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The Correlation between Blood Flow Rate with Arteriovenous Fistula Thrombosis in Patients with End-Stage Renal Disease at Dr. Zainoel Abidin General Hospital in Banda Aceh

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ABSTRACT

Introduction: Thrombosis is a complication that may arise in End-Stage Renal Disease (ESRD) patients with an arteriovenous fistula (AVF), usually caused by stenosis (narrowing of the vein more than 50% of its diameter) and changes in blood flow rate (BFR). The aim of this study is to explore the relationship between blood flow rate and the incidence of AVF thrombosis in patients with ESRD at Dr. Zainoel Abidin General Hospital Banda Aceh.
Methods: In this study, a cross-sectional design was employed to investigate ESRD patients who had undergone the AVF procedure at Dr. Zainoel Abidin General Hospital Banda Aceh from October to November 2023. The study examined Blood Flow Rate values obtained via Doppler ultrasound. The data were analyzed using SPSS version 26 and the contingency coefficient (Cramer's V) to assess the relationship between the variables.
Result: 51 patients were sampled. The average BFR value six weeks after surgery in the event of thrombosis and non-thrombosis was 274 ml/min and 786,8 ml/min. There was a significant correlation between BFR values with the incidence of AVF thrombosis ($p = 0.000$ and Cramer's $V = 0,658$)
Conclusion: Inadequate blood flow through the fistula may contribute to clot formation, leading to fistula failure in patients undergoing hemodialysis. Optimizing monitoring and early intervention for blood flow in AVF may help reduce the incidence of thrombosis and improve patient outcomes.

Keywords: Arteriovenous fistula, Blood flow rate, Thrombosis, End-stage renal disease.
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INTRODUCTION

Description of the research area, pertinent background information, and the hypotheses Hemodialysis (HD) is a common treatment for kidney failure, along with peritoneal dialysis and transplantation. It involves using a catheter, arteriovenous graft (AVG), or arteriovenous fistula (AVF) for intravenous access.[1] AVF maturation typically takes 4 to 6 weeks. During this time, the National Kidney Foundation's Kidney Dialysis Outcomes Quantitative Initiative (KDOQI) recommends that the blood flow rate must reach at least 600 ml/min, the vein diameter must exceed 0.6 cm, and the vein depth must be less than 0.6 cm for cannulation. If the fistula does not mature properly, it will not be able to serve as a dialysis access. Unfortunately, 10% of AVFs and 20% of AVGs become blocked by thrombus, neointimal hyperplasia, or stenosis each year. On average, AVF failure rates reach 35,9% after 135 days of use.[2,3]

In an arteriovenous fistula (AVF), the joining of vessels causes the blood flow, which was previously laminar, to become turbulent. This activates several mechanisms, increasing Wall Shear Stress (WSS) and the levels of vascular remodeling mediators. Hence, as an adaptation response, the vessel will dilate and thicken.[4] The success of AVF maturation depends on vascular remodeling and the inhibition of neointimal hyperplasia.[5] Thrombosis refers to the formation of a blood clot (thrombus) in a blood vessel, which can obstruct blood flow and is the most common cause of 75% AVF access failure.[6,7] Thrombosis can occur within the first 24 hours to 1-2 months after the procedure. The clots that form tend to be harder, leading to vein constriction and reduced blood flow.[8]

It is essential to have an effective strategy to detect early thrombosis in hemodialysis to increase the success of arteriovenous fistula (AVF) placement, since it requires good vascular access. One such strategy is the use of Doppler Ultrasonography (DUS). DUS is a test that has a high sensitivity of 91% and specificity of 100% for assessing AVF maturation and detecting early complications like stenosis and thrombosis.[9] Measuring the blood flow rate (BFR) is one of the ways to do that. According to a retrospective study of 121 patients, brachial artery flow volume ≥ 1000 mL/min and a PAV diameter ≥ 3.5 mm predicted a well-functioning fistula.[10] The KDOQI guidelines state that a BFR AVF < 500 ml/minute or a 25% reduction

in flow within three to six months carries a higher risk of stenosis or thrombosis. However, the Renal Association Clinical Practice Guidelines suggest a BFR < 300 ml/min as the standard for intervention since it is associated with a 64% risk of failure.[11,12]

This study aimed to investigate the correlation between blood flow rate with the incidence of arteriovenous fistula thrombosis in patients with End-Stage Renal Disease (ESRD) at Dr. Zainoel Abidin General Hospital Banda Aceh.

METHODS

Definitions

AVF thrombosis is characterized by the absence of a bruit and weak or no thrill, even though pulsation may occur at the anastomosis. Additionally, it can be identified by the presence of a thrombus, with a decreased blood flow rate of less than 600 ml/min on DUS examination.[11,13,14]

Study design and participants

This quantitative study uses analytical-descriptive methods with a prospective cross-sectional design. It aims to find the relationship between blood flow rate and the incidence of arteriovenous fistula thrombosis in patients with ESRD at Dr. Zainoel Abidin General Hospital Banda Aceh. The study was conducted at the Thoracic, Cardiac, and Vascular Surgery polyclinic from 02 October 2023 to 30 November 2023. The sample consisted of 51 people selected using a total sampling method, with specific inclusion and exclusion criteria. Inclusion criteria included patients with ESRD who underwent the AVF procedure at Dr. Zainoel Abidin General Hospital Banda Aceh and were willing to undergo DUS examination 6 weeks after the procedure. Exclusion criteria included patients who did not attend appointments according to the schedule, died, underwent reoperation, or had complications such as hematoma, aneurysm, or anastomosis leakage.

RESULTS

Characteristics of participants

According to Table 1 of this study, there were 51 participants, of whom 22 were men (43.14%) and 29 were women (56.86%). Among 45 participants, 45 (88.24%) did not experience thrombosis, while 6 (11.76%) did.

Characteristics of blood flow rate six weeks after surgery

According to the data presented in Table 2, it is evident that after six weeks of surgery, 76.47% (39 people) of the patients exhibited mature blood flow rate values (>600 ml/min). However, 23.53% (12 people) had a blood flow rate considered not mature, with values below <600ml/min.

Correlation between blood flow rate values six weeks after surgery with the incidence of AVF thrombosis

According to the bivariate study presented in Table 3, there is a significant correlation between blood flow rate and the incidence of AVF thrombosis (p=0.000 and Cramer's v=0.658). The mean blood flow rate in patients with AVF thrombosis was 274 ml/min, and in patients with no AVF thrombosis, 786,8 ml/min.

DISCUSSION

In this study, most participants were male and aged 46 to 55 years. Essentially, individuals in the early and late stages of aging have a higher risk of developing chronic kidney failure due to reduced kidney function and other health conditions. It's worth noting that AVF cannulation failure is likely to occur due to the prevalence of vascular disorders that may be present.[15] As per Virchow's triad, thrombosis occurs due to a combination of three factors: endothelial dysfunction,

Table 1. Characteristics of age, gender, and incidence of thrombosis in the sample.

Characteristics	Frequency (N=51)	Percentage (%)
Age		
< 26 years	2	3,92
26-35 years	4	7,84
36-45 years	12	23,53
46-55 years	18	35,29
56-65 years	12	23,53
> 65 years	3	5,88

Table 2. Characteristics of blood flow rate six weeks after surgery.

Characteristics	Frequency (N=51)	Percentage (%)
Blood Flow Rate		
Not Mature	12	23,53
Mature	39	76,47

Table 3. Correlation between blood flow rate values six weeks after surgery with the incidence of AVF thrombosis.

Variable	Thrombosis (N=6)		BFR Mean (Thrombosis) ml/min	Not Thrombosis (N=45)		BFR Mean ml/min	P Value	Cramer's V
	n	%		n	%			
Blood Flow Rate								
Not Mature	6	11,76	274	6	11,76	768,8	0,000*	0,658
Mature	0	0,0		39	76,47			

Note: *significant at p<0.05

altered blood flow, and hypercoagulability. Additionally, the male dominance may be related to sex hormones, as men tend to have higher epidermal growth factor receptor (EGFR) expression values. This can affect vascular remodeling, inflammatory response, platelet activation, cell proliferation and migration, etc. Abnormal EGFR expression can contribute to pathological changes in vessel walls that cause thrombosis.[16] Lastly, the study concludes that thrombosis is a relatively uncommon complication of AVF creation when compared to graft or central venous catheter (CVC) procedures and is usually associated with prior operative intervention.

According to this study, there is strong and significant relationship between the incidence of arteriovenous fistula thrombosis and blood flow rate. According to Gjorgjievski et al. (2019), primary AVF failure is defined as the inability to cannulate the AVF within 3-4 weeks. This can happen due to inadequate maturation, early thrombosis, etc. However, the formation of AVF thrombosis involves complex mechanisms. Systemic factors such as hypotension, hypercoagulable state, hematoma, intimal injury during the creation can cause early fistula thrombosis within the first 24 hours to first week after fistula implantation.[7] Of the 178 samples taken in the study, 29 (16.29%) showed primary AVF failure, and 18 (10.11%) experienced early thrombosis.[8] Another research by Besarab et al. suggests that BFR values < 700-1,000 ml/min and/or reduced flow > 25% are optimal predictors for stenosis, with a 91% efficiency level.[17]

Late thrombosis most likely occurs when there is a progressive neointimal hyperplasia in the venous outflow system, structural deterioration, or repeated mechanical trauma from needle cannulation which may occur within a few months to years after the dialysis.[7] Measurement of access flow is the most reliable and validated surveillance tool. Low BFR can lead to stasis and blood pooling in the vessels. Moreover, increased levels of shear stress, activation of clotting factors in stagnant blood flow, and inadequate clearance of clotting factors and other procoagulant substances will be more conducive to thrombus formation.[18] Early DUS monitoring helps pinpoint the issue potentially causing the primary failure by measuring the flow through a single accessory vein and confirming its significance in the underdevelopment of the AVF.[12] Proper maturation is undetermined if the brachial artery flow volume tends to decrease with time, and the fistula will likely become unsuitable for use in dialysis due to low flow or thrombosis issues.[9]

In patients with ESRD, the body's coagulation function and endothelial dysfunction undergo changes. When the endothelium deteriorates, endothelial cells release various substances, such as plasminogen activator inhibitor-1, von Willebrand factor, thromboxane A2, fibrinogen, and tissue factor, which can indicate the degree of endothelial disruption.[19] A continuous increase in blood viscosity can lead to arterial pressure elevation and blood clotting, resulting the formation of thrombus and emboli, which can cause AVF failure [15]. In a 2013 study by Salmela et al., 25% of patients with thrombosis had shortened PT (less than 17 seconds) and an increased D-dimer greater than 2.0 mg/L (26%). D-dimer levels exceeding 500 ng/mL have a sensitivity of 96.2% and a specificity of 50% for thromboembolic disorders.[20] However, in this study, it is unclear how many patients were using oral anticoagulants, which would decrease the rate of thrombosis.

Several factors related to the research variable make it imperative for the clinician to conduct a thorough and precise examination. However, this research has certain limitations. The sample size in the study was quite small, resulting in insufficient variation to accurately describe the optimal results. Additionally, we did not collect data on the illnesses patients experienced or the medications they were taking. Therefore, it is necessary to conduct further research on a larger scale and with a more comprehensive approach to complete this study.

CONCLUSION

This study established a significant relationship between blood flow rate (BFR) values and the incidence of arteriovenous fistula (AVF) thrombosis in patients with end-stage renal disease (ESRD). Doppler ultrasound proved an effective tool for assessing BFR and identifying early signs of thrombosis. Therefore, monitoring blood flow and early intervention can significantly reduce the risk of thrombosis and other complications, thereby improving long-term patient outcomes.

DISCLOSURES

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Conflict of Interest

All the authors declare that there are no conflicts of interest in this research.

Author Contribution

All authors contributed equally to this research.

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