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Ramifications, maturation and complications of arteriovenous fistula for long-term dialysis and its evaluation by Sonographic Doppler and elastography by acoustic radiation force impulse

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Abstract

Background: In the context of end-stage renal disease (ESRD), kidney transplantation and hemodialysis emerge as critical therapeutic avenues. However, the emergence of secondary complications is a prevailing concern. To address this, we undertook an innovative study utilizing sonography Doppler ARFI to comprehensively evaluate myopathy and the complexities associated with arteriovenous fistula (AVF) in ESRD patients.

Methods: We conducted a prospective observational study encompassing 65 ESRD patients who had undergone AVF for hemodialysis. The study was conducted in strict adherence to rigorous guidelines and received ethical and scientific committee approvals. A proficient team of radiologists carried out periodic assessments, employing ARFI values in tandem with ultrasonography and Doppler techniques. Patient evaluations were conducted at 0, 2, and 4 months subsequent to the creation of the AVF.

Results: The study cohort exhibited a distribution of 67.7% males and 32.3% females. The AVF placements encompassed 50.8% radial artery to cephalic vein connections and 49.2% brachial artery to cephalic vein connections. Initial AVF assessments at the onset (0 months) unveiled an absence of complications, with corresponding ARFI values well within the normal range. Progressing to the 2-month mark, 52.3% of patients displayed uncomplicated AVFs, indicative of proficient functionality and characterized by diminished ARFI values attributed to the steal phenomenon. Conversely, 47.5% of cases exhibited complications alongside normative ARFI values. Upon reaching the 4-month interval, 40% demonstrated uncomplicated AVFs with notably reduced ARFI values, while 60% presented complexities while still retaining ARFI values within the expected range.

Conclusion: Our study introduces a groundbreaking methodology for evaluating complications linked to AVFs through the utilization of sonography Doppler ARFI. The integration of ARFI values with Doppler techniques facilitated a comprehensive comprehension of both AVF successes and failures. The timely identification of myopathy significantly contributed to the efficacy of diagnoses and management strategies. Despite the relative scarcity of comparable research, our study differentiates itself through its systematic clinical rigor and technical methodologies within a tertiary medical environment. The outcomes of our study exhibit promising implications for elevating the prognosis of ESRD patients, consequently enhancing both their physical tolerance and overall quality of life.

Keywords: ESRD, AVF, Sonography Doppler ARFI

Introduction

Chronic kidney disease and end-stage renal disease (ESRD) require renal transplantation as a permanent solution, and the long-term temporary alternative is purification dialysis. Among various ways of purifying blood from chemical pollutants, hemodialysis is considered superior. For this purpose, an arteriovenous fistula (AVF) is performed to facilitate venous dilatation and maturation through endothelial changes, rendering it suitable for multiple venipunctures using a large gauge needle [1]. Sonodoppler can reveal matured outflow veins and facilitate the first puncture [2]. Rayner *et al.* [3] incorporated the rule of six in K-DOQI guidelines [1], where the flow volume should be >600 ml/min and the diameter >6 mm. The brachial artery's flow rate should be 80 to 120 ml/min [4, 5]. After AVF creation, the vein gradually shows arterialization from day one to a few weeks [5]. Brachial artery flow volume was measured before AVF creation and at 1, 7, 28, and 258 days in RCP by Lomonte *et al.*

They found that on the first day, the flow rate was 250 to 500 ml/min, increasing to a maximum of 500 to 900 ml/min on the 28th day [6].

The reasons for non-maturation are due to failure of arterial dilatation, venous dilatation, and accelerated or decelerated veno-neointimal hyperplasia. Other complications include thrombosis, stenosis, aneurysm, arterial steal syndrome, and heart failure (If AVF volume is more than 2000 ml/min).

Myopathy is an inevitable condition and is usually underdiagnosed in ESRD and hemodialysis patients [7]. Signs include proximal limb muscle weakness, wearing, low endurance, exercise limitation, and fatigability [8]. Dialysis patients are less active [9], have reduced exercise capacity [10], and poor functioning [11-12]. This was previously unnoticed due to the lack of a reliable tool [13]. Approximately 50% of dialysis patients develop obvious myopathy [14-15], while other studies show myopathy in varying grades and clinical and subclinical forms in patients [16]. Several studies have shown that dialysis patients are weaker, with loss of muscle volume and muscle bulk, resulting in asthenia [14, 17-20]. Muscle atrophy, myopathy, and neuromuscular function alterations occur in the central nervous system during dynamic activity, affecting nearly normal portions of muscle fibers or combinations of these systemic mechanisms [21-22]. Some literature mentions that ESRD myopathy is more common in dialysis patients compared to those without dialysis [23-25]. The main causes include acidosis, altered serum calcium, inactivity, malnutrition, inadequate dialysis, or hyperparathyroidism [18, 24]. Low physical activity leads to atrophy [23]. Campistol divided myopathy into three factors: classic factors, muscle mitochondrial alteration-related factors, and functional factors. Type 2 fibers are involved in CKD [24]. Some reports suggest that fiber typing is potential evidence of neuropathic processes, with noted mitochondrial and other structural abnormalities constituting myopathy [26-28]. ARFI was performed in the forearm brachii and flexor carpi radialis and in the arm Brachioradialis. To standardize machine values, we used non-CKD and CKD values. Several muscle biopsy studies have been conducted in patients with renal failure [24, 27-28]. Abnormal muscle architecture is more prominent in ESRD hemodialysis patients when compared to CKD patients who have not yet started dialysis [23]. There are two types of elastography: qualitative and quantitative. Among quantitative methods, ARFI with a representative numerical value is the most accepted and convincing in the research literature.

To address this, we conducted an innovative study utilizing sonography Doppler ARFI to comprehensively evaluate myopathy and the complexities associated with arteriovenous fistula (AVF) in ESRD patients."

Methodology

The aim of the study is to predict the necessary maturation of Arterio-Venous fistulae and the early prediction of its success and failure by utilizing sonography Doppler ARFI. The objectives include detecting the time taken for AVF maturation and identifying correctable reasons if there is a delay in it for long-term dialysis, as well as utilizing optimum and maximum imaging resources in the form of the sonography Doppler ARFI unit scale for AVF vasculo musculature.

Materials and Methods: A prospective observational study

was conducted in the departments of radiology and imaging sciences, vascular surgery, and dedicated high-end nephrology units at Apollo Main Hospital Chennai. The perfectly suitable sample size of 65 patients with end-stage renal disease (ESRD) who underwent arterio-venous fistula construction for hemodialysis purposes was followed for a period of 1 year.

In this study, we adhered to stringent guidelines, protocols, obtained scientific committee approval, ethical committee approval, and secured patient-understandable informed consent from respective boards and participants. Patients who underwent an arterio-venous fistula (AVF) for hemodialysis and had end-stage renal disease were included, while patients with a history of musculoskeletal diseases were excluded from this research. The high-resolution ultrasonic scanner, Siemens Acuson S3000, was equipped with sonography, color, power, and pulsed Doppler ARFI capabilities, utilizing a transducer with a broad frequency spectrum of 7–12 MHz.

Statistical Analysis

All continuous variables were represented as mean \pm SD. Categorical variables were expressed as percentages. Comparison of continuous variables was performed using an independent sample t-test, while the chi-square test or Fisher's exact test was used for categorical variables. Receiver operating characteristic (ROC) analysis was carried out to determine the optimal cut-off value of ARFI by finding optimal sensitivity and specificity. Data entry was performed using Microsoft Excel 2007, and data validation and analysis were conducted using IBM SPSS version 25.0. A significance level of $P < 0.05$ was considered statistically significant.

Imaging Protocol

To establish and calibrate our musculature ARFI, we conducted the study group to standardize ARFI numerical values. Each patient was positioned in a supine posture with elbow extension for B-mode and Doppler evaluation of the Arterio-Venous fistula, as well as ARFI imaging of the Biceps brachii, Brachioradialis, and Flexor carpi radialis muscles. Sono Doppler assessment of the Arterio-Venous fistula was performed on the arm for Brachiocephalic Arterio-Venous fistula and on the forearm for Radiocephalic Arterio-Venous fistula. The diameter of the fistula and the arterial end's draining vein were obtained using B-mode, while flow velocity across the Arterio-Venous fistula was assessed using color, power, and pulsed Doppler, with measurement of peak systolic velocity (PSV). Diameter values were measured in centimeters (cm), and PSV values were measured in centimeters per second (cm/s).

For ARFI imaging of the Biceps brachii, Brachioradialis, and Flexor carpi radialis muscles, a linear ultrasound transducer was utilized on both the arm and forearm. Scanning for the Biceps brachii muscles extended up to 8 cm above the elbow joint, while for the Brachioradialis and Flexor carpi radialis muscles, scanning was performed up to 8 cm below the elbow joint. All ARFI-VTQ values were duly recorded. A fixed-dimension region of interest (1×0.5 cm box) was applied to the Biceps brachii, Brachioradialis, and Flexor carpi radialis muscles, with corresponding ARFI-VTQ values recorded. ARFI-VTQ values were measured in meters per second (m/s) and were acquired for the Biceps brachii muscle, Brachioradialis muscle, and

Flexor carpi radialis muscle. The ARFI numerical measurements were carried out five times in each scalable area, and the mean values of the muscles were utilized to enhance accuracy.

Results

Our study included a gender distribution of 67.7% males and 32.3% females. The AVF radial artery to cephalic vein site accounted for 50.8%, while the brachial artery to cephalic vein site constituted 49.2%. At 0 months, there were no complications associated with AVF, and the mean ARFI value fell within the normal range.

The Effect of following complications of Arterio-venous fistulae in our study and by way of its flow pattern and luminal patency and the ARFI recording is as follows:

1. Partial thrombosis,
2. Cellulitis with infective abscess in the vicinity of arteriovenous fistulae,
3. Extraneous compression by collection or hematoma,
4. Pseudoaneurysm,
5. Complete intra-luminal narrowing/thrombosis.

This study revealed similar ARFI changes in the above types of complications of 1- 5 during the period of study and follow-up of the patients and the mean ARFI value found to be 2.5 m/sec (Mentioned in following table-1). At 2 months, 52.3% displayed no complications (Similar to figure 1 and 2), characterized by a reduced ARFI value indicating satisfactory AVF function due to steal effect, causing a decrease in ARFI value associated with myopathy. Conversely, 47.5% experienced other complications, despite having an essentially normal ARFI value, suggesting the absence of arterial steal. At 4 months, 40% exhibited no complications with a reduced AFRI value, indicating functional AVF, while the remaining 60% of patients

encountered various complications with ARFI values within the normal range. Additional findings revealed that 13.8% (total 9) of patients were below 40 years of age (total 33), 50.8% were in the 41-60 year age group, and 35.4% (total 23) were older than 60 years. In terms of gender, 67.7% (total 44) were males, and 32.3% (Total 21) were females. The surgical sites encompassed 50.8% (total 33) radio-cephalic and 49.2% (Total 32) brachio-cephalic cases (Table - 1).

This study revealed similar ARFI changes in the aforementioned types of complications during the study period and patient follow-up. Among the group of 65 hemodialysis patients, no Arterio-Venous fistula complications were observed at 0 months, with a mean ARFI-VTQ value of 2.6 m/sec.

After 2 months, 52.3% (total number 34) of these patients exhibited a normal Arterio-venous fistula with no complications, and the mean ARFI VTQ value decreased to 1.8, indicating proximal myopathy. Conversely, 47.7% (total number 31) of these cases presented complications of the Arterio-venous fistula, as described above, leading to reduced flow, and the mean ARFI-VTQ value was found to be 2.5 m/sec.

At 4 months of hemodialysis, 40% (Total number 26) of the patients showed a normal Arterio-venous fistula with no complications, and the mean ARFI VTQ value decreased to 1.8, suggesting proximal myopathy. Furthermore, partial thrombosis was identified in 8 cases (12.3%), while cellulitis with infective abscess was observed in 5 cases (7.7%). Hematoma was noted in 10 cases (15.4%), pseudoaneurysm occurred in 6 cases (9.2%) (Refer Figure 5,6), and complete intraluminal narrowing/thrombosis was present in 10 cases (15.4%) (Refer Figure 3, 4). The mean values for all these complications are provided in Table-1.

Table 1: Doppler- arfi - at 2 months and 4 months

Doppler ARFI	At 2 months, (n=65)		8	
	n (%)	Mean	n (%)	Mean
Without any complication	34 (52.3)	1.8	26 (40)	1.8
Partial Thrombosis	10 (15.4)	2.5	8 (12.3)	1.5
Cellulitis with infective abscess in the vicinity of AVF	8 (12.3)	2.5	5 (7.7)	2.5
Extraneous compression by collection or hematoma	8 (12.3)	2.5	10 (15.4)	2.5
Pseudoaneurysm	4 (6.1)	2.5	6 (9.2)	2.5
Complete intra luminal narrowing/thrombosis	1 (1.5)	2.5	10 (15.4)	2.5

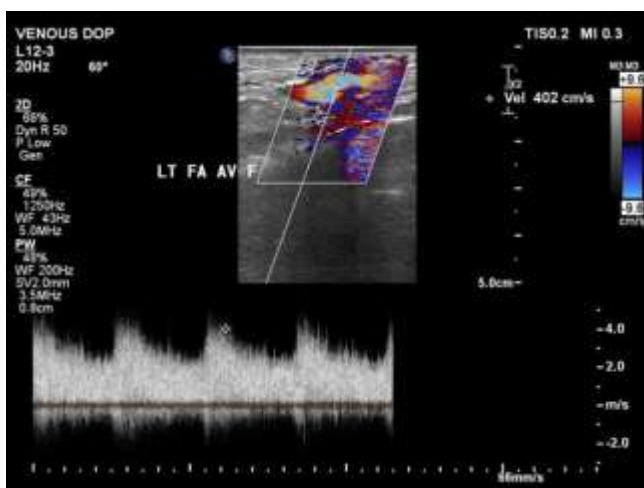


Fig 1: Normal AVF showing normal flow at 2 months in normally functioning AV fistula.



Fig 2: ARFI value of Brachioradialis muscle is 1.6 m/sec at 2 months in Normally functioning AV fistula.



Fig 3: AVF showing short segment narrowing at 4 months.



Fig 6: ARFI value of Flexor carpi radialis muscle is 2.5 m/s at 4months with Pseudoaneurysm.

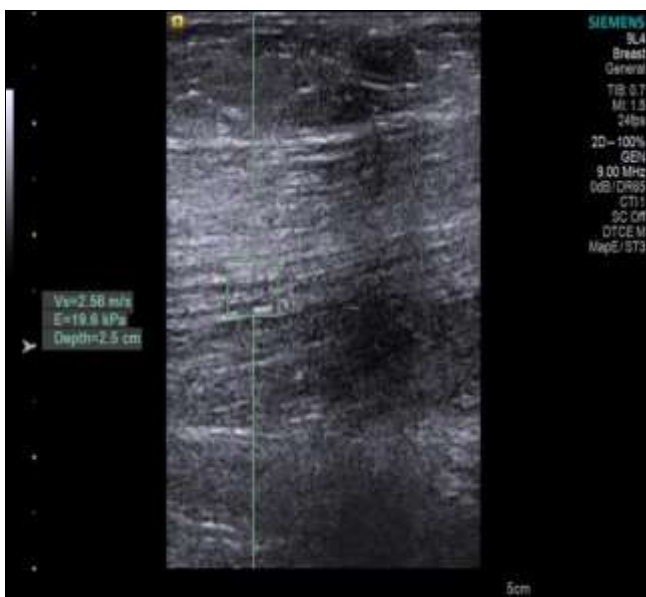


Fig 4: Flexor carpi radialis muscle showing an ARFI value of 2.5 m/sec in AVF narrowing with reduced flow at 4 months.

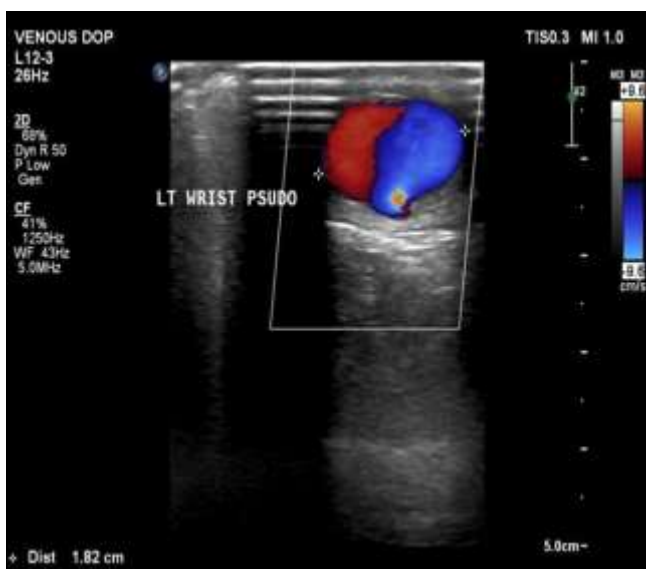


Fig 5: AVF showing pseudo aneurysm with swirling flow at 4 months

Discussion

The global prevalence of chronic kidney disease is alarmingly high, and its progression to end-stage renal disease is influenced by various factors such as age, gender, dietary habits, primary renal glomerular diseases, and secondary comorbidities like cardiac, hepato-biliary, hypertension, and diabetes-related conditions [8, 11]. Once a patient is diagnosed or predisposed to renal disease, preventive measures can be implemented in many instances; however, ESRD necessitates a definitive solution, such as renal transplantation, while dialysis remains the only option for both transplantable and non-transplantable patients [20]. The process of dialysis is an ongoing requirement, typically taking 6 to 8 hours on alternate days to mitigate the severe consequences and potential hazards associated with ESRD. [7, 13, 15, 17]. Achieving this task effectively involves the establishment of an arteriovenous fistula (AVF) as the standard approach. Maintaining the functionality of AVF and promptly identifying correctable complications are the core aspects addressed in this study. Multidisciplinary collaboration plays a pivotal role in ensuring the success of arteriovenous communication, highlighting its indispensable nature [5].

Sonography Doppler technology contributes significantly to this field, offering valuable insights when interpreted by skilled professionals. Elastography, specifically quantitative ARFI, has been integrated into this research, proving its value across clinical, laboratory, surgical, and cytological domains. The normal range of ARFI values falls between 3.5 to 2.5 m/sec. In ESRD cases, ARFI values averaged around 2 m/sec. The successful AVF function in ESRD patients displayed a gradual reduction in ARFI values, possibly reaching as low as 1.4 m/sec due to arterial steal, indicating a marker of myopathy in numerical terms. Conversely, an unnoticed, gradual failure was associated with higher ARFI numerical values, reaching up to 2.5 m/sec.

At the 2-month mark, 52.3% of the patients displayed a normal Arterio-venous fistula with reduced ARFI values indicative of proximal myopathy, while 47.7% experienced complications, leading to reduced flow and slightly elevated ARFI values. The 4-month data showed that 40% had normal functioning AVF, with decreased ARFI values signaling proximal myopathy, while 60% encountered

complications, resulting in reduced flow and corresponding ARFI values.

These findings corroborate the estimated 50% prevalence among dialysis patients, as indicated by Clyne N. [7] in 'Physical working capacity in uremic patients' and Arnold R. *et al.* [15] in 'Neurological complications in Chronic kidney disease.' The ARFI-VTQ values differed significantly (p -value > 0.0001) between normal and myopathic muscles when subjected to sonodoppler elastography, with myopathic muscles displaying lower ARFI-VTQ values, indicating reduced stiffness. Previous studies have highlighted type II muscle fiber atrophy in CKD and ESRD myopathy, contributing to the softer nature of affected muscles. Notably, quantitative ARFI values for Biceps brachii, Brachioradialis, and Flexor carpi radialis muscles in the adult population lack documentation in the existing literature.

Limitations of the Study

Despite adhering to stringent selection, employing experienced professionals, and following rigorous guidelines for inclusion and exclusion, the study's small sample size poses a limitation. Variations in ARFI changes may arise due to physiological and comorbidity factors, and other confounding variables were not comprehensively studied. The study's single-center nature also warrants consideration, suggesting the potential benefits of multicenter endeavors with larger participant cohorts.

Conclusion

Our study sheds light on the physio pathological ramifications of AVF complications, documented through Sonography Doppler ARFI VTQ values in specific muscles. This technique proves non-invasive, secure, cost-effective, and time-saving, presenting an efficient means of early detection and management of myopathy. By improving exercise tolerance and enhancing the patients' quality of life, effective myopathy management is pivotal.

In summary, Acoustic Radiation Force Impulse (ARFI) imaging, a form of shear wave elastography, demonstrates its utility as a feasible method for discerning normal and myopathic muscles in chronic hemodialysis patients. This non-invasive technique can serve as a screening tool for differentiating between these conditions, contributing to more accurate diagnoses. The application of ARFI is appealing due to its accessibility, affordability, and compatibility with prevalent ultrasound machines. Detection and management of myopathy can significantly enhance patients' quality of life. While limitations such as the small sample size exist, larger studies could further validate these findings. Continued research in muscle sonoelastography, particularly ARFI, could solidify its role as a practical, painless, and cost-effective approach for myopathy screening.

Conflict of interest: Nil

Ethical clearance

Institutional ethical committee approval was obtained, and Informed consent was obtained from all the study participants.

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