent n / %	SFJ Incompetent n / %	χ^2 value	p-value
C1-C6	38 (38%)	62 (62%)	29.44	< 0.05
CEAP Class	**Perforator Present**	**Perforator Absent**	**χ^2 value**	**p-value**
C1-C6	86 (86%)	14(14%)	27.96	< 0.05
CEAP Class	**GSV >5mm**	**GSV <5mm**	**χ^2 value**	**p-value**
C1-C6	63 (63%)	37(37%)	14.42	< 0.05

Table 4. Skin ultrasound findings across different CEAP clinical classes

S. No	CEAP clinical class (n)	Skin ultrasound findings	Percentage (%) (n)
1	C1 (n = 4)	Normal skin architecture; no dermal edema, no cutaneous or subcutaneous thickening	100% (4)
2	C2 (n = 43)	Dermal edema	41.9% (18)
		Cutaneous layer inflammatory infiltration	16.3% (7)
3	C3 (n = 16)	Dermal edema	43.8% (7)
		Anechoic lacunae	25% (4)
		Subcutaneous layer thickening	43.8% (7)
4	C4a (n = 13)	Dermal edema	92.3% (12)
		Cutaneous layer thickening	30.8% (4)
		Subcutaneous layer thickening	46.2% (6)
		Disappearance of dermo-hypodermal junction	84.6% (11)
		Cutaneous and subcutaneous layer inflammatory infiltration	15.3% (3)
5	C4b (n = 10)	Dermal edema	80% (8)
		Cutaneous layer thickening	50% (5)
		Subcutaneous layer thickening	50% (5)
		Disappearance of dermo-hypodermal junction	90% (9)
		Subcutaneous layer inflammatory infiltration	30% (3)
6	C5 (n = 6)	Cutaneous layer thickening	33.3% (2)
		Subcutaneous layer thickening	33.3% (2)
		Disappearance of dermo-hypodermal junction	100% (6)
7	C6 (n = 8)	Dermal edema	87.5% (7)
		Subcutaneous layer thickening	75% (6)
		Anechoic lacunae	25% (2)
		Subcutaneous layer inflammatory infiltration	87.5% (7)

Table 5. Association between skin ultrasound findings and CEAP clinical class

CEAP Class	Sub cutaneous layer thickening present	Sub cutaneous layer thickening absent	χ^2 value	p-value
C1-C6			35.02	<0.05
CEAP Class	Cutaneous layer thickening present	Cutaneous layer thickening absent	χ^2 value	p-value
C1-C6			49.32	<0.05
CEAP Class	Dermal Edema present	Dermal edema absents	χ^2 value	p-value
C1-C6			22.35	<0.05
CEAP Class	Anechoic lacunae present	Anechoic lacunae absent	χ^2 value	p-value
C1-C6			33.93	<0.05
CEAP Class	DHJ present	DHJ absent	χ^2 value	p-value
C1-C6			80.37	<0.05
CEAP Class	Inflammatory infiltration present	Inflammatory infiltration absent	χ^2value	p-value
C1-C6			28.34	<0.05

Table 6. Skin ultrasound findings across studies

Finding	Present study	Caggiati 2016 [6]	Girdhani et al [7]
Dermal edema	C2, C3, C4a, C4b, C6	C5 (not mentioned) Seen in C2, C3	C2, C3, C4a, C4b, C6
Cutaneous thickening	C2, C4a, b, C5	C4, C6 C5-Not mentioned	C2, C4a, C4b, C5, C6
Subcutaneous layer thickening	C3, C4a, C4b, C5, C6	C3, C4, C6	C2, C3, C4a, C4 b, C5, C6
Anechoic lacunae	C3, C6	C3	C3, C4B, C6
Loss of DHJ	C4a, C4b, C5	C4, C6 C5-Not mentioned	C3, C4, C5, C6
Inflammatory infiltration	C2, C4a, C4 b, C5, C6	C2, C4, C6 C5-Not mentioned	C2, C4a, C4b, C5, C6

Figures

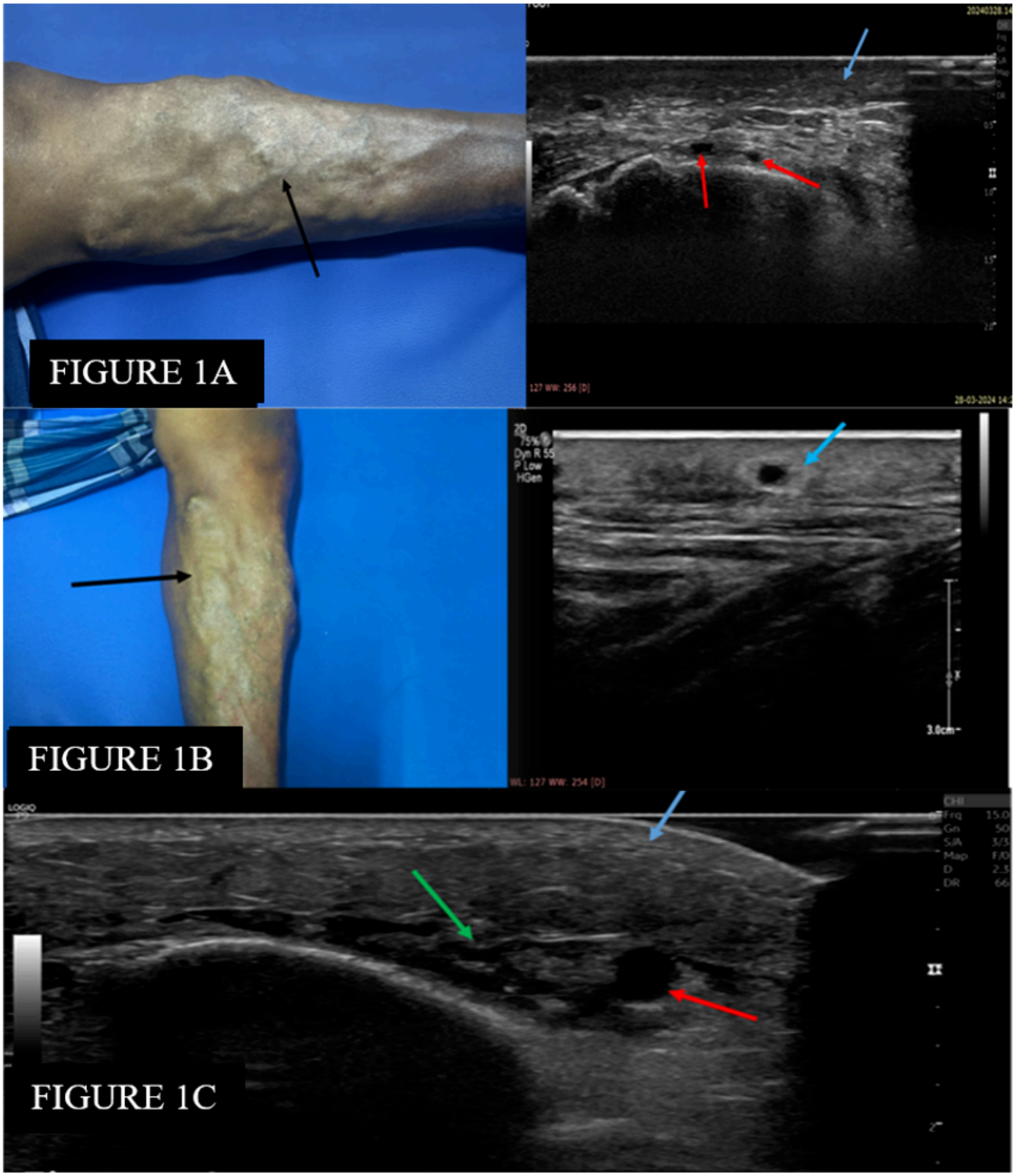


Figure 1

a: Dermal edema in normal appearing C2 leg Clinical photograph of leg shows dilated superficial veins suggestive of varicosities (black arrow) with no skin changes High resolution ultrasound image of leg showing diffusely decresed dermal echogenicity with loss of subepithelial low echogenic band suggestive of dermal edema (blue arrow) overlying varicose veins (red arrows);

b and c: Inflammation in normal appearing C2 leg Clinical photograph of leg shows dilated superficial veins suggestive of varicosities (black arrow) with no skin changes. High resolution ultrasound image of leg showing diffusely increased dermal echogenicity with echogenic halo (blue arrow) surrounding the dilated superficial vein suggestive of inflammatory infiltration in dermis and around the vein. High resolution ultrasound image of leg showing diffusely increased dermal echogenicity (blue arrow) overlying a varicose vein (red arrow) with edema of subcutaneous layer surrounding the vein (green arrow).

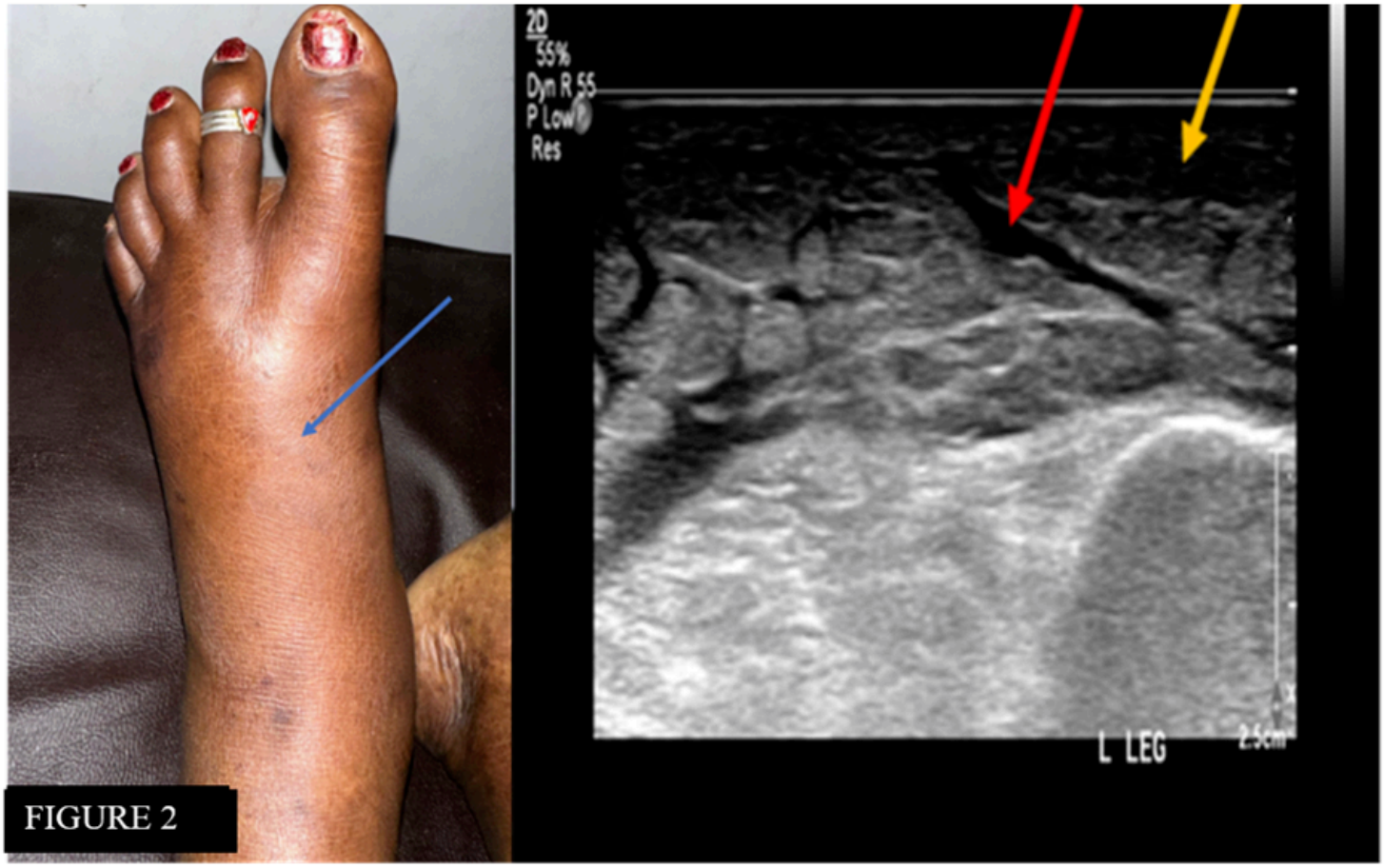


Figure 2

Clinical photograph shows swollen leg in a female patient with varicose veins (blue arrow). High resolution ultrasound images of leg showing dermal edema (yellow arrow) with subcutaneous layer thickening due to anechoic lacunae of varying size, extension and orientation (red arrow).

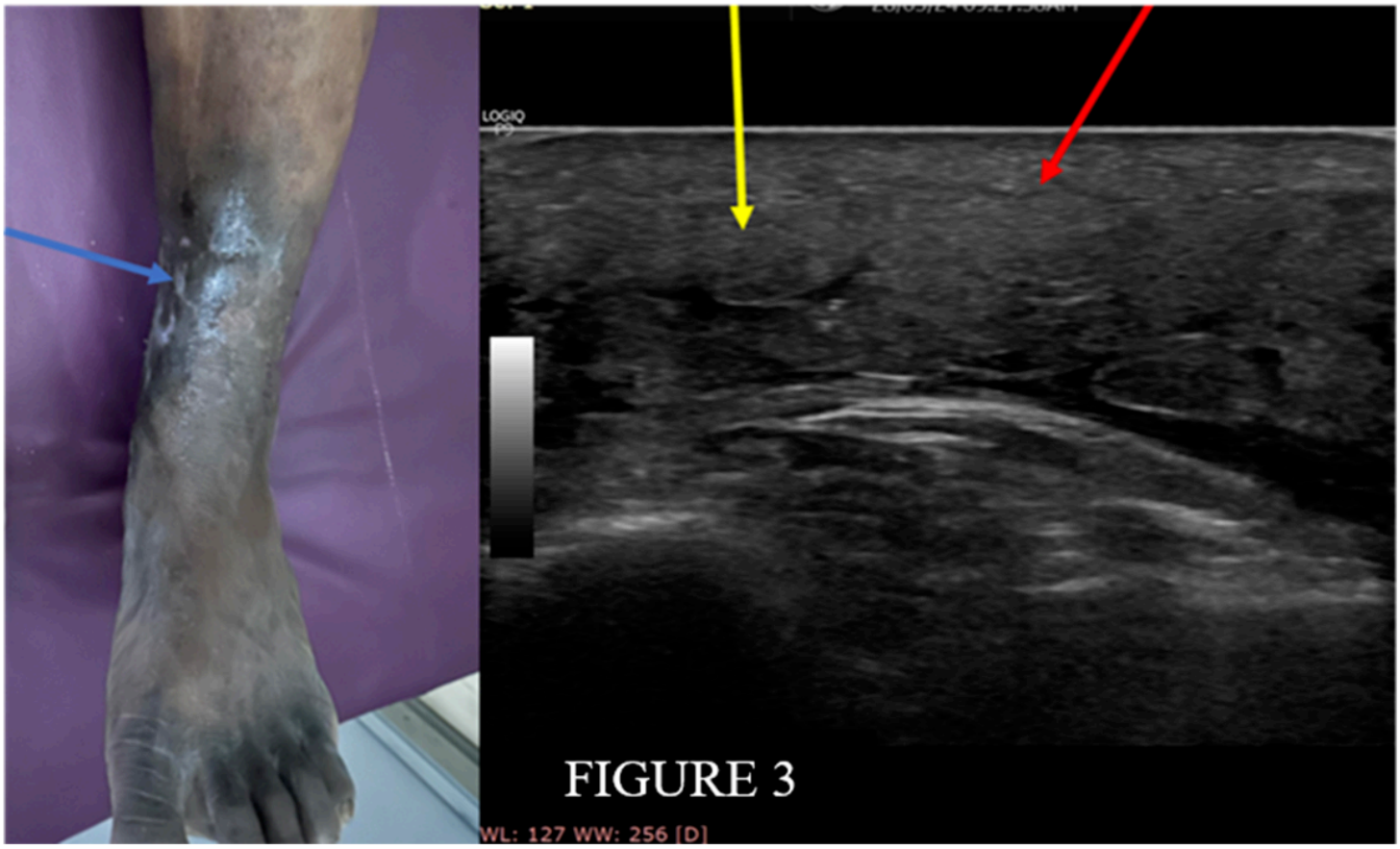


Figure 3

Venous eczema and pigmentation -Clinical photograph shows venous eczema and pigmentation in a patient with varicose veins (blue arrow) High resolution ultrasound image of leg showing dermal hyperechogenicity extending to the underlying subcutaneous layer (red arrow) with disappearance of dermo-hypodermal junction (yellow arrow).