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Role of Doppler Ultrasound in Assessment of Local Factors Affecting Maturation of Arteriovenous Fistula in Haemodialysis Patients

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ABSTRACT

Background: The creation of a native arteriovenous fistula (AVF) is a crucial procedure for patients undergoing haemodialysis (HD). Doppler ultrasound (DUS) has recently been acknowledged as a standard method for vascular mapping, however it has been noted that there is a lack of evidence to support this recommendation.

Objective: This study aimed to determine the efficacy of DUS in detecting the expected parameters associated with the maturation of AVFs in HD patients.

Patients and methods: We performed DUS examinations on all AVFs created at our institute for this retrospective study. Patient characteristics as well as concomitant diseases and DUS parameters pre- and post-operative were analysed. Variables associated with maturation were analysed in multivariate models by logistic regression.

Results: Successful maturation was observed in 58% of the patient cohort. Univariate analysis indicated that a larger diameter of the selected vein and a shorter distance between the vein and artery preoperatively were significantly associated with successful maturation (P = 0.032 and 0.047, respectively). Both the diameters of the outflow vein and inflow artery, along with the fistula flow volume, were significantly elevated in patients who achieved successful maturation (p=0.00). The multivariable logistic regression analysis indicated that the diameters of both the outflow vein and inflow artery, along with the blood flow volume at the fistula site post-surgery, significantly influenced the successful maturation.

Conclusions: The importance of DUS aids in evaluating the risk of failure, thereby enhancing the durability of vascular access and improving patient outcomes.

Keywords: Arteriovenous fistula (AVF), Doppler ultrasound (DUS), Haemodialysis (HD).

INTRODUCTION

For patients receiving haemodialysis (HD), the creation of arteriovenous fistulas (AVFs) is essential to the success of their treatment [(1)]. The exact prediction of AVF maturation is still a considerable problem that is faced on a daily basis, even with improvements in monitoring and assessment methods. Therefore, it is necessary to acknowledge this to increase awareness and understanding regarding the recurring issue of maturation failure in AVF [(2)].

Utilising Doppler ultrasound (DUS) for mapping is vital in the selection of vessels for AVF, which helps to decrease the rate of maturation failure [(3)]. The most recent updates to vascular access guidelines indicate that there is insufficient evidence to advocate for routine vascular mapping via DUS for all patients. Nevertheless, they recommend conducting preoperative DUS for those patients who present risk factors associated with maturation failure [(4)]. In this context, a previous study investigated the DUS factors related to the maturation of AVF. The findings indicated that successful maturation was linked to an increase in vein diameter and systolic blood pressure [(5)].

Mendes *et al.* [(6)] assessed how the diameter of the cephalic vein influences the successful maturation of AVF and found that a diameter exceeding 2 mm enhances AVF maturity. On the other hand, research has indicated that the diameter of blood vessels by itself is not a dependable measure of the maturation of AVFs. It is essential to consider other factors, such as the distensibility of the veins and the reactive hyperaemia of the selected artery [(7)]. Additionally, the diameter and depth of the AVF, as well as the postoperative blood flow rate, are predictors of overall survival in patients with an AVF, and a previous study found that an AVF is likely to mature early when the postoperative flow rate exceeds 300 ml/min. This implies that patients who do not meet this criterion may gain advantages from an earlier intervention with an alternative approach [(8)].

Therefore, identifying blood vessels that are more suited for the maturation of AVF and understanding the factors associated with higher AVF maturation rates highlight the importance of Doppler Ultrasound (DUS). The purpose of this study was to determine the efficacy of DUS in detecting the expected parameters associated with the maturation of AVFs in HD patients.

PATIENTS AND METHODS

This retrospective study encompassed patients suffering from chronic kidney disease who were referred to the radiology department between October 2021 and March 2022.

Inclusion criteria: The study included adult' patients > 18 years who were candidates for creation of native AVF in the upper limb . Upon reviewing the DUS data, we

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concluded that it was necessary for study participants to have access to measures from two DUS examinations—one performed before the surgery and another conducted six weeks after the creation of the AVF.

Exclusion criteria: Participants aged 80 years or older, experienced severe heart failure or arrhythmias and were unable to maintain stability during the DUS examination or exhibited vascular abnormalities that required the use of another interventional procedure. Furthermore, the absence of a DUS examination or the existence of only one examination.

Evaluation of vascular access: Before the DUS scan, a vascular surgeon with experience creating AVFs conducted a clinical evaluation of each patient's vascular access.

Pre-operative: The pulses at the elbows and wrists and the superficial veins in the forearm and upper arm (with tourniquet) were assessed. Vessels were deemed appropriate if the artery had a good pulse and the vein was patent and of good calibre. The most distal possible site was selected for AVF formation.

Post-operative: Two days following the surgical procedure, a clinical examination was conducted to assess the patency and positioning of the arteriovenous fistula (AVF) and to detect any possible complications.
DUS was conducted according to a standardized protocol that had been previously outlined, both prior to and six weeks after the surgical procedure [(9)]. A skilled radiologist with experience in DUS and over six years of expertise in vascular mapping of the upper limb from our department performed all DUS evaluations. Toshiba Aplio 300 ultrasound system (Toshiba Medical Systems, Tokyo, Japan) equipped with a high-frequency linear probe that operates at 7–10 MHz was used to evaluate each patient. A thorough assessment was performed in a sequential manner employing both transverse and longitudinal scanning methods that included both arteries and veins. Additionally, colour Doppler imaging was utilised as a standard procedure for monitoring purposes.

Maturation of AVF: Successful maturation in a clinical context is demonstrated by the capacity to provide and maintain adequate blood flow for haemodialysis without the need for supplementary interventions or the closure of the fistula. Additionally, the presence of a palpable thrill and a continuous murmur over the venous outflow of the arteriovenous fistula (AVF) further indicates successful maturation [(10)]. Following a six-week period, the maturation of the arteriovenous fistula (AVF) was evaluated through Doppler ultrasound (DUS). Successful maturation was indicated by a vein diameter of a minimum of 4 mm, an AVF flow rate of at least 300 mL/min, and an outflow vein depth that was less than 6 mm from the skin surface . Failure to meet these criteria is classified as primary failure to mature [(11)].

Variables: We analysed the demographic and gender characteristics of the patients and the related comorbid conditions (diabetes mellitus and hypertension), as well as the location of the fistula.
Pre-operative: DUS parameters assessed included the diameters of the selected artery and vein. Furthermore, measurements were taken to determine the depth of the chosen vein from the skin surface and the distance between the selected vein and the neighbouring artery .
Postoperatively: A B-mode ultrasound examination was carried out to detect any possible complications such as haematoma, stenosis, or thrombosis. Measurements were obtained for the diameters of the inflow artery and the outflow vein. Furthermore, the blood flow volume through the AVF was evaluated, along with the depth of the outflow vein from the skin.
All relevant parameters were documented in a structured study proforma and were recorded by a single radiologist who was blinded to the DUS findings.

Ethical approval: This research received approval from Sohag Faculty of Medicine's Ethical Committee for Research. Code of Ethics (Soh-Med-21-10-21). After receiving all of the information, each participant signed a permission. The study protocol was proposed in accordance with the Declaration of Helsinki.

Statistical analysis

The differences among the variables under investigation were evaluated using the χ^2 test for categorical data and the independent Student t-test for continuous data. The results were expressed as percentages and as mean ± standard deviation, with a P value ≤ 0.05 indicating statistical significance. Parameters that were significant in the univariate analysis were further examined using logistic regression. A multivariate model was developed incorporating variables identified as potential confounders. Data analysis was conducted using SPSS Statistics for Windows (version 20.0; SPSS Inc., Chicago, Ill.).

RESULTS

Fifty consecutive patients eligible for AVF creation were enrolled in the study. The mean age was 47±17.33 years (range, 41 to 69 years). Twenty-seven (54%) were male, and twenty-three (46%) were female. Most participants (47%, n=27) had hypertension, eight (16%) had diabetes mellitus, and 10 (20%) had diabetes mellitus plus hypertension. In terms of AVF type, all patients underwent radiocephalic anastomoses. Out of the 50 fistulas included in our study, 13 were accessed on the right side, while 37 were accessed on the left side. By week 6, 29 (58 %) AVF had reached maturity (Figures 1 and 2).

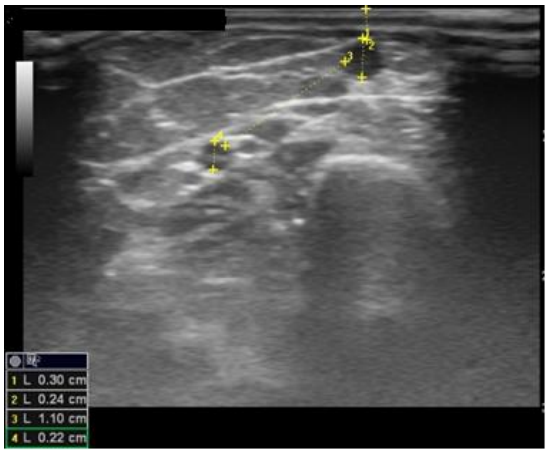

Figure (1): Vascular measurements in a patient considered for endovascular arteriovenous fistula. Transverse gray-scale ultrasound image showed measurements of the inner lumen diameter of the artery (a) and vein (v), distance between the artery and veins (yellow line), and depth from skin.

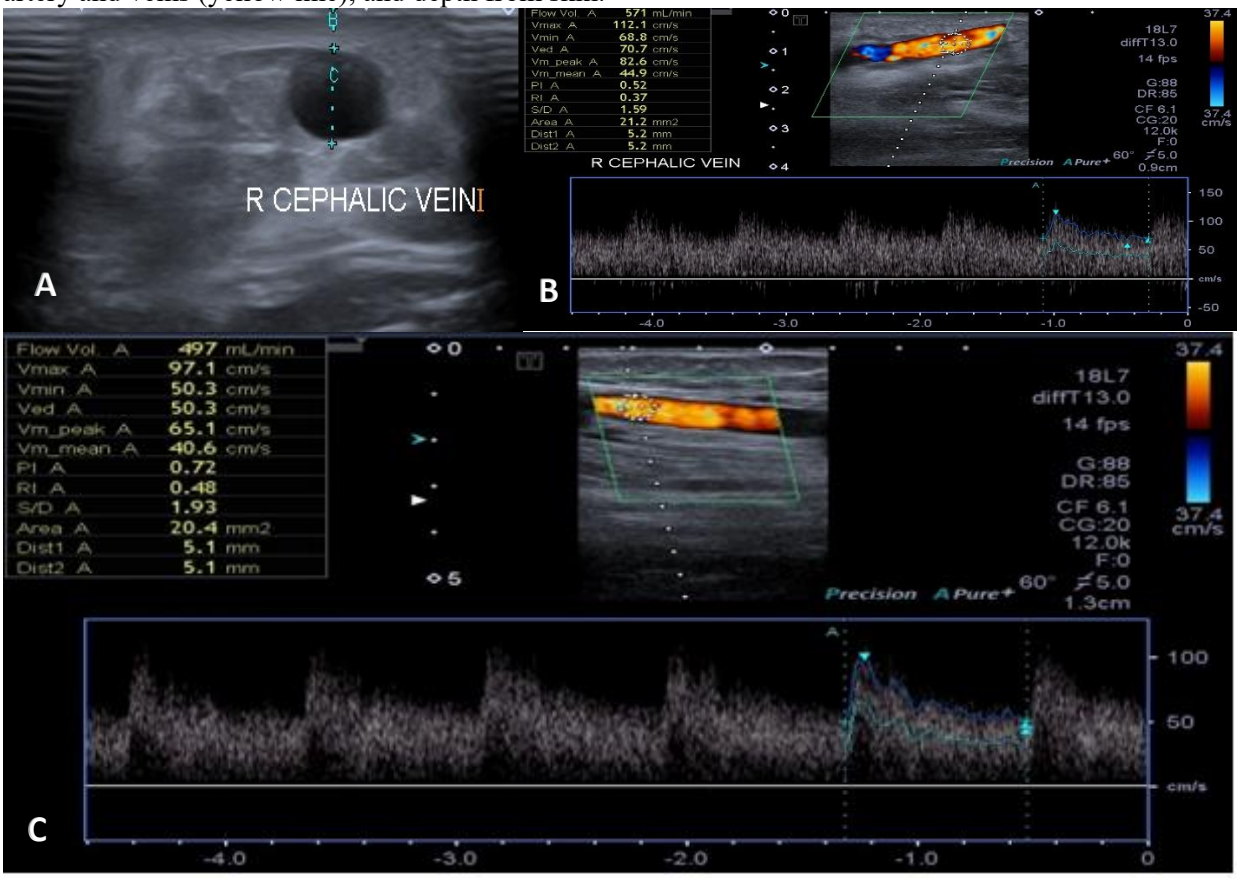

Figure (2): Mature arteriovenous fistula. **(A)** Transverse gray-scale US image showed the cephalic vein diameter is greater than 6 mm and depth is less than 6 mm from the skin surface**. (B)** Longitudinal ultrasound image showed the flow volume measurement is obtained within the outflow vein 10 cm from the anastomosis and is greater than 300 mL/min. **(c)** Color Doppler ultrasound with pulsed waveform on inflow artery that showed turbulent flow of brachial artery with monophasic low resistance flow on spectral waveform.

Causes contributing to the failure of AVF maturation were found in 21 (42 %) patients; three patients (6%) were unable to sustain an adequate flow rate for at least three dialysis sessions, 1 (2%) patient had a haematoma, 6 (12%) patients had anastomosis thrombosis, 8 (16 %) patients had vein stenosis, 2 (4%) patients had a vein diameter less than 6 mm and 1 (2 %) patient had an outflow vein depth less than 6 mm below the skin surface. The successful maturation rate was higher for the left side fistula (42 %) in comparison to the right side (16 %). No significant statistical differences were observed in patient characteristics, comorbidities, or the location of the fistula between the two groups concerning AVF maturation (Table 1 & figures 3, 4 and 5).

Table (1): Demographics and clinical characteristics of the study population, along with DUS parameters (n=50)

Variables	Results
Age mean ± SD	47±17.33
Gender n (٪) Male Female	 27 (54) 23 (46)
Comorbidity n (٪) HTN DM DM& HTN No	 27 (54) 8 (16) 10 (20) 5 (10)
Side of fistula n (٪) Left Right	 37 (74) 13 (26)
Cephalic vein diameter (mm) Mean± SD Range	3.00±0.85 1.9-5.5
Radial artery diameter (mm) Mean± SD Range	3.27±0.86 2.0-5.0
Vein depth from skin (mm) Mean± SD Range	5.28±4.34 2.0-30.0
Vein distance from nearby artery (mm) Mean ± SD Range	21.27±13.36 2.0-40.5

HTN: hypertension; DM diabetes mellitus, DUS: Doppler ultrasound

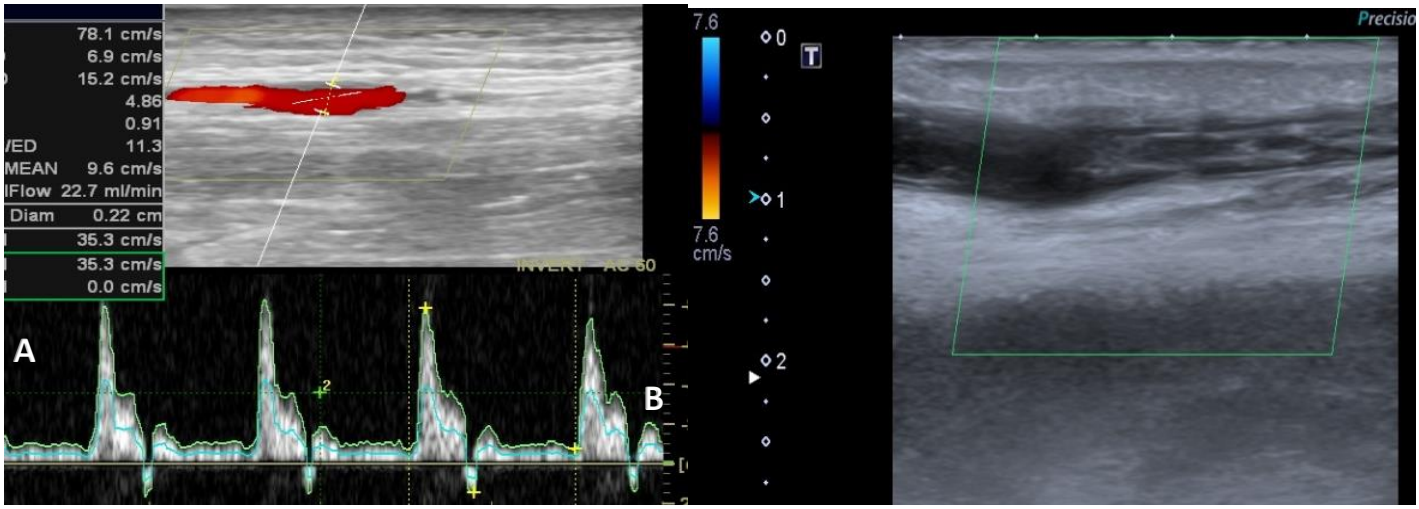

Figure (3): Radio cephalic arteriovenous fistula thrombosis in a 50-year-old man with arm pain and loss of thrill. **(A)** Longitudinal spectral Doppler ultrasound image of the left radial artery proximal to the AVF showed a high-resistance waveform with reversed diastolic flow. Normally, there is low-resistance flow in the artery proximal to a patent AVF or AVG anastomosis. **(B)** Longitudinal spectral Doppler ultrasound image of the left cephalic draining vein showed an avascular echogenic occlusive clot, with loss of blood flow and spectral waveform in the cephalic vein.

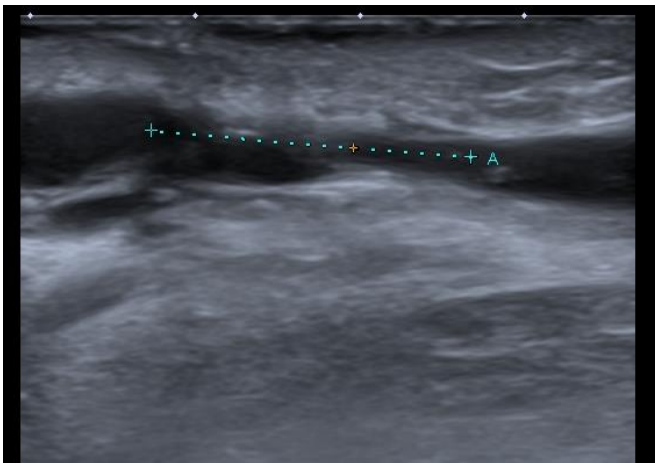

Figure (4): Doppler ultrasound image of the cephalic venous outflow showed focal area of significant stenosis

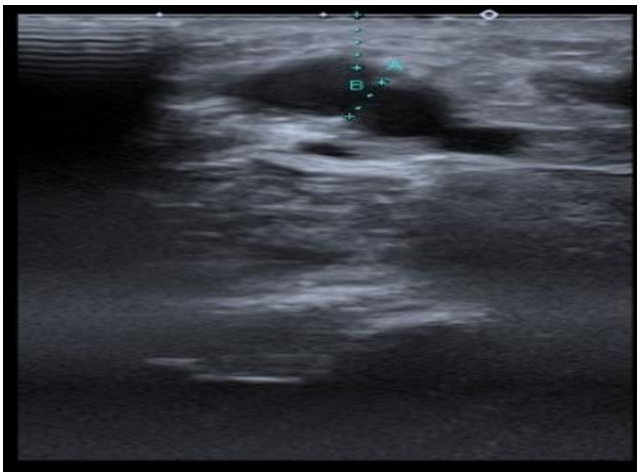

Figure (5): Post-operative ultrasound image of the anastomosis site of the radio-cephalic arteriovenous fistula (AVF): (A) diameter of the anastomotic site and (B) depth from the skin surface.

The results from the DUS indicated that the pre-operative average cephalic vein diameter, which was measured at 3.22 ± 0.86 mm, along with a reduced distance between the vein and artery, recorded at 16.89 ± 14.32 mm, were significantly associated with the mature group when compared to the failed group (P= 0.032 and 0.047 respectively) (Table 2).

Table (2): Univariate analysis of factors influencing fistula maturation prior to the creation of AVF

Parameters	**Failed AVF** N (21)	**Successful AVF** N (29)	**P-value**
Age, years, Mean±SD	49.33±17.71	45.55±17.18	0.452
Gender, n (٪) Male Female	 12 (24) 9 (18)	 15 (30) 14 (28)	0.704
Comorbidity n (٪) HTN DM DM& HTN No	 17 (34) 6 (12) 7 (14) 3 (6)	 10 (20) 2 (4) 3 (6) 2 (4)	0.845
Side of fistula, n (٪) Left Right	 16 (32) 5 (10)	 21 (42) 8 (16)	0.764
Vein diameter (mm) Mean ±SD	2.70±0.75	3.22±0.86	**0.032***
Artery diameter (mm) Mean ±SD	3.14±0.82	3.37±0.88	0.362
Vein depth from skin (mm) Mean ±SD	4.10±1.97	6.14±5.33	0.101
Vein distance from artery (mm) Mean ±SD	 24.45±11.88	 16.89±14.32	 **0.047***

HTN: hypertension; DM diabetes mellitus, AVF: arteriovenous fistula, DUS: Doppler ultrasound. ***:** significant ≤ 0.05

For the DUS studies performed 6 weeks following AVF creation, the mean diameters of the outflow vein and inflow artery were 5.54 ± 1.79 and 4.70 ± 1.14 mm respectively, as well as the mean flow volume of the fistula was 550.12±509.78 ml/min (Figure 6). Complications were observed in 15 (30%) patients. A haematoma occurred in one patient (2%) and resolved on its own following basic medical treatment, 6 (12 %) patients developed venous and arterial thrombosis, and 8 (16 %) patients developed fistula stenosis as illustrated in table (3).

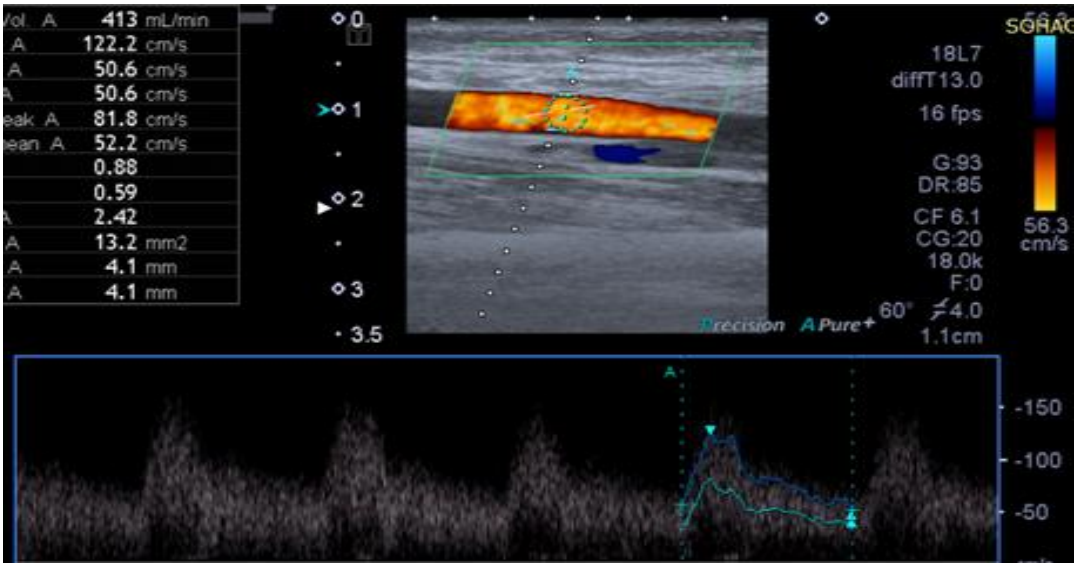

Figure (6): Technique used for blood flow volume measurement. Longitudinal ultrasound image at a straight segment of the vessel identifies an area without turbulent flow. The Doppler gate was increased in size to encompass the entire vessel diameter and was corrected to an angle of 60 degrees or less, parallel to the posterior vessel wall. Only the antegrade flow was measured.

Table 3: Post-operative DUS related- parameters

Parameter	Measurement (post-operative)
Diameter of out-flow vein (mm) Mean± SD Range	 5.54±1.79 2.2-6.4
Diameter of In-flow artery (mm) Mean± SD Range	 4.70±1.14 2.6-5.8
Fistula flow volume (ml/min) Mean ± SD Range	 550.12±509.78 300.5 – 600.4
Depth of out-flow vein (mm) Mean± SD Range	 4.036±1.63 2.0- 6.1
Complication n (%) Hematoma Thrombosis Stenosis	 1 (2) 6 (12) 8 (16)

DUS: Doppler ultrasound.

The diameters of the outflow vein and inflow artery, as well as the flow volume of the fistula were all significantly higher in the patients with successful maturation compared to those with failure (P= 0.00, 0.00, and 0.003 respectively). On the other hand, the failure group showed a significant increase in complications compared to the successful mature group (p = 0.00) (Table 4). The logistic regression analysis test included all the variables in our study that had a P value of ≤ 0.05. It was found that post-operative high diameter of outflow vein and inflow artery and flow volume of fistula were independent predictors for successful AVF maturation as shown in table (5). The overall prediction accuracy of the model was 80.3 %.

Table 4: Relationship between post-operative DUS-related parameters and the maturation of AVF, analyzed through univariate methods.

Parameters	**Failed AVF** N (21)	**Successful AVF** N (29)	**P-value**
Out-flow vein diameter (mm) Mean ± SD	3.99±1.64	6.66±0.77	**0.000 ***
In-flow artery diameter (mm) Mean ± SD	3.88±1.05	5.30±0.77	**0.000 ***
Fistula flow volume (ml/min) Mean ± SD	176.34±186. 50	820.79±499. 28	**0.003 ***
Out-flow vein depth (mm) Mean ± SD	3.91±1.94	4.13±1.38	0.632
Complications n (%)	14 (66.7)	1 (3.4)	**0.00***

AVF: arteriovenous fistula; DUS: Doppler ultrasound; ***:** significant ≤ 0.05

Table (5): Multivariate logistic regression analysis of preoperative and postoperative factors influencing fistula maturation

Variables	P- value
Out-flow vein diameter (mm)	**0.001***
In-flow artery diameter (mm)	**0.001***
Fistula flow volume (ml/min)	**0.002***
Complications	**0.001**
Vein diameter (mm)	0.214
Vein distance from artery (mm)	0.32

DISCUSSION

Currently, there is insufficient evidence to support the use of DUS to evaluate AVF. This is primarily due to research limitations, including the variability of criteria for determining AVF maturity between studies, which complicates comparison of results. Furthermore, most studies have addressed each criterion separately, and therefore the timing of DUS evaluation remains controversial [12].

The aim of this research was to evaluate the efficacy of DUS both before and after surgery in detecting the expected parameters associated with the maturation of AVFs in patients receiving HD. The investigation spanned six weeks during which clinical evaluations were performed alongside DUS to track the maturation of AVFs. We employed multivariable logistic regression to analyse the relationships between the ultrasound measurements.

The study found that demographic factors such as age, gender, and comorbidities had no impact on the maturation of the AVF, which is consistent with results from earlier studies [13, 14, 15]. A previous meta-analysis revealed that older patients, particularly those aged 50 to 70 years, demonstrated an increased rate of primary AVF failure [16]. **Wan *et al.*** found that for every 20-year increase in age, there was a significant association with a more than 54% rise in the risk of AVF immaturity [17]. Elderly individuals are more susceptible to hypertension and diabetes mellitus. These risk factors poorly predict AVF non-maturation, as they impair endothelial function, leading to decreased vascular relaxation and increased infiltration of inflammatory cells in blood vessels [18].

The study's patient population consisted of women, who represented 46% of the cohort. Our observations indicated a slight advantage for the male gender. However, this difference is not statistically significant. Despite a higher number of male participants in this study, the figures remain consistent with findings from another research in this field [19].

According to current studies, being female is a negative predictor of AVF maturation [20, 21]. Women are statistically more prone to developing kidney failure compared to men. However, the progression of the disease occurs at a quicker rate in men, which raises the chances of requiring dialysis and an arteriovenous fistula [22].

The forecast of AVF maturation relies on preoperative Doppler ultrasound evaluations, which offer essential information regarding vascular structure and blood flow dynamics [23]. When the preoperative assessment was limited to clinical evaluations, the failure rate associated with the creation of an AVF could reach 25%. However, incorporating DUS examination prior to surgery reduced this rate to 5.6%. The use of DUS measurements has now become a standard component of the preoperative evaluation process [24]. A prior investigation revealed that preoperative DUS significantly enhances the development of AVF and increases their suitability for dialysis. Additionally, it effectively raises the number of patients able to utilise the fistula for HD. These favourable results are likely attributed to DUS's ability to identify suitable vessels that may not be detected through a standard clinical assessment [25].

Univariate analysis conducted in our study indicated a significant association between the maturation of the AVF and both the preoperative diameter of the selected vein and its distance from the artery. Studies have shown that patients with a larger vein diameter identified during preoperative vein mapping are more likely to achieve better long-term patency of AVFs and have a lower risk of fistula maturation failure. To ensure the selected veins are suitable for AVF creation, it is recommended to conduct DUS assessments prior to the surgical procedure [26, 27]. **Luavao *et al.*** [28] also examined AVF maturation and functional progression in a group of 158 individuals. The diameter of the chosen vein was found to be the only independent predictor of maturation in the multivariate logistic regression analysis ($p = 0.002$). A comprehensive review identified 804 studies that examined the correlation between successful AVF maturation and the diameter of the chosen vein. Each study concluded that the vein's diameter is a reliable indicator of successful maturation. Nevertheless, consensus on the precise minimum venous diameter necessary for accurate maturation prediction remains elusive, with current research indicating that this diameter falls between 2.5 mm and 4 mm [29]. These results are close to the values observed in our study, which were 3.00 ± 0.85 mm. According to **Khavanin *et al.*** [30], there is an association between the rate at which fistulas successfully mature and the average vein diameter, which is 2.40 mm [30].

Regarding the distance between the chosen vein and artery. Our findings are consistent with surgeons' efforts to develop procedures that reduce the distance between the chosen vein and the artery. The transposition of the radial artery to the cephalic vein in the distal forearm is an important procedure in this regard. This approach aids

in reducing the extensive venous mobilisation required to establish an AVF [31].

This study successfully met its goal in 58% of the cases analysed. Four key post-operative factors were recognised as predictors of successful maturation: An increase in the diameters of both the inflow artery and outflow vein, enhanced flow volume through the fistula, and the lack of complications. The results of our research indicated that the multiple regression statistical model confirmed the predictive significance of these postoperative factors concerning the maturation of the arteriovenous fistula (AVF). Our results align with an earlier meta-analysis which indicated that a mere 60% of fistulas achieve effective dialysis. This is due to the fact that, even after successful maturation of AVF, a considerable number of cases necessitate reintervention because of ongoing stress from repeated puncture and fistula stenosis [32].

The development of the anastomosis initiates the maturation process. During this development, vascular remodeling occurs, which is characterised by increased wall shear stress, resulting in an increase in arterial and venous blood flow and diameter. This action eventually helps to normalise the pressure applied to the vessel walls, as per Poiseuille's Law [33]. There is a significant link between vessel diameter and AVF flow, implying that blood flow is the most important element controlling the vein's ultimate diameter [27].

The occurrence of early complications after the creation of an arteriovenous fistula (AVF) is often a significant negative indicator of successful maturation [34]. A previous study found that early complications, particularly thrombosis, pose a serious challenge [35]. Timely identification and management of these complications enhance the likelihood of the AVF being functional for haemodialysis. The creation of AVF necessitates vascular mapping both prior to and following the surgical procedure, and DUS can fulfil this requirement. It recognises possible complications and aids in establishing the most suitable timing for the puncture of the AVF [36]. Previous studies have shown that DUS can reduce the need for further invasive interventional procedures, underscoring its significance in the continuous monitoring of AVF [6]. Furthermore, the prompt detection of AVF failure enables timely interventions, which may include the replacement of the vascular access [37].

LIMITATIONS

Limitations of our research encompass the retrospective evaluation of arteriovenous fistula (AVF) outcomes, with a limited sample size and a short-term follow-up period. Furthermore, the study was carried out at a single institution, and we did not consider additional factors that influence the successful maturation of AVFs.

CONCLUSION

Monitoring of all native fistulas through DUS, performed both before and after surgery, provided the advantage of identifying suitable vessels for AVF and decreased the incidence of primary fistula failure. This prompt identification allowed for immediate action, thereby significantly lowering the likelihood of complications.

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Lists of Abbreviations
AVF: Arteriovenous fistula, **DUS:** Doppler ultrasound, **HD:** Haemodialysis.

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