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ARFI Elastography of Venous Thrombosis and Adjacent Muscles in Assisting Treatment Management and Prognostication in Tertiary Care Hospital

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ABSTRACT

Introduction: Deep Vein Thrombosis (DVT) is a condition with potentially severe consequences, including Pulmonary Embolism (PE) and post-thrombotic complications. This study aimed to investigate the characteristics, detection, and management of DVT using Acoustic Radiation Frequency Impulse (ARFI) technology, considering factors like age, comorbidities, and thrombus stage.

Materials and Methods: The study, conducted at Apollo Hospital Chennai, retrospectively analyzed data from 247 patients with DVT. High-end Sonodoppler ARFI was used. Inclusion criteria covered clinically suspected DVT cases and patients with a history of PE and elevated D-Dimer levels. Exclusion criteria applied to non-consenting or suboptimal imaging patients. Statistical analysis employed SPSS software.

Results: Out of 247 patients, 124 controls had mean ARFI values of 0.96 m/sec for veins and 2.52 m/sec for muscles. DVT patients in the acute, subacute, and chronic stages showed distinct ARFI values. Age, gender, and comorbidities were associated with DVT. Thrombus characterization revealed differences in ARFI values.

Moreover, the study revealed significant correlations between ARFI values and various clinical parameters. Vein and muscle ARFI values displayed progressive increments across thrombus stages, aiding in the differentiation between acute, subacute, and chronic DVT. Notably, a statistically significant correlation was observed between ARFI values and liver function tests, platelets, and D-dimer levels, further underscoring the diagnostic potential of ARFI in assessing DVT.

Conclusion: ARFI technology is valuable in diagnosing and managing DVT. It aids in early detection and prognosis, especially in acute-on-chronic cases. However, larger sample sizes are needed to establish ARFI values for chronic DVT. This study highlights ARFI's potential in improving DVT management and outcomes.

Keywords: *ARFI, Acute DVT, Chronic DVT.*

INTRODUCTION

DVT incidence is one in a thousand; autopsy reports showed PE deaths are due to missed DVT. Causes include the elderly, non-ambulation, injury involving vein endothelium, oral contraceptives, oral hormone replacement therapy, obesity, family history, cardiac failure, malignancy, pregnancy, and smoking. (1) Complications encompass PE and sudden death, post-phlebitic syndrome, and post-anticoagulation treatment complications. (2)

Prevention of DVT through ambulation, exercise, smoking cessation, and weight reduction is crucial. (3) The thrombosis formation mechanism involves altered collagen in the subendothelial layer of the tissue matrix and the facilitation of the circulatory system. (4) If the inner wall is breached or the endothelium is discontinued, collagen and tissue factors are exposed to moving cellular blood, thus slowly initiating the formation of thrombotic layers filling the lumen. (5)

The gold standard is sonography duplex Doppler with a compression technique. However, there is another angle apart from diagnosis: the age of the thrombus, nature, morphology, location, and particularly the significant role of management and invasive treatment perspective as early as possible for the best outcome. (6) This situation is well handled by sonography Doppler with the addition of elastography using high-end equipment to increase accuracy in every aspect of clinical, laboratory, and sono Doppler ARFI. (7)

This elastography, a quantitative ARFI, plays a significant role in DVT and has been proven in many structures in the body for diagnosis and assisting in treatment. (4) It represents a novel approach to assessing the progression of DVT in sono Doppler elastography. The exact age determination of DVT is essential for appropriate treatment, especially in acute staging. In the USA, where 600,000 people develop PE, leading to 60,000 deaths, appropriate treatment depends on the maturity of the thrombus. (6) A mature thrombus is stable with minimal migration. Acute DVT can be divided into three phases: 1. Acute loose clot (1-3 to 5 days), 2. Phase (3 to 5 to 14 days) attached to the wall, and 3. Phase (15 days and above) fully organized with minimal risk of PE. (1)

The Royal Society Open Sciences mentions that in addition to elastography, the application of direct forces with ARFI has recently been developed as an alternative to conventional sonography. (7) ARFI involves impulses in milliseconds to the tissue where mechanical properties directly reflect and can be averaged for interpretation. (2) ARFI application on the coagulation of blood in ex vivo experimentation, coupled with mechanical resonance and analytical modes of wave scattering in viscoelasticity, mimicked venous thrombosis in a phantom during the acute phase by using a gelatin agent as a phantom, yielding similar results. (3) Generally, the biomechanics of tissues can exhibit anisotropy, angle, viscosity, nonlinear behavior direction-dependent of elastowave, impulse rate, and extent. A simple elastic modulus is elastography in various modes of improvement in finding various characteristics of given tissues like the liver, thyroid, kidneys, prostate, muscles, and others, which have been proven beyond doubt. (8) Perhaps the earliest effort in elastography dates back to 2002 in an Ontario conference sponsored by the University of Texas and Rochester University. Cosgrove of European Ultrasound and the World Federation of Ultrasound set guidelines in elastography practice principles. (4) Acute thrombosis carries a significant risk of PE, with a shift towards CDT. The role of ARFI in finding the age of the clot provides advantages in treatment and cost-effectiveness. (5) Another descriptive nomenclature of venous thrombosis as soft, intermediate, and hard by morphology is depicted by sono Doppler with strong support from elastography, aiding in the differentiation of acute and subacute thrombosis. Clinical, laboratory, and imaging facilities, along with adjacent soft tissue changes, help in better delineation and management. (6)

Venous thrombosis is a common condition, and this research aimed to investigate its characteristics, location, extent, underlying factors, age, gender, and comorbidities, with a particular focus on rapid detection and correlation with clot and adjacent muscle using ARFI (Acoustic Radiation Frequency Impulse) through strict adherence to established protocols and guidelines. The primary objective of this study was to detect

and characterize venous thrombosis, including acute, subacute, chronic, and mixed stages, in order to assist in determining suitable management strategies. Additionally, the secondary objective involved the utilization of clinical, laboratory, and high-end Sonography Doppler ARFI techniques to establish, record, and follow up on the findings.

MATERIALS & METHODS

The study was conducted at the Department of Radiology and Imaging Sciences, Apollo Hospital Chennai as a Retrospective Study. The study was conducted from December 2022 to May 2023. A total of 247 patients who presented with venous thrombosis in various locations, including the lower and upper extremities, IVC, iliac, and jugular veins, were included in the study. The equipment used for this research comprised a high-end Sonodoppler ARFI Unit. Inclusion criteria encompassed all clinically suspected cases of deep vein thrombosis (DVT) and patients with a history of pulmonary embolism and elevated D-Dimer levels. Exclusion criteria applied to patients who did not provide consent were non-cooperative, or presented with suboptimal imaging windows.

Statistical Analysis:

Descriptive statistics were presented with Frequency (Percentage) and Mean ± SD for the categorical and continuous factors respectively. Normality of the data were checked by using Shapiro-Wilk test. Student's t-test/Mann Whitney U test were used to find out the significant difference between case and control. Chi-square/Fisher's exact test were used to find out the association between patients details and group. *P*-value <0.05 consider as statistical significance. All analysis was carried out by using SPSS software (IBM, 28.0)

RESULT

Out of 247 patients, 124 normal controls with an average age of 53.5 years participated in acute, sub-acute, and chronic stages.

1. ARFI Control of the vein: The numerical mean value is 0.9 m/sec.
2. ARFI control of peri-venous muscle: The mean value is 2.5 m/sec.

DVT patients in the acute stage showed values of 1.8 m/sec, while sub-acute patients showed 3.0 m/sec, and those in the immediate chronic stage exhibited values above 3 m/sec. Long-term chronic DVT patients had values of 4 m/sec or higher. The mean and standard deviation (SD) of control and DVT ages were 59.3±13.8 and 53.6±14.4, with an overall mean and SD of age at 56.4±14.3, where the P-value is 0.025, signifying statistical significance.

In terms of gender distribution, among the total population, 84 (67.7%) were male, with 46 (74.2%) in the control group and 38 (61.3%) in the DVT group. Among females, the total population was 40 (32.3%), with 16 (25.8%) in the control group and 24 (38.7%) in the DVT group.

Regarding comorbidities, 28 (45.2%) individuals in the control group had DM, while 34 (54.8%) individuals in the DVT group had DM. HTN was present in 36 (58.1%) individuals in the control group and 30 (48.4%) individuals in the DVT group.

The parameters including Vein, FEM, IVC, JUG, AVF, Axillary Vein, Iliac, Portal vein, Thigh Muscle, Paravertebral Iliopsoas, Neck, Arm, Iliopsoas, Platelets, and D-Dimer were statistically significant with p-values <0.001. Liver function tests were also significant with a p-value of 0.002.

In a previous observation, acute and hyper-acute cases were observed within 1-4 days, subacute cases between 5-14 days, and chronic cases at 14-180 days and above.

The characterization of thrombus types based on ARFI measurements is as follows:

Hyperacute: moving, slightly hyperechoic thrombus, slightly compressible, poor doppler, ARFI 1 to 1.4 m/sec, muscle 2 - 2.5+.

Acute: vein dilated, non-compressible, absent color doppler, ARFI VEIN 1.2-1.6

+/- 0.4, muscle ARFI 2.5 to 3 +/- 0.5 sec due to edema and compartment pressure.
Subacute: non-compressible, no color, dilated, ARFI VEIN 2.0 to 3 +/- 0.5, ARFI muscle 2.5 - 3.

Chronic thrombosis: fibrosed walls/small lumen, partial recanalization, or complete fibrosis, with ARFI values of 2-2.5 for thrombus and muscle 2.5+/- 0.5.
A total of 124 controls were included, with an ARFI of 0.96 m/sec being the mean average of normal veins. The mean average of normal muscle ARFI was 2.52 m/sec. Out of these, 5 cases were positive, including 2 acute, 1 subacute, and 3 chronic cases.

Vein ARFI classification:
1. Hyperacute (partially compressible): ARFI 1 to 1.4 m/sec.
2. Acute: dilated, hypoechoic, increased ARFI 1.5 to 1.9 m/sec.
3. Subacute: ARFI 2 to 2.4 m/sec.
4. Chronic: above 2.5 m/sec.

Muscle correlation classification:
1. 2.1 to 2.4 m/sec.
2. 2.5 to 2.9 m/sec.
3. 2.5 to 2.9 m/sec.
4. 3 m/sec or above.

The mean age is 56.4 +/- 14.3 for both control and DVT groups, with a P-value of < 0.025. The femoral vein and muscle complex showed an 80.6% association with a P-value of < 0.002. Liver function tests also showed a P-value < 0.002, while Platelets D-dimer was associated with a P-value of < 0.001.
ARFI Vein: ARFI venous control individual value is 1.01+/- 0.1. DVT positive venous value is 1.9+/- 0.8, with a P-value of < 0.001.
ARFI Muscle: The control individual of muscle complex is 2.4+/- 0.4. DVT-positive muscle ARFI is 2.6+/- 0.3, associated with a P-value of < 0.018.
ARFI CG (Control Group) - shows 1.01+/- 0.1 (range 0.7 - 1.6).
DVTG (DVT Group) - showed 1.9+/- 0.8 (range 0.8-3.8), with a P-value of < 0.001.
Muscle CG is 2.4+/- 0.4 (range -0.2-3.2).
DVTG is 2.6+/- 0.3 (range 1.8 - 3.7), associated with a P-value of < 0.018.
The ARFI cut-off Values in vein and muscle for normal patient was 0.8 +/- 0.20 m/s and 2.0 +/- 0.15 m/s, The ARFI cut-off Values in vein and muscle for Acute thrombosis was 1.2 +/- 0.30 m/s and 2.7 +/- 0.14 m/s, The ARFI cut-off Values in vein and muscle for Subacute thrombosis was 1.6 +/- 0.20 m/s and 2.6 +/- 0.34 m/s, The ARFI cut-off Values in vein and muscle for chronic thrombosis was 2.5 +/- 0.27 m/s and 3.6 +/- 0.45 m/s (Ref table-1)

Table 1: ARFI Cut-off Values in Normal Patients and Various stages of DVT.

PARAMETERS	VEIN	MUSCLE
NORMAL	0.8 +/- 0.20 m/s	2.0 +/- 0.15 m/s
ACUTE	1.2 +/- 0.30 m/s	2.7 +/- 0.14 m/s
SUBACUTE	1.6 +/- 0.20 m/s	2.6 +/- 0.34 m/s
CHRONIC	2.5 +/- 0.27 m/s	3.6 +/-0.45 m/s

The radiographic images of ARFI cut-off Values in vein and muscle were represented in Figures 1,2,3,4 for Normal vein and muscle, Acute DVT, Sub-acute DVT and Chronic DVT Respectively. (Ref-Figure-1, Figure-2, Figure-3, Figure-4)

Figure: 1 Normal vein and muscle

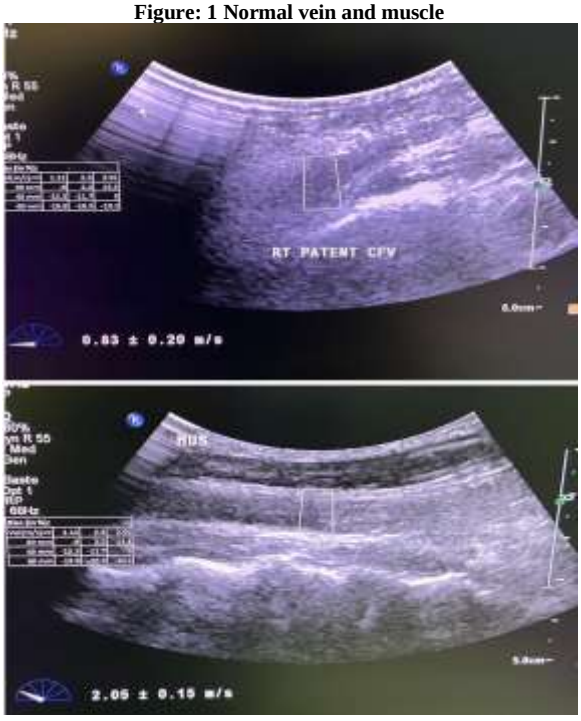


Figure 2: Acute thrombosis

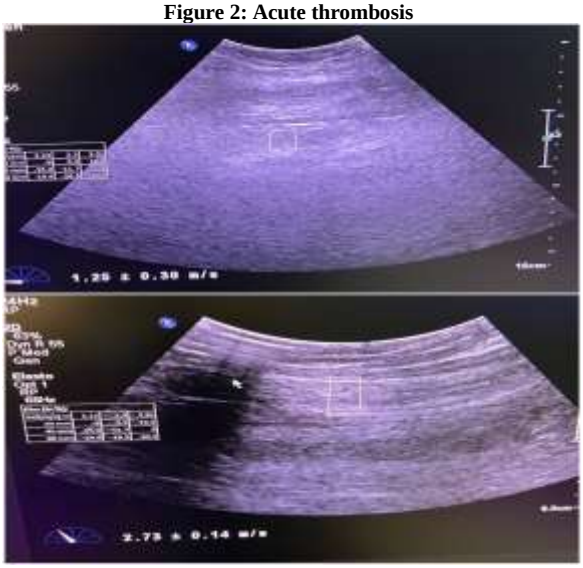


Figure 3: Subacute thrombosis

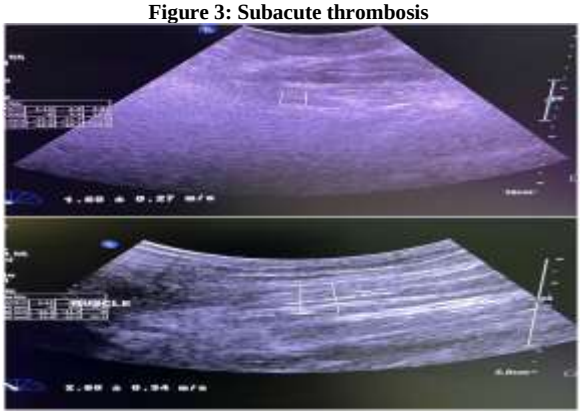
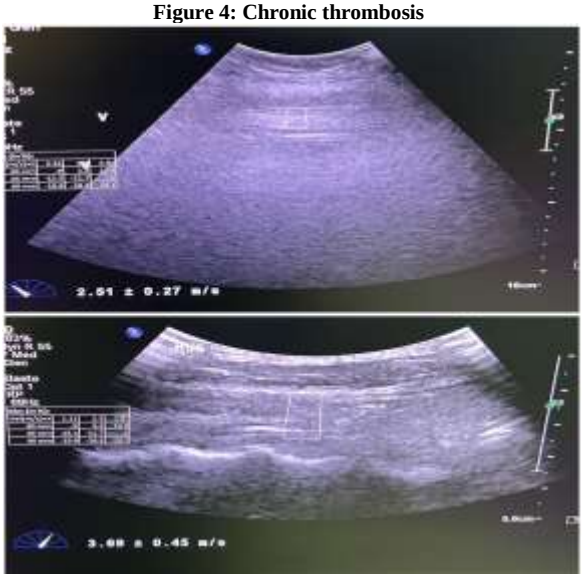


Figure 4: Chronic thrombosis



DISCUSSION

An extensive literature analysis, coupled with our practical approach, yielded results that are consistent with previous studies. (5,7,8) Additionally, our research unveiled novel findings through independent assessment by a senior radiologist, presenting the data in a clear format.

We initiated a control group to establish baseline ARFI values for larger veins and muscles, following the designated protocol. This interpretation served a dual purpose: firstly, to compare numerical ARFI values of veins across the stages of acute, subacute, and chronic, as per our methodology. Secondly, we employed ARFI measurements of muscle in these three stages, which generally aligned with prognostication based on numerical values. However, we observed greater consistency in the acute and subacute stages, while some variability was noted in cases of chronic thrombus. This variability may be attributed to assumptions based on patient history and interval scans, especially in cases of minor acute layer thrombosis. Here, sonodoppler played a more significant role in isolation.

It is imperative to mention that our treatment approach includes the administration of low molecular weight heparin and oral anticoagulants for a duration of 3 to 6 months, as well as the adoption of intravenous thrombectomy and thrombolysis. In cases where wall damage and valvular damage lead to complications, the role of phase detection becomes paramount.

Venous thrombosis and its initial viscosity represent crucial factors in the context of DVT SWIRE. The combination of ARFI measurements makes a significant difference, emphasizing the importance of not overlooking basic sonography Doppler. (6,7,8)

In our classification, the mean average for acute thrombosis is 5.7 days, while for chronic thrombosis, it extends beyond 8 months. It is worth noting that these references are correlated with symptoms and DVT echogenicity, proving to be purposeful in the context of post-thrombotic syndrome. Furthermore, it is important to consider that venous thrombosis may be associated with occult malignancy.

In cases of portal vein thrombosis due to tumor invasion, higher values were

observed compared to non-tumour-related thrombosis in portal veins, particularly in the presence of cirrhosis.

CONCLUSION

The major role of this lies in trans-catheter thrombolysis before the clot adheres to the vein wall, transitioning from the acute to subacute phase. Since ARFI is a unit value, it plays a phenomenal role in concordance with acute DVT even before clinical onset. ARFI measurements of muscle and the veno-muscular complex provided sufficient correlative information in cases of acute and subacute DVT, as well as in the context of chronic DVT. Furthermore, ARFI reinforces its utility in the prognosis and management of acute-on-chronic DVT. The sample size is the limitation of this study. More patients with chronic DV need to be evaluated for the establishment of ARFI values.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

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