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Brachial artery and cephalic vein diameter as maturation predictors of brachiocephalic arteriovenous fistula in end-stage renal diseases with type 2 diabetes mellitus

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ABSTRACT

Introduction: Arteriovenous fistula (AVF) is the gold standard for vascular access for hemodialysis in end-stage renal disease (ESRD) patients. There is a high rate of AVF maturation failure, especially in DM patients, and it takes longer for maturation in diabetes mellitus (DM) patients. This study aimed to obtain the recommendations for the minimum diameter of the brachial artery and cephalic vein as a predictor of brachiocephalic AVF maturation in ESRD patients with type 2 diabetes mellitus after six weeks to eight weeks of AVF creation.

Methods: This study is a retrospective cohort study using secondary data from patients with brachiocephalic arteriovenous fistula. The examined variables were brachial artery diameter, cephalic vein diameter, and brachiocephalic arteriovenous fistula maturation. Comparative analysis and ROC curve analysis were performed.

Results: A total of 72 patients met the inclusion and exclusion criteria. Forty-four (61,11%) patients were mature at six weeks, while 47 (65,28%) were mature at eight weeks postoperatively. At week six, the mature group had a significantly larger cephalic vein diameter (3,20±0,94 vs. 2,65±1,02, p=0,002). At week eight there was a significantly larger brachial artery (4,22±0,70 vs 3,78±0,60, p=0,012), and cephalic vein diameter (3,28±0,98 vs 2,43±0,82, p=0,000) in the mature group.

Conclusion: The best threshold value for preoperative brachial artery diameter predicting AVF maturation eighth week was 3.85 mm. The best threshold value for preoperative cephalic vein diameter predicting AVF maturation at the sixth week was 2.45 mm, and at the eighth week, it was 2.45 mm.

Keywords: brachiocephalic arteriovenous fistula maturation; brachial artery diameter; cephalic vein diameter; diabetes mellitus; hemodialysis.

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INTRODUCTION

End-stage renal disease (ESRD) has become a national and global health-related problem with high morbidity and mortality rates.[1] Treatment of kidney disease ranks the second-highest financing from Indonesian National health insurance.[2] In 2018, diabetic nephropathy was ranked as the second most common etiology of ESRD, accounting for 28% of patients following hypertension.[2]

Currently, arteriovenous fistula (AVF) is the gold standard for vascular access for hemodialysis.[2] AVF takes time to reach maturation before it can be used. AVF has a relatively high maturation failure rate. The maturation failure rate varies between 20-60%. In Europe, it ranges from 7-10%, and in America, it ranges from 40-45%.[3]

Diabetes mellitus in ESRD patients causes atherosclerosis, especially in small and medium blood vessels in the antecubital fossa area, potentially decreasing the diameter of the arteries and thereby reducing arterial flow to the AVF.[3] In addition, uremia and hemodialysis in patients with ESRD further increase oxidative stress and endothelial dysfunction that triggers neointima hyperplasia and stenosis of AVF.[4] A meta-analysis concluded that DM patients have a higher maturation failure rate with statistically significant results (OR 1.682 [95% CI, 1.429-1.981]).[5]

Blood vessel diameter is one of the main predictors of fistula maturation.[6] A previous study showed that vein diameter was the main predictor of AVF maturation with a cut-off of > 2 mm.[7] The guideline also recommends a minimum diameter of ≥ 2 mm for veins and ≥ 2mm for arteries being used as vascular access.[8] Zhang et al. showed a maturation failure rate of 55.56% of patients with cephalic veins diameter < 2mm.[9]

This study aims to analyze the minimum recommended diameter of the brachial

artery and cephalic vein as predictors of brachiocephalic AVF maturation in ESRD patients with type 2 diabetes mellitus at six and eight weeks after AVF creation.

METHODS

A retrospective cohort study was conducted using secondary data from all ESRD patients with type 2 diabetes mellitus who underwent brachiocephalic AVF surgery in three hospitals from July 2019 to March 2020.

The variables examined were brachial artery diameter, cephalic vein diameter, and brachiocephalic AVF maturation. Demographical data collected were age, gender, and blood pressure. The data are presented in a table with the mean, standard deviation, or sum and proportion. AVF Maturity was determined by the "rule of 6s" from the vascular access guidelines of The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI).

The correlation between the brachial artery and cephalic vein diameter on brachiocephalic AVF maturity was analyzed using a T-Test. The value of $p<0.05$ indicates a statistically significant correlation. The receiver operating characteristic (ROC) curve determines the preoperative ultrasound predictor values, including the diameter of the brachial artery and cephalic vein and hemodynamic parameters in mature AVF.

RESULTS

Seventy-two subjects met the inclusion criteria and exclusion criteria. Table 1 shows the demographic and preoperative ultrasound data.

Table 2 compares demographical characteristics between mature and immature patients six weeks after brachiocephalic AVF creation. There were no significant differences between the mature and immature groups. Table 3 shows that at the sixth week, subjects with mature AVF had a significantly larger preoperative cephalic vein diameter than the immature (3.20±0.94 vs. 2.65±1.02, p=0.002). This result indicates that the preoperative cephalic vein diameter in ESRD patients with DM influences brachiocephalic AVF maturation in the sixth week.

Table 4 compared demographical characteristics between mature and immature patients eight weeks after

Table 1. Demographic, Clinical Data, and Characteristics of Perioperative Ultrasound.

Variable	Total
Patients	72
Age (years), Mean± SD	57±9
Male (%)	34 (47.22%)
Female (%)	38 (52.78%)
Systolic blood pressure (mmHg), Mean±SD	146±21
Diastolic blood pressure (mmHg), Mean±SD	84±9
Internal brachialis artery diameter (mm), Mean ±SD	4.07±0.69
Internal cephalic vein diameter (mm), Mean±SD	2.98±1.01

Table 2. Patient Baseline Data between Mature and Immature Groups at 6th weeks Postoperative.

Variable	Mature (n=44) (61.11%)	Immature (n=28) (38.89%)	p-value
Male (%)	24(54.5%)	10(35.7%)	0.119
Female (%)	20(45.5%)	18(64.3%)	
< 50 years	11(25%)	3(10.71%)	0.135
≥ 50 years	33(75%)	25(89.28%)	
Normotension (Systole<140/ Diastole <90)	16(36.37%)	5(17.86%)	0.09
Hypertension (Systole ≥140/ Diastole ≥90)	28(63.63%)	23(82.14%)	

Table 3. Data on Brachial Artery and Cephalic Vein Diameter between Mature and Immature Groups at 6th week Postoperative.

Variable	Mature (n=44)	Immature (n=28)	p-value
Internal brachialis artery diameter (mm), Mean±SD	4.19±0.72	3.87±0.62	0.066
Internal cephalic vein diameter (mm), Mean±SD	3.20±0.94	2.65±1.02	0.002

Table 4. Patient Baseline Data between Mature and Immature Groups at 8th week Postoperative.

Variable	Mature (n=47) (65.28%)	Immature (n=25) (34.72%)	p-value
Male (%)	25(53,2%)	9(36%)	0.164
Female (%)	22(46.8%)	16(64%)	
<50 years	12(25.53%)	2(8%)	0.073
≥50 years	35(74.47%)	23(92%)	
Normotension (Systole <140/ Diastole <90)	16(34.04%)	5(20%)	0.212
Hypertension (Systole ≥140 / Diastole ≥90)	31(65.96%)	20(80%)	

Table 5. Data on Brachial Artery and Cephalic Vein Diameter between Mature and Immature Groups at 8th week Postoperative.

Variable	Mature (n=47)	Immature (n=25)	P Value
Internal brachialis artery diameter (mm), Mean±SD	4.22±0.70	37.8±0.60	0.012
Internal cephalic vein diameter (mm), Mean±SD	3.28±0.98	2.43±0.82	0.000

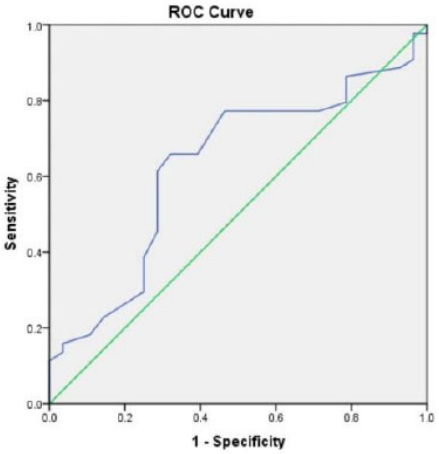

Figure 1. ROC curve depicting the sensitivity and specificity of brachial artery diameter at 6th week to predict AVF maturation.

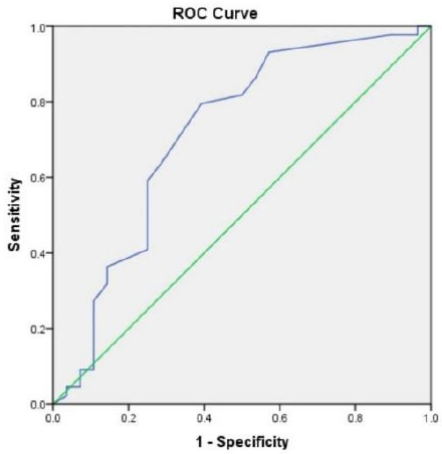

Figure 3. ROC curve depicting the sensitivity and specificity of cephalic vein diameter at 6th week to predict AVF maturation.

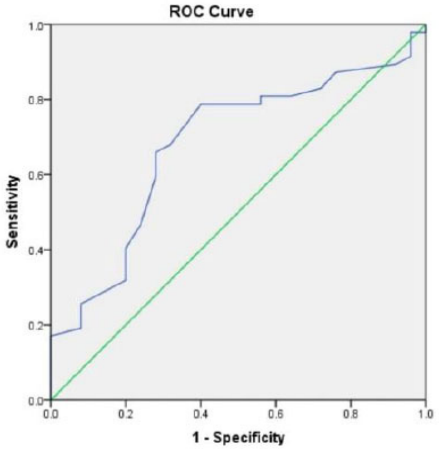

Figure 2. ROC curve depicting the sensitivity and specificity of brachial artery diameter at 8th week to predict AVF maturation.

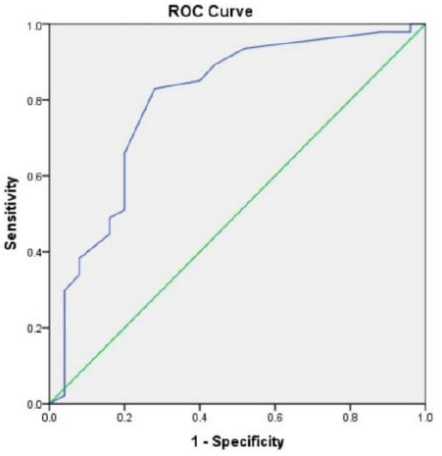

Figure 4. ROC curve depicting the sensitivity and specificity of cephalic vein diameter at 8th week to predict AVF maturation.

brachiocephalic AVF creation. Table 5 shows that subjects with mature AVF at week 8 had a significantly larger brachial artery diameter (4.22±0.70 vs. 3.78±0.60, p=0.012) and cephalic vein diameter (3.28±0.98 vs. 2.43±0.82, p=0.000).

From the ROC curve and the Area Under the Curve (AUC) analysis, the predictive value of the preoperative brachial artery diameter to predict Brachiocephalic AVF maturation was 62.9% (95% CI: 49.5%-76.3%) at weeks 6 and 68% (95% CI: 55.1%-80.9%) at the eighth week. In the analysis using the ROC curve, the best threshold value for preoperative brachial artery diameter predicting AVF maturation at the sixth week was 4.1 mm. (sensitivity 65.9% and specificity 67.9%), and at the eighth week was 3.85 mm (sensitivity 78.7% and specificity 60%) (Figure 1 and Figure 2).

From the ROC curve and AUC analysis, the predictive value of preoperative cephalic vein diameter to predict Brachiocephalic AVF maturation was 71.7% (95% CI: 58.7%-84.7%) for 6th week and 79.8%. (95% CI: 68.2%-91.3%) for 8th week. In the analysis using the ROC curve, the best threshold value for preoperative cephalic vein diameter predicting AVF maturation at 6th week was 2.45 mm (sensitivity 79, 5% and specificity 60.7%), and at 8th week was 2.45 mm (83% sensitivity and 72% specificity) (Figure 3 and Figure 4).

DISCUSSION

In this study, in the sixth week, 44 subjects (61.11%) had mature AVF, and 28 subjects (38.89%) had immature AVF. In the eighth week, there were 47 (65.28%) mature AVF and 25 (34.72%) immature AVF. In Lee et al. study, the AVF maturation failure rate was 13.59% out of 103 patients with DM.[10]

Vernaglione et al. found that AVF maturation failure was relatively high in women. This was thought to be caused by women generally having narrow blood vessels. A high maturation failure rate was found mainly in radiocephalic AVF creation.[11] In contrast, a study by Feldman et al. found no significant correlation between sex and AVF maturation.[12] In our study, there was no significant association between sex and brachiocephalic AVF maturation either at the sixth week or eighth week(p=0.119 and p=0.164).

A meta-analysis of cohort studies showed that elderly individuals (50-70 years) had a high rate of radiocephalic AVF maturation failure[13] In Kim et al. study showed that the elderly have thick enough intima-media, resulting in loss of elasticity of the arterial vessels and the narrowing of the lumen.[14] However, Lok et

al.'s retrospective single-center study of 440 subjects showed no correlation between age and AVF maturity.[15] In our study, there was no significant relationship between age and brachiocephalic AVF maturation either at the sixth week or eighth week (p=0.135 and p=0.073).

Hypertension is a factor that plays a role in the failure of AVF maturation through the mechanism of damage to endothelial function, where there is a decrease in vascular relaxation/vasodilation and triggers the infiltration of inflammatory cells into the blood vessel wall.[16,17] In a single-study cohort study conducted by Kim et al., there was no positive relationship between hypertension and AVF maturation.[18] In our study, there was no significant association between hypertension and brachiocephalic AVF maturation either at week six or week eight (p=0.09 and p=0.212).

In this study, patients with mature AVF had a significantly higher mean cephalic vein diameter than immature at the sixth week (3.20 ± 0.94 vs. 2.65 ± 1.02, p=0.002) and the eighth week (3.28 ± 0.98 vs. 2.43± 0.82, p=0.000). Patients with mature AVF had a significantly higher mean brachial artery diameter than immature at the eighth week (4.22±0.70 vs. 3.78±0.60, p=0.012). Lee et al. study of 162 patients found that the mean cephalic vein diameter in mature patients was higher than in immature patients at the eighth week, but it was not significant (2.9±0.7 vs. 2.8±0.17, p=0.542). The mean brachial artery diameter in mature patients was higher than in immature patients but also not significant (4.18±0.67 vs. 3.90±0.61, p=0.082).[10]

In our study, the threshold values for predicting AVF maturation were preoperative brachial artery diameter of 3.85 mm (sensitivity 78.7% and specificity 60%) and cephalic vein diameter of 2.45 mm (83% sensitivity and 72% specificity). In a study conducted by Ferring et al. on 36 patients, the threshold value of the brachial artery was 3 mm, and the cephalic vein was 3 mm. However, this study was not carried out in patients with DM.[19] The study conducted by Maya et al. on 322 patients found that the threshold value for AVF of the brachial artery was 2.5 mm, and the cephalic vein was 2.5 mm.[20] This study also cannot be performed in patients with DM.

Although the diameter of the brachial artery and cephalic vein can be used as a predictor of maturation in patients with ESRD due to diabetes, other considerations are still needed to include other factors such as patient comorbidities (hypertension, peripheral vascular disease, coronary artery disease, cerebral vascular), BMI, smoking history, coagulation factors, blood lipids, and electrolytes. This study has limitations where the number of samples is still relatively small, and the study population is only in 3 vascular centers located in adjacent locations.

Further research is needed to carry out external validation using the threshold value above with a homogeneous sample. In addition, studies can be carried out in several different vascular centers to obtain a more diverse population and consider all variables affecting brachiocephalic AVF maturation in ESRD patients with DM.

CONCLUSION

The best threshold value for preoperative brachial artery diameter predicting AVF maturation eighth week was 3.85 mm (sensitivity 78.7% and specificity 60%). The best threshold value for preoperative cephalic vein diameter predicting AVF maturation at the sixth week was 2.45 mm (sensitivity 79.5% and specificity 60.7%), and at the eighth week is 2.45 mm (sensitivity 83% and specificity 72%).

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There is no funding to be declared.

ETHICAL STATEMENT

Prior ethical approval from the institute's ethics committee was following the Declaration of Helsinki. Written informed consent for publication data was obtained from the participants.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

AUTHOR'S CONTRIBUTIONS

DP: Project administration, Methodology, Supervision, Resources; OW: Formal analysis, Data Curation, Writing - Original Draft, Writing - Review & Editing; AK: Methodology, Formal analysis, Supervision, Writing - Original Draft; RS: Resources, Conceptualization, Writing - Review & Editing; AM: Resources, Writing - Review & Editing; BFA: Formal analysis, Writing - Review & Editing; MFF: Formal analysis, Writing - Review & Editing. All authors have read and approved the final manuscript.

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