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Original research

IMAGING DIAGNOSIS AND TREATMENT RESULTS OF ARTERIOVENOUS FISTULAS STENOSIS COMPLICATION AMONG HEMODIALYSIS PATIENTS

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ABSTRACT

Introduction: *Percutaneous transluminal angioplasty (PTA) presents several advantages in addressing arteriovenous fistula (AVF) stenosis compared to surgical approaches. In addition, Doppler ultrasonography (DUS) serves as a noninvasive technique for stenosis measurement and access flow volume calculation. This study aimed to evaluate the agreement in stenosis diagnosis using PTA and DUS before intervention and to assess the effectiveness of the PTA method after intervention.*

Method: *A non - controlled intervention study involved 15 chronic HD patients with a mature AVF in place for over three months, presenting AVF stenosis ≥ 50%, who underwent PTA intervention. Correlation analysis was employed to assess the similarity of AVF stenosis evaluations using DUS and PTA. The study also compared pre - and post - intervention indicators to evaluate the effectiveness of PTA intervention.*

Results: *The results indicated a strong positive correlation between the two techniques (r = 0.997, r2 = 0.994, p < 0.001). Following intervention, all patients were considered successful, with significant reductions observed in various indicators, including alterations in murmurs along AVF, VAPR, the number of patients with AVF stenosis ≥ 50% on DUS, and none with Qmin < 500 mL/min.*

Conclusion: *This study recommends utilizing DUS to evaluate stenosis before contemplating PTA intervention, owing to the correlation and similarity observed in the results of AVF stenosis examination between these two techniques. Ultimately, our research endorses PTA intervention as the preferred method for HD patients with AVF stenosis, considering the observed enhancements in clinical, hemodialysis, and DUS parameters.*

Keywords: *Doppler ultrasonography, percutaneous transluminal angioplasty, arteriovenous fistula stenosis, hemodialysis*

I. BACKGROUND

More than 10% of the world's population, totaling around 800 million individuals, grapple with chronic kidney disease (CKD). In Vietnam, approximately 12.8% of the population, equivalent to around 8.74 million people, is affected by CKD [1, 2]. Hemodialysis (HD) is the predominant long-term treatment for end - stage renal disease patients. In 2018, globally, 2,823,000 out of 3,171,000 undergoing renal replacement therapy received HD [3]. The primary vascular access types for HD are arteriovenous fistulas (AVF), arteriovenous grafts (AVG), and central venous catheters (CVC) [4]. AVF is the most commonly chosen, with 63% of HD patients opting for it, while AVG accounts for 16.7%, and various catheters make up the remaining 19.6%,

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according to data from the United States Renal Data System spanning 2012 to 2020 [5]. Around 15 - 20% of hospitalizations for CKD patients on maintenance hemodialysis result from vascular complications [6]. Stenosis is the most common issue within these complications, occurring at the anastomosis site or nearby. Stenosis can hinder proper blood flow during hemodialysis, causing local re - filtration problems and compromising the quality of the procedure. Early detection of stenosis, especially when it affects venous return, poses a challenge [7, 8].

In recent times, there has been a growing inclination towards utilizing Percutaneous Transluminal Angioplasty (PTA) to address stenosis, driven by its numerous advantages compared to surgical methods. PTA is a well-established and deemed safe and effective for treating vascular access dysfunction. Notably, it can be conducted as an outpatient procedure, allowing for a relatively quick recovery [9]. Detecting AVF stenosis during PTA using an imaging diagnostic technique called Digital Subtraction Angiography (DSA). DSA integrates X-rays and utilizes algorithms for image processing, eliminating background from two images captured before and after injecting a contrast agent into the blood vessels. The image is computer-generated, created through digitalization and used as a mask. When subtracted from later images, only the features not present during its creation are fully highlighted. The mask density serves as a discernible “ghost image” facilitating the clear identification of the assessed vascular structures. This feature enables the use of diluted radiocontrast (50% or less), ensuring a diagnostic-quality image even with minimal contrast volumes [10].

Doppler Ultrasonography (DUS) is a method comparable to, and in certain aspects, superior to angiography. DUS offers advantages such as noninvasive visualization of stenosis causes and surrounding tissues, along with the ability to calculate access flow volume (Qa). In contrast, angiography typically assesses stenosis significance through a luminal diameter reduction of ≥ 50%, often linked to clinical or physiological abnormalities [11]. Futhermore, DUS is a non - invasive method of examining the AVF system, can be repeated many times, is safe and inexpensive. This method is recommended by the European Society for Vascular Surgery for all patients planning to have a coronary artery bypass graft (class I level A recommendation) [12]. However, to employ DUS before PTA, it is essential to assess the agreement between DUS and PTA concerning the extent of AVF stenosis. Hence, our study aimed to assess the concordance in stenosis diagnosis using PTA and DUS before intervention. Additionally, we examined the effectiveness of the PTA method after intervention in hemodialysis patients with AVF stenosis ≥ 50%.

II. MATERIAL AND METHODS

2.1. Study design

We conducted an non-controlled intervention study involving 15 chronic HD patients with a mature AVF in place for over three months, and had AVF stenosis ≥ 50%. Data was gathered at Cho Ray Hospital, Ho Chi Minh City, affiliated with the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam, from September 2020 to September 2022. All chronic HD patients had a physical examination (PE), DUS, and hemodynamic parameters measured during HD.

2.2. Study population

Firstly, 324 HD patients with an AVF created at least three months were included the study. The three - month AVF maturity criterion aimed to reduce the likelihood of attributing complications to the initial AVF surgery, ensuring observed issues are more likely tied to disease progression. Patients with acute, severe medical conditions or impediments to study participation due to physical and/or mental health conditions were excluded.

These patients were examed the percentage of AVF stenosis using DUS. Using these methods, 83 patients out of a total of 324 patients participated in the study were determined to have AVF stenosis ≥ 50%. Patients with AVF stenosis ≥ 50% were recommended PTA intervention. The final sample of the research comprised 15 patients who consented to PTA intervention and had already signed the consent statement. Those who declined PTA intervention engaged in discussions with the doctor, exploring alternative treatments, weighing optimal methods and associated costs. They considered continuing with the AVF until its functionality diminishes or opting for surgical replacement with a new AVF.

2.3. Study procedures

Initially, the study gathered patient characteristics included age, gender, body mass index (BMI), comorbidities such as hypertension and diabetes, the duration of dialysis, prior CVC placements, and history of AVF creation. Next, an experienced nephrologist conducted PE on the AVF arm. Two tests were performed: the arm elevation test, positive if the AVF did not collapse when the arm was raised, and the pulse augmentation test, positive if the pulse did not strengthen when the vein was occluded [13]. Several other clinical features were also examined including: swollen fistula arm, collateral veins in ipsilateral arm, and murmurs change along the AVF. These characteristics were measured before and after PTA intervention to evaluate the effectiveness of reducing clinical symptoms in patients.

Each patient underwent DUS to map the AVF. A specialized cardiovascular ultrasonography expert utilized a 7.5MHz probe and the Winno E10 color flow duplex machine for this mapping procedure. AVF stenosis was identified when there was a reduction of at least 50% in the inner diameter compared to the adjacent vessel on the inflow side [11]. The calculation of access blood flow (Q) was conducted using the formula: Q = Cross - sectional area (cm^2) × minimal velocity (cm/s) × 60, with the cross - sectional area (cm^2) determined by π d2/4 (where "d" represents the diameter) [14]. Access blood flow was evaluated at four specific locations along the AVF, including the brachial artery supplying the AVF (Qa), the anastomosis, and 5cm and 10cm away from the anastomosis. The minimum blood flow value among these four sites was denoted as Qmin. To calculate the access recirculation (AR), the following formula was applied: AR (%) = 100 x (S-A) / (S-V), where "S" indicated the concentration of Blood Urea Nitrogen (BUN) in the peripheral vein, "A" in the arterial line, and "V" in the venous line during HD. Blood samples were collected after reducing or halting the dialysate flow at the end of the dialysis session. It was crucial to confirm the correct needle positions and line orientations before withdrawing blood for BUN measurements [15]. Similar to clinical characteristics, all parameters measured on DUS before PTA intervention were measured repeatedly in the post - intervention period. In addition, HD parameters were also investigated, including spKt/V, intra - access pressure vein (Pvi), intra - access pressure artery (Pai), Delta Pai-Pvi, and venous access pressure ratio (VAPR).

Patients with AVF stenosis ≥ 50% underwent intervention using the PTA technique, utilizing a direct access approach from the AVF with a 6F - 7F sheath (1F = 0.33mm). The stenosis site was identified through DSA. Subsequently, a 0.035-inch diameter guidewire (1 inch = 25.4mm) was threaded along with a catheter through the lesion, followed by balloon angioplasty with pressures reaching up to 25 atmospheres, sustained for 1 - 3 minutes. Post-PTA intervention, the patient's AVF was reassessed for any residual stenosis. If the AVF remained narrowed ≥ 70%, stent placement might be considered. The sheath was then removed, and a 3.0 nylon thread was sutured at the sheath placement site, with bleeding controlled through focused pressure [16].

Assessment after PTA intervention deemed "successful" when residual stenosis under 30%. "Clinical success" was defined as (1) facilitating adequate blood flow for HD with clinical improvement and enhancements in HD parameters, notably, two values indirectly evaluating AVF function (Urea - based access recirculation and spKt/V); (2) uninterrupted HD for the patient. Complications were categorized based on The Society of Cardiovascular and Interventional Radiology 2017 standards: (1) hematoma at the needle puncture site, (2) prolonged bleeding at the intervention site requiring blood transfusion; (3) perforation of the vessel wall [17].

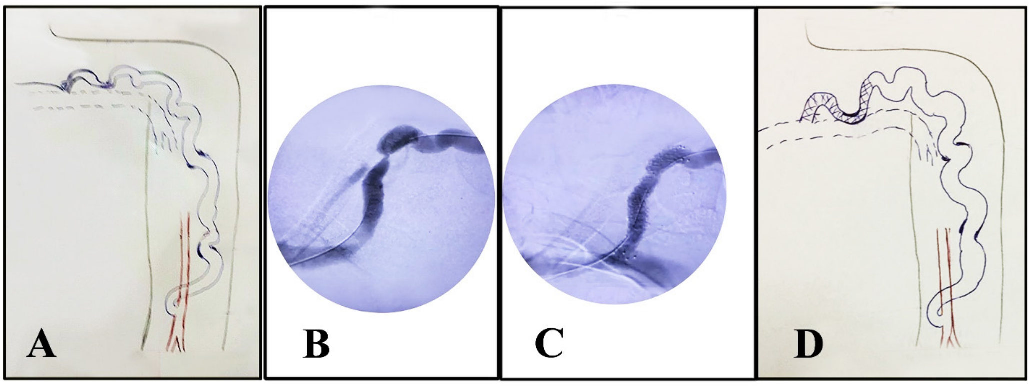


Figure 1. Doppler ultrasound mapping AVF (a), (d) before and after treatment, and Percutaneous Transluminal Angioplasty AVF (b), (c) before and after treatment

Male patient, 38 years old, admission number 3190000209, diagnosis of AVF stenosis 80.43% on ultrasound Doppler (cephalic arch) and 81.1% on PTA+high venous pressure during hemodialysis

2.4. Statistical analysis

Data were analyzed and presented in tables and figures using SPSS version 20.0 software. Quantitative variables were expressed using median and interquartile range (IQR), while qualitative variables were represented as frequencies and percentages. To assess disparities between clinical examinations, HD parameters, and DUS parameters before and after PTA interventions, the Wilcoxon signed-rank test was utilized for continuous factors, and McNemar's test was employed for categorical factors. Statistical significance was considered achieved when the p-value was less than 0.05 (two - tailed). Spearman's rank correlation coefficient (rho) and a scatter plot were employed to identify the correlation between AVF stenosis as determined by PTA and DUS. The correlation strength, degree, and statistical significance of this relationship were assessed through the correlation coefficient (r), r-squared, and p-value.

III. RESULTS

3.1. Correlation and similarity in stenosis assessment based on DUS and PTA

The study enrolled 15 HD patientsHD with AVF stenosis of at least 50% who received PTA intervention. The median age of the patients was 50 years (IQR: 37 - 64 years) and most of them (60.0%) were men. BMI was 19.5kg/m^2 (IQR: 18.6 - 22.3kg/m^2). More than half of the patients (66.7%) had hypertension and some of them (20.0%) had diabetes. The patients had been on dialysis for a median of 6 years (IQR: 4 - 8 years). Most of the patients had a history of CVC placements (73.3%) and AVF creation (86.7%) (table 1).

Table 1: Baseline characteristics of end stage renal disease patients

Characteristics	Total (N = 15)
Age #	50 (37 - 64)
Male (n, %)	9 (60.0%)
BMI (kg/m2) #	19.5 (18.6 - 22.3)
Hypertension (n, %)	10 (66.7%)
Diabetes mellitus (n, %)	3 (20.0%)
Dialysis vintage (years) #	6 (4 - 8)
History of previous CVC placements (n, %)	11 (73.3%)
History of previous AVF creation (n, %)	13 (86.7%)

Note: #: Median (Interquartile range); (n, %): frequency (percentage)

AVF: arteriovenous fistula;.BMI: Body Mass Index; CVC: Central Venous Catheter.

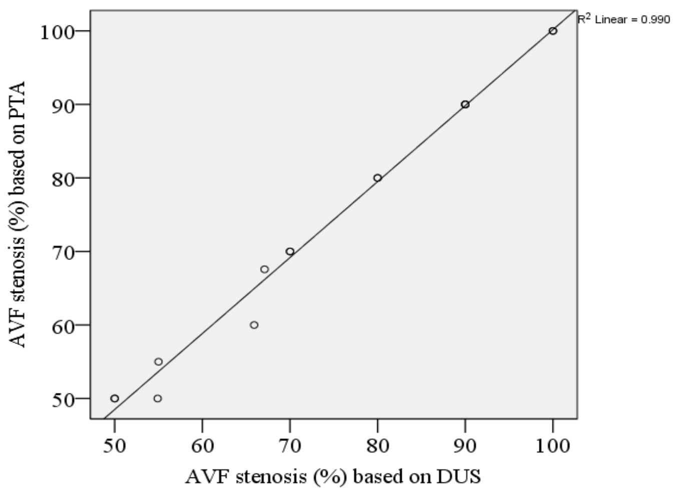
The results showed that when comparing the assessment of AVF stenosis parameters using DUS and PTA methods, there was consistent in terms of both the level and location of the stenosis. Among the 15 HD patients, 9 exhibited stenosis within a 5 cm range from the anastomosis, with 6 experiencing venous stenosis. Stenosis rates ranged between 50% and 79% in 8 cases and were 80% or higher in 7 cases. These findings were summarized in Table 2.

Table 2: Comparison between AVF stenosis diagnosed by DUS and PTA

Indicators (N = 15)	DUS	PTA
Stenosis at different sites		
Brachial artery (Qa)	0	0
Anastomosis	0	0
5 cm from the anastomosis	9	9
Venous stenosis	6	6
AVF Stenosis		
50 - 79%	8	8
≥ 80%	7	7

AVF: arteriovenous fistula: DUS: Duplex Duppler Ultrasound: PTA: Percutaneous transluminal angioplasty.

Figure 2 presented a correlation between AVF stenosis as measured by DUS and PTA. The findings demonstrated a highly robust positive correlation between the two techniques. The correlation coefficient r = 0.997, and r2 = 0.994 implying that 99.4% of the variability in AVF stenosis can be accounted for by the linear connection between DUS and PTA with p-value < 0.001.



r = 0.997
r2 = 0.994
p < 0.001

Figure 2: Correlation between AVF stenosis measured through DUS and PTA (n = 15)

3.2. The effectiveness of the PTA intervention in hemodialysis patients with AVF stenosis ≥ 50%

Out of a total of 83 HD patients, 15 consented to undergo PTA. Immediately following the intervention, all patients were deemed successful, as confirmed by DSA scan results showing the prompt resolution of AVF stenosis post-angioplasty. No patients reported complications such as bleeding, infection, or thrombosis after the intervention. Following revascularization, there were statistically significant reductions in various indices, including changes in murmurs along the AVF, VAPR, the number of patients with AVF stenosis ≥ 50% on DUS, and non of patients with Qmin < 500 mL/min. Additionally, various clinical examination indicators, hemodialysis parameters, DUS, and access flow at different sites demonstrated improvement, although these differences were not statistically significant, likely due to the limited size of the study sample.

Table 3: Clinical examination, hemodialysis parameters, Duplex Doppler Ultrasound data of patients before and after PTA intervention

Indicators (N = 15)	**Before PTA intervention**	**After PTA intervention**	**p-value**
Clinical examinations			
Swollen fistula arm (n, %)	3 (20.0)	1 (6.8)	0.157b
Collateral veins in ipsilateral arm (n, %)	4 (26.7)	3 (20.0)	0.5637b
Murmurs change along AVF (n, %)	14 (93.3)	4 (26.7)	0.002b
Positive pulse augmentation test (n, %)	14 (93.3)	12 (80.0)	0.317b
Positive arm elevation test (n, %)	15 (100.0)	14 (93.3)	0.317b
Hemodialysis parameters #			
Urea - based AR (%)	3.45 (2.22 - 6.25)	3.13 (2.17 - 4.55)	0.427a
spKt/V	1.48 (1.23 - 1.78)	1.69 (1.45 - 1.88)	0.191a
Pvi	19 (13 - 53)	22 (17 - 48)	0.474a
Pai	30 (16 - 56)	30 (20 - 47)	0.667a
Delta Pai-Pvi	1 (-2 - 6)	1 (-1 - 4)	0.628a
VAPR	1.55 (1.24 - 1.73)	0.45 (0.22 - 0.59)	< 0.001a
Duplex Doppler Ultrasound (n, %)			
AVF stenosis ≥ 50%	15 (100.0)	3 (20.0)	0.001b
AVF thrombosis	3 (20.0)	0	0.317b
Qmin < 500mL/min	15 (100.0)	0	0.001b
Access flow (mL/min) at different sites # (n = 8)			
Brachial artery (Qa)	797 (573.5 - 1194)	1089.5 (1034.5 - 1777)	0.0499a
Anastomosis	784 (368 - 1197.5)	905.5 (668.5 - 1306)	0.124a
5 cm from the anastomosis	759.5 (346.5 - 1325.5)	1187 (942 - 1599.5)	0.093a
10 cm from the anastomosis	663 (276.5 - 1409)	839 (656.5 - 1232.5)	0.161a

Note: #: Median (Interquartile range); (n, %): frequency (percentage)
a Wilcoxon signed - rank test, b McNemar's test

AR: access recirculation; AVF: arteriovenous fistula; PTA: Percutaneous transluminal angioplasty; Qa, blood flow at brachial artery feeding AVF; Qmin, The minimal blood flow value of the 4 sites (brachial artery feeding the AVF, anastomosis, 5 cm and 10cm from the anastomosis); PiaV, intra - access pressure vein; VAPR, venous access pressure ratio.

IV. DISCUSSION

AVF is preferred over AVG as it carries a lower risk of infection, graft stenosis, and access loss. Almasri et al.'s study indicated the need of an intervention (defined as both surgical and endovascular) was 60% for AVG compared to 45% for AVF over a two - year period [18]. However, complications were still common with AVF, with approximately 45 - 67% of AVFs developing stenosis requiring intervention within one year. Factors such as high age, female gender, and comorbidities are associated with complications related to AVF stenosis [19]. This study investigated the characteristics of HD patients, revealing a median age of 50 years. Hypertension was the prevalent underlying medical condition among the patients, accounting for 66.7%. The median duration of dialysis was 6 years, with a substantial history of CVC placements (73.3%) and AVF creation (86.7%). These factors may pose a risk for complications include AVF stenosis. Our findings noted that the BMI among the patients was within the normal range, with a median value of 19.5 kg/m² (Table 1). However, recent research has similarly demonstrated a significant positive correlation between BMI and recurrent AVF stenosis. One plausible explanation is that individuals with obesity experience more vigorous intimal hyperplasia, resulting in earlier instances of stenosis [20].

In the assessment of the AVF system, it is clear that DUS stands out as a leading noninvasive tool for examining the peripheral vasculature's anatomy [21]. Beyond the carotid artery, criteria for duplex scanning to assess stenosis levels in various vascular regions, such as the legs, renal arteries, and splanchnic arteries, have been previously established [22]. Table 2 illustrates consistent results in the assessment of AVF stenosis parameters using DUS and PTA methods, showing alignment in both the level and location of stenosis. Specifically, 9 cases exhibited stenosis within a 5 cm range from the anastomosis, and 6 cases involving venous stenosis. Stenosis rates ranged from 50% to 79% in 8 cases and were 80% or higher in 7 cases. Futhermore, the correlation analysis revealed a highly robust positive correlation between the degree of stenosis measured by DUS and PTA ($r = 0.997$, $r^2 = 0.994$, and p-value < 0.001), as shown in Figure 2. This results aligns with recent studies addressing the same subject. Wo K et al. conducted a study in 780 HD patients exhibiting AVF stenosis characterized by peak systolic velocity ≥ 500 cm/s. The study aimed to establish DUS criteria for identifying significant AVF stenosis, using angiography as the gold standard for comparison. The findings indicated that DUS accurately predicted a AVF stenosis ≥ 50%, with a sensitivity of 89% (95% CI: 87 - 91) and a positive predictive value (PPV) of 99% (95% CI: 99 - 100) [23]. Similarly, Baz et al.'s study findings revealed no significant distinctions in mean AVF stenosis (%), mean length of stenosis segment, and mean narrowest part as assessed by both DUS and angiography methods (p-values = 0.115, 0.271, and 0.233, respectively) [24]. Lastly, Cosovic et al. conducted a study to assess the efficacy of DUS in detecting significant (≥ 50%) AVF stenosis and identifying its location within the AVF, comparing it with angiography. The findings indicated that out of 63 patients experiencing a substantial decrease in blood flow according to DUS, 51 (80.9%) revealed a haemodynamically significant stenosis. Among these, angiography was conducted in 45 cases (88.2%), all of which confirmed the presence of significant stenosis. This study also suggested that DUS is probably dependable for confirming the existence of AVF stenosis, in conjunction with flow criteria [25].

Concerning PTA intervention efficacy, all patients demonstrated success, as verified by DSA scan results indicating the immediate resolution of AVF stenosis post - angioplasty. No complications, such as bleeding, infection, or thrombosis, were reported post-intervention. Revascularization led to statistically significant reductions in indices, including changes in AVF murmurs, VAPR, patients with AVF stenosis ≥ 50% on DUS, and none with Qmin < 500 mL/min (Table 3). In recent years, there has been a push for both endovascular and surgical interventions to enhance fistula maturation and augment the availability of functional vascular accesses. Common clinical treatments for immature AVF now include Proximal AV neo - anastomosis, endovascular accessory vein ligation/occlusion, PTA, stent graft placement in long segment stenosed veins, and AVF reconstruction. Notably, PTA and AVF reconstruction stand out as the primary approaches to address stenosis [26]. In a study by Yu et al., the effectiveness of PTA and AVF reconstruction was compared in 44 HD patients. The findings indicated that both technical and clinical success were attained in 100% of the 44 cases. No notable differences in patency rates were observed between the two groups ($p > 0.05$) [27]. Likewise, Gu et al. conducted a study assessing the effectiveness of ultrasound - guided PTA for AVF stenosis. The results demonstrated a significant increase in the flow rate of the brachial artery, from 334.59 ± 187.24 to 1026.19 ± 268.46 mL/min, and an enlargement in the stenosis diameter from 1.08 ± 0.32 to 3.54 ± 0.71 mm. Meanwhile, the peak systolic velocity of the stenosis decreased from 417.96 ± 168.73 to 271.46 ± 100.42. These findings clearly indicate a high level of technical and clinical success in treating juxta - anastomotic site stenosis using PTA [28].

Our study had certain limitations. Firstly, it was conducted at a single HD center with a relatively small participant pool, limiting the generalizability of our findings to a broader population of HD patients. Secondly, the diagnosis of AVF stenosis heavily relied on DUS mapping, and only a small subset of HD patients with AVF stenosis ≥ 50% consented to PTA intervention. Consequently, it was challenging to include patients with both AVF stenosis parameters based on both PTA and DUS, resulting in a reduced sample size and diminished value for inferential statistical analyses. Ultimately, limited time and resources prevented us from conducting extensive long - term follow - ups to fully showcase the intervention's effectiveness. Thus, we recommend future studies to continue monitoring patients to accurately assess the intervention's impact.

V. CONCLUSION

DUS offers several advantages over PTA, including noninvasive visualization of stenosis causes and surrounding tissues, along with the capability to calculate access flow volume. Its noninvasive nature allows for repeated examinations, ensuring safety and cost - effectiveness. Therefore, we suggest employing DUS for assessing stenosis before considering PTA intervention, given the correlation and similarity in the results of AVF stenosis examination between these two techniques. Finally, our study supports PTA intervention as the preferred method for HD patients with AVF stenosis, given the observed improvements in clinical, HD, and DUS parameters.

Ethical statement

The research received approval from the Ethical Committee for Biomedical Research at the University of Medicine and Pharmacy in Ho Chi Minh City (Approval Number: 320/HĐĐĐ-ĐHYD, on June 12th, 2020) and at Cho Ray Hospital (Approved based on the decision number 320/HĐĐĐ-, on June 25th, 2020). Prior to participation, all enrolled patients provided written informed consent.

Conflict of interest

The authors declare that there is no conflict of interest.

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