ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

The Accuracy of Brachial Artery Volume Flow as a Predictor of Brachiocephalic Arteriovenous Fistula Maturation

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Abstract

Objective: This study aims to investigate brachial artery volume flow accuracy in predicting AVF maturity. Methods: This was a cross-sectional study involving 80 patients that underwent AVF creation in Cipto Mangunkusumo Hospital, Jakarta, Indonesia. Parameters recorded include demographic data, ultrasound parameters in six weeks after AVF creation, and complications. Diagnosis tests were performed to determine the area under the curve (AUC), cut-off, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Results: Of 80 patients that underwent brachiocephalic AVF, we found that 64 (80%) successfully mature, and 16 (20%) failed to mature. Receiver operating characteristic (ROC) for brachial artery volume flow in predicting brachiocephalic AVF had AUC of 97,6 %. With cut-off brachial artery volume flow of 700 ml/minute, the sensitivity, specificity, PPV, NPV, and accuracy were 98.44 % (95 % CI 91.6-99.7%), 87.5 % (95 % CI 63,9 % - 96.5 %), PPV 96.9 % (95% CI 89.4-99.15%) NPV 84.6 % (95 % CI 66.5 % - 93.8 %) 93.33 % (95 % CI 70.1-98.8%), respectively. Conclusions: Brachial artery volume flow six weeks after AVF creation is an accurate parameter in predicting brachiocephalic AVF maturity.

Keywords: *Brachial artery volume flow, Maturity, Arteriovenous fistula.*

Introduction

Chronic Kidney Disease (CKD) is defined as abnormalities of kidney structure and function with Glomerular Filtration Rate (GFR) less than 60 mL/min / 1.73 m2, which occurs for more than three months [1]. This disease is increasingly concerned because of its prevalence, which continues to increase, and the management costs incurred are very high. Within almost 30 years, the prevalence of CKD has increased by 29.3%, until 2017, the prevalence of this disease to 9.1%[2].

Eventually, patients with CKD will need kidney replacement therapy. In America 87.9% of CKD patients will undergo hemodialysis, 9.3% undergo peritoneal dialysis, and 2.6% undergo kidney transplants [3]. For patients undergoing hemodialysis, vascular access is needed since blood from the patient's body flowed to the dialysis machine. National Kidney Foundation's vascular access guide, Kidney Disease Outcomes Quality Initiative (K/DOQI) [1, 4, 5] states AVFs as the best access for hemodialysis because thrombosis rates are low and costs are relatively cheaper [6, 7]. AVs can only be used when mature. Based on KDOQI guidelines, the AVF maturity criteria appropriate for cannulation are defined as the "rule of 6s," i.e., 6 mm venous diameter, the venous flow rate of 600 mL/min and deep vein from 6 mm skin [8].

Theoretically, the most accurate measurement of volume flow is to measure volume flow in draining veins, but due to the high level of measurement variation, which depends on the level of pressure applied by the probe, this technique is starting to be abandoned. [9] As for now, the measurement through the brachial artery is being developed. The brachial artery is recommended because of its large diameter, laminar blood flow, and less turbulence.

Thus more stable value will be obtained. This study aims to assess the accuracy of the brachial artery volume flow, which represents the draining vein volume flow. Besides, determining the brachial artery volume cut-off. The cut-off then can be utilized as a brachiocephalic fistula maturity reference to do hemodialysis.

Methods

This cross-sectional study design was applied to determine the relationship between brachial artery volume flow in brachiocephalic AVF with maturity using of Doppler ultrasonography in patients undergoing hemodialysis. This study was conducted at Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Ethical clearance was obtained from the Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia No Ket-437/UN2.F1/ETIK/PPM.00.02/2019. All patients with stage 5 CKD with brachiocephalic AFVs six weeks after their creation, were included in the study. The sample selection used by the total sampling method. The number of research subjects was 80 patients. This study collected demographic data, data related to USG, and AVF complications data from the subjects.

Demographic data included age, sex, and comorbidities. An ultrasound examination was performed with Doppler (inStar 1000) US Imaging, Beijing, China. By using B-mode after brachial artery and draining vein are found, the long axis is sought and assessed whether there is stenosis or not. Peak systolic velocity (PSV) is assessed by placing an angle steer <60. The volume of the brachial artery flow is measured by placing a linear probe in the 2 cm proximal anastomosis brachial artery. The diameter is measured in the inner to the inner lumen of the brachial artery.

The parameters assessed on Doppler ultrasound examination were brachial artery diameter, PSV brachial artery, EDV brachial artery, draining vein diameter, volume flow draining, and distance of vein draining to the skin surface. PSV is recorded in cm/s and draining vein and brachial artery volume in ml/min. Data were analyzed using SPSS 20.0 for windows.

Initially, a descriptive analysis was performed to assess the characteristics of the subjects, including age, sex, comorbid disease, brachial artery PSV, brachial artery diameter, the diameter of draining vein, and complications. Then brachiocephalic AFVs at 6 weeks of age were compared between mature and nonmature group.

The main expected outcome was a cut-off blood volume flow of brachial artery flow in mature brachiocephalic AVF using a diagnostic test of Receiver Operator Curve (ROC) charts. The statistical test used was the unpaired T-test if the data distribution was normal, and the data variance was similar. If the data distribution was not normal or the data variance was different from the test used, then the Mann Whitney test is applied. P values <0.05 were considered statistically significant.

Result

We included 80 subjects in this study. The mean age of the patients was 50 ± 13 years, with proportions of men and women being equal, ie, 48.8% and 51.2%. In the USG parameters showed the mean volume of the flow rate of the brachial artery was 1633 ± 1068 ml/min, the mean volume flow rate of the draining vein was 2265 ± 1772 ml/minute, the mean diameter of the brachial artery was 6 ± 1 mm, the mean diameter of the draining vein was 9 ± 10 mm and mean PSV of the brachial artery was 157 ± 71 cm/s. Most patients had hypertension, as much as 52.5%.

Table 1: Subject characteristics

Variable	n (%)	Mean ± SD
Age (years)		50 ± 13
Gender		
Men	39 (48,8)	
Women	41 (51,2)	
USG parameter		
Volume flow (ml/min)		
a. Brachialis		1633 ± 1068

b. Draining vein		2265 ± 1772
Diameter		
a. Brachialis		6 ± 1
b. Draining vein		9 ± 10
PSV a. brachialis (cm/s)		157 ± 71
Comorbidities		
Diabetes Mellitus	24 (30,0)	
Diabetes Mellitus + Hypertension	8 (10)	
Hypertension	42 (52,5)	

In comparison between groups, 64 patients (80%) experienced maturity, and 16 patients (20%) experienced failure of maturation. In the group that experienced maturity failure, the values of the brachial artery and draining vein volume flow, brachial artery diameter, and draining vein and brachial artery PSV were lower. This difference in value was significant with p <0.05, respectively. Regarding complications, complications were more often found in the group that failed to mature, whereas in the group that failed to mature stenosis was found in 10 patients (62.5%) and thrombosis in 3 patients (18.8%).

Table 2: Comparison between mature and nonmature AVF

Variable	Mature Brachiocephalic AVF	Nonmature Brachiocephalic AVF	p
Total (n)	64	16	
Age (years) (mean ± SD)	50 ± 14	51 ± 11	0,987
Gender [n(%)]			
Men	28 (35,0)	11 (13,8)	0,096
Women	36 (54,0)	5 (6,2)	
USG parameter [mean ± SD]			
Volume flow (ml/min)			
a. Brachialis	1901 ± 1030	563 ± 152	0,001
b. Draining vein	2707 ± 1717	500 ± 73	0,001
Diameter			
a. Brachialis (mm)	6 ± 1	4 ± 0	0,001
a. Draining vein (mm)	10 ± 11	4 ± 0	0,001
PSV a. brachialis (cm/s)	175 ± 69	87 ± 8	0,001
Complication			
Without complication	62 (96,8 %)	3 (18 %)	0,001
Stenosis	2 (3,2 %)	10 (62,5 %)	
Thrombosis	0 (0 %)	3 (18,8 %)	

In the receiver operating characteristic (ROC) measurement for brachial artery flow in distinguishing the brachiocephalic AVF maturity, an area under the curve (AUC) of 97.6% was obtained. The highest sensitivity and specificity values were obtained when the brachial artery volume flow was 700 ml/min. This brachial artery volume flow value is determined as a cut-off value for the limitation prediction of brachiocephalic AVF maturity with a sensitivity, specificity, PPV, and NPV of 98.44% (95% CI 91.6-99.7%), 87.5% (95% CI 63.9-96.5%), 96.9% (95% CI 89.4-99.15%) and 84.6% (95% CI 66.5-93.8%), respectively. The accuracy was 93.33% (95% CI 70.1% - 98.8%) (Figure 1-3 and Table 3-4).

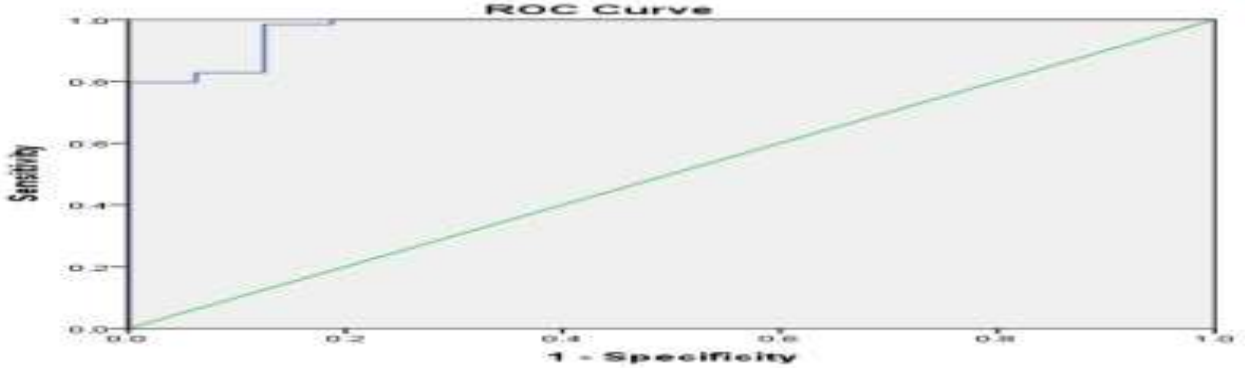

Figure 1: ROC curve with AUC 0,974 (p<0.001)

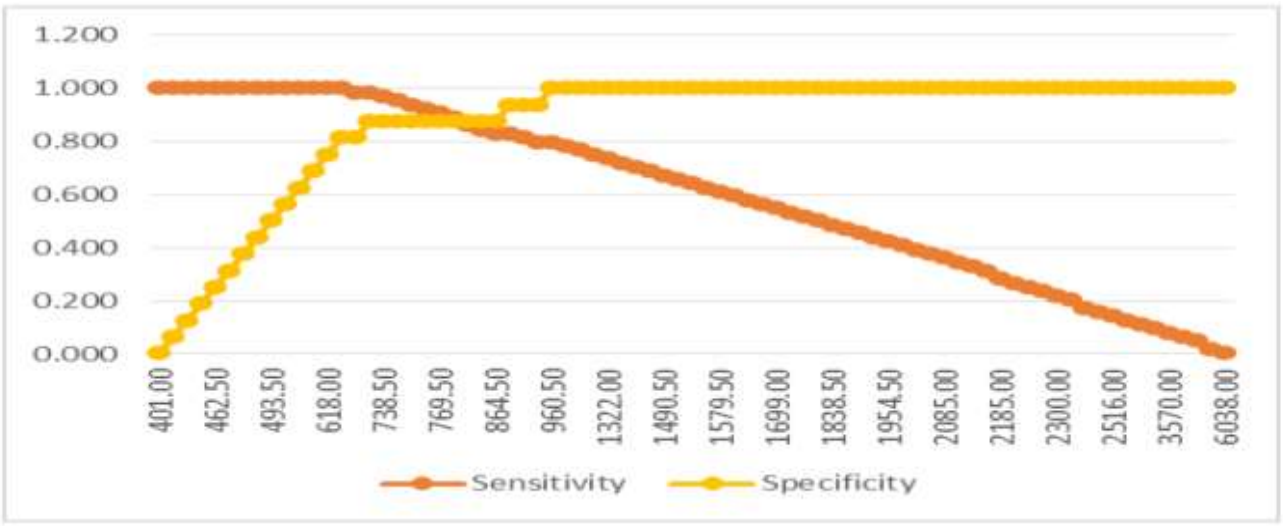

Figure 2: Cut-off curve of volume flow rates sensitivity and specificity

Table 3: Brachial artery volume flow accuracy to diagnose mature brachiocephalic AVF

		Mature	Nonmature	Total
Volume flow	≥ 700	63	2	65
	< 700	1	14	15
		64	16	80

Table 4: Sensitivity, specificity, PPV, NPV and, diagnostic accuracy of brachialis artery volume flow to determine brachiocephalic AVF maturation

		AVF maturation	
		Mature	Non-mature
Volume Flow artery Brachialis	Positive ≥ 700 ml	63	2
	Negative < 700 ml	1	14

Parameter	**(%)**	**95 % CI (%)**
Sensitivity	98,44	(91,67 – 99,72)
Specificity	87,5	(63,98 – 96,50)
Positive predictive value	96,92	(89,46 – 99,15)
Negative predictive value	93,33	(70,18 – 98,81)
Diagnostic accuracy	96,25	(89,55 – 98,72)

Discussion

Demographic Characteristics of the Subjects

In this study, the mean age of patients undergoing AVFs creation was 50 ± 13 years. As for other studies, the subject's age varies. Carrie et al. found the mean age of patients was 65.1 ± 16.8 years [10] whereas, in the study of Pogula et al. in India, the mean age of patients was 50.72 ± 12.62 in males and 49.32 ± 12.97 in females.[11] This difference in onset might be influenced by the underlying disease that caused the patient to develop kidney failures, such as diabetes mellitus (DM) and hypertension (HT). In developing countries, such as Indonesia and India, services to DM and HT are relatively poor with relatively low patient compliance. This causes microvascular complications such as chronic kidney disease to occur earlier [12]. In addition, this study also found that the proportion of male and female subjects balanced with the most basic disease is hypertension (52.5%).

Comparison between Mature and Non-mature Groups

In a comparison between groups, 64 patients (80%) had the maturity, and 16 patients (20%) had failed maturity. This maturation rate is almost the same as previous studies, such as the study of Jenifer et al. whose AVF maturity rate at 8 weeks was 71.43% [13].

In both groups, there were no significant differences related to age and sex. As for concomitant diseases, the presence of diabetes mellitus turned out to have a significant influence on the failure of AVF maturity. Of the 16 study subjects who were not mature, found 11 (68.75%) subjects had DM. This is in line with a meta-analysis from Yan et al. Which found that AVF failure rates in DM patients were higher than patients without DM (OR 1.682; 95% CI 1.429 - 1.981) [14].

Changes in metabolism in diabetes cause endothelial damage deregulation of growth factors, and an increase in extracellular matrix deposition. Impaired endothelial function can be explained as an impaired balance of vasodilation and vasoconstriction of blood vessels. All of these mechanisms cause a decrease in nitric oxide and an increase in platelet aggregation, which will ultimately increase the likelihood of thrombosis.

Thrombosis results in failure of AVF maturity [14].In this study, the volume flow in the brachial artery and mature AVF draining vein was higher than that of non-immature AVF. This was undoubtedly something normal. However, the comparison between the volume of brachial artery flow and mature AVF draining veins showed different values. The volume flow in draining veins should be around 90% of the volume flow in the brachial artery.

Despite that, this study found the volume flow in the draining vein was higher than in the brachial artery. Each volume flow was (2707 ± 1717) and (1901 ± 1030). This could be caused by variability in venous diameter during measurement, where the higher the venous diameter, the higher the volume flow [15].

In this study, the diameter of the brachial artery was 6 ± 1 mm, and draining vein 10 ± 11 mm. The comparison of brachial artery diameter between the mature and non-mature groups reported that the diameter of the mature arteries (6 ± 1) mm was higher than that of the non-mature (4 ± 0) mm groups. The mature group showed an increase in diameter size, which was higher than the immature group. Based on research conducted by Lomonte et al., an increase in arterial diameter began to occur from the first 24 hours and significantly increased on the 7th day to the 28th day.

The increase in blood vessel diameter is caused by an increase in shear stress-mediated by an increase in nitric oxide and other endothelium-dependent relaxing factors that attempt to return shear stress to normal [16].Furthermore, the parameters of the PSV a brachialis also found significant differences between the mature and failed groups (p = 0.001). In the mature group, the brachial PSV was 175 ± 69 cm/s, while in the immature group was 87 ± 9 cm /s.

The higher PSV of a brachial group in maturity is in line with the higher volume of mature brachial arteries flow in the mature group. Evaluation of complications or abnormalities after the creation of AVF showed that the abnormalities were more prevalent in the group failed to mature (p = 0.001). In the mature group, only 3.2% experienced abnormalities (in the form of stenosis), while 82% in the failed failure group experienced abnormalities, consisting of stenosis in 62.5% subjects and thrombosis in 18.8% subjects.

Brachial Artery Accuracy as an Arteriovenous Fistula Maturity

In this study, the best cut-off for brachial artery volume flow as a predictor of brachiocephalic AVF maturity was 700 ml/min. These results were similar to previous studies or slightly lower. Among them is the research of Burak et al. that found a cut-off of 770 ml/min [9] and Sae Hee Ko et al.'s research of 800 ml/min [17].

With a cut off of 700 ml / minute the sensitivity is 98.44% (95% CI 91.6 -99.7%), the specificity is 87.5% (95% CI 63.9% - 96.5%), positive predictive value 96.9% (95% CI 89.4% - 99.15%), negative predictive value of 84.6% (95% CI 66.5% - 93.8%) and accuracy of 93.33 % (95% CI 70.1% - 98.8%).

Thus, brachial artery AVF is quite accurate in determining the maturity of AVF. Wise et al. suggested that there were several reasons to recommend measuring the volume flow of the brachial artery in assessing access, such as the volume of flow in the brachial artery having a good correlation with the volume flow in draining vein. Besides, measuring volume flow in other access is more difficult because of variations in diameter, branches, shape of turns, turbulence, and a more superficial location. Meanwhile, the artery has laminar flow, flat wall shape, and is not affected by ultrasound probe pressure [18].

Conclusions

The variation of volume flow draining vein in brachiocephalic AVF could reduce the accuracy of AVF maturity prediction. Turbulence and variation in diameter are factors that affect the overestimation of volume flow in the access. Furthermore, through ROC-AUC analysis, the brachial artery is obtained accurately in determining the maturity of AVF access.

The best cut-off that can be used is 700 ml/minute, which will be obtained at the cut-off sensitivity, specificity, PPV and NPV 94.4 %, 87.5 %, PPV 96.9 %, and NPV 93.33%. Further studies are required to investigate parameters that could be used in predicting brachiocephalic AVF maturity.

Acknowledgement

We thanked Cipto Mangunkusumo General Hospital for their hospitality and support for this research.

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