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Original Article

Effect of Venoplasty on Arteriovenous Fistula Dysfunction on Quick of Blood Values of Hemodialysis Patients

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Introduction: Percutaneous transluminal angioplasty (PTA) is the gold standard in the management of AVF dysfunction. [1,2] On the other hand, the management of stenosis with PTA induces an acceleration of neointimal hyperplasia with the occurrence of restenosis.[3,4,5] The aim of this study was to assess the increase of quick of blood (Qb) hemodialysis (HD) patients after venoplasty with AVF dysfunction and its patency within 3 months post procedure, and examine the factors associated with venoplasty failure to maintain optimal Qb.

Method: This study used a quasi-experimental design, in which all subjects received the treatment under study without a control group, due to ethical issues; because venoplasty is the standard protocol for AVF dysfunction in the place of this study. Qb measurements were made before and after HD, and 3 months thereafter, to evaluate AVF patency.

Result: There were 25 cases that included 23 patients with 2 patients had to be re-venoplasty. An increase in Qb averaged 221.3−196.7 mL / min or about 25 mL / min in the 3-month period after venoplasty with significant results (p = 0.044). The location of stenosis in juxta anastomosis has a 14 times greater chance of venoplasty failure (p = 0.037) than stenosis in the area of draining vein or central vein. Diabetes Mellitus (DM) increased the odds of venoplasty failure 12 times greater (p = 0.038) than cases without this comorbid..

Conclusion: This study proves the increase in Qb of hemodialysis patients after venoplasty for AVF dysfunction, and it was found that the location of juxta anastomosis stenosis and the presence of DM are the two main factors that have the potential to increase the chance of venoplasty failure.

Keywords: venoplasty, quick of blood, stenosis
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INTRODUCTION

Indonesian Renal Registry (IRR) data 2017, the number of new patients undergoing HD in Indonesia continues to increase, where there are 30,831 new patients in 2017, and 77,892 active patients. In America, the total cost for vascular access is estimated at 2.9 trillion USD. [6,7] Adequate HD can be evaluated on the results of post HD ureum reduction ratio (URR). Qb is one of the factors affecting URR results. The European Best Practice Guidelines, Kidney Disease Outcomes Quality Initiative (KDOQI) and the Indonesian Nephrology Association (PERNEFRI) recommend a URR of at least 65%. [6,8,9] In patients with end stage renal disease (ESRD), AVF is the preferred access to HD, but often complicated by stenosis. Stenosis in AVF dysfunction can be managed with endovascular procedures such as percutaneous balloon venoplasty. [3,10,11] Duque et al. said primary failure was defined as AVF which never matured to support cannulation, failed in the first 3 months after initial cannulation ranged from 30 to 50%, most commonly in juxta- anastomotic stenosis associated with intimal hyperplasia (IH) .[12] This relates to the pathophysiology of AVF which requires adequate inflow and outflow of blood flow that can be inhibited by vascular disease and poor cardiac output. AVF failure results in the need for repeat operations, longer use of intravenous catheters, and more expensive costs.[13,14]

Angioplasty plays an important role in saving access to hemodialysis and has an excellent success rate in primary failure. [15] PTA reduces the need for surgical intervention or AVF elimination.[1,16] However, 10-30% re-stenosis is reported in one year after the procedure. Tariq et al, in a case study of re-stenosis, the first case was found after 6 months.[11] On the other hand, the management of stenosis with PTA, induces an acceleration of neointimal hyperplasia with recurrence of stenosis. In 20% of cases, restenosis occurs within 1 week post-procedure and 40% in 1 month.[3,4,5]

Table 1. Characteristics of AVF dysfunction cases with venoplasty, in μ ± *SD* or n (%)

Characteristic	Total (n =25)	AV Fistula BC (*n* =18)	AV Fistula RC (*n* =7)	*p-value*
Age, μ±*SD*	62.5±10.0	64.0±10.5	58.6±7.8	0.228
Gender				
Men	11 (44)	5 (28)	6 (86)	0.021
Woman	14 (56)	13 (72)	1 (14)	
Comorbid				
Heart disease	2 (8)	2 (11)	0 (0)	1.000
Hypertension	18 (72)	13 (72)	5 (71)	1.000
Diabetes	12 (48)	10 (56)	2 (29)	0.378
Location of Stenosis				
Draining Vein / Central Vein	9 (36)	7 (39)	2 (29)	1.000
Juxta Anastomosis	16 (64)	11 (61)	5 (71)	
Quick of Blood Before, After, and 3 Months after Venoplasty, μ ± SD				
Before	142.4±26.6	139.2±2.8	152.5±22.2	0.400
After	196.7±25.1	197.8±23.4	193.3±32.0	0.716
After 3 months	221.3±33.1	221.8±38.7	220.0±11.5	0.929
Venoplasty Results in 3 Months (according to Quick of Blood Value)				
≥ 200 mL/menit	12 (48)	8 (44)	4 (57)	0.673
< 200 mL/menit	13 (52)	10 (56)	3 (43)	

NOTE: SD standardization, BC brachiocephalic, RC radioadiophalic. a Test on numeric variables, χ2 or Fisher's Exact on categorical variables

METHOD

This study used a quasi-experimental design, all subjects received treatment without a control group, due to ethical issues; where venoplasty is the standard protocol for handling AVF dysfunction. Qb measurements were made before and after hemodialysis, and 3 months thereafter. There were 25 cases that included 23 patients with 2 patients had to be re-venoplasty. Data processing centered on the Surgery Department of Prof. R. D. Kandou Manado Hospital. Venoplasty is performed in the cath lab with diagnostic facilities and interventions according to standard operating procedures. Prior to the procedure, a clinical evaluation was carried out, Doppler ultrasound to assess AVF patency, location of the lesion, presence of stenosis or thrombosis and hemodialysis adequacy assessed in Qb. The operator is a vascular surgeon. Proximal and distal diameters of the lesion were evaluated, followed by venography and venoplasty using plain old balloon angioplasty 6 mm, inflation procedures according to the target proximal and distal diameter of the lesion and maximum pressure according to balloon rated burst pressure (RBP) within 2-4 minutes. The study was conducted in accordance with the applicable ethical principles of human subject research and has received ethical clearance from the Research Ethics Commission.

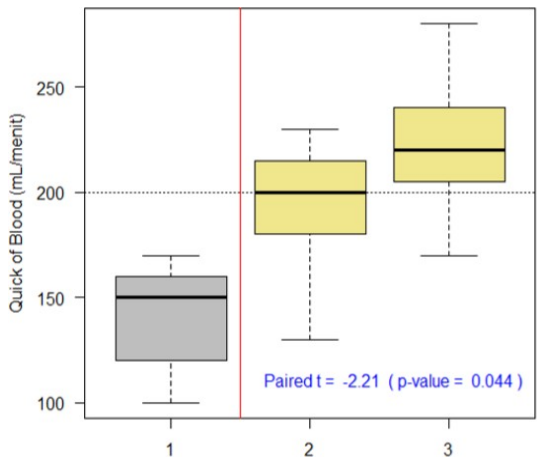


Figure 1. Quick of Blood Measurement Results: (1), (2) immediately after, and (3) three months after venoplasty

RESULTS

Table 1 shows the characteristics of cases with a mean age above 60 years. More cases of women than men (56% vs 44%). Most suffer from DM and nearly 75% have hypertension. AVF of 18 (72%) cases in the brachiocephalic region and the rest were radiocephalic AVF. The increase in Qb during the study was seen descriptively by comparing the results of examinations before, immediately after, and 3 months after venoplasty.

The number of cases with Qb at the end of the third month after venoplasty was ≥200 mL / min and relatively no different from the total cases whose Qb was <200 mL / min, i.e. 12 (48%) and 13 (52%) cases, respectively.

Figures 1, 2, and 3 show the distribution of Qb values. The first graph is supplemented by the results of the Qb difference statistical test in the last two measurements. Table 7 shows the average Qb

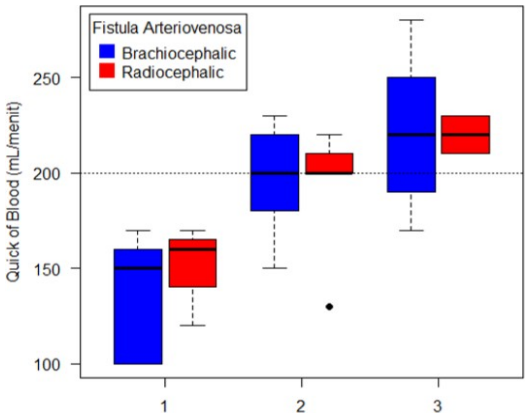


Figure 2. Qb values according to AVF location at the third inspection time

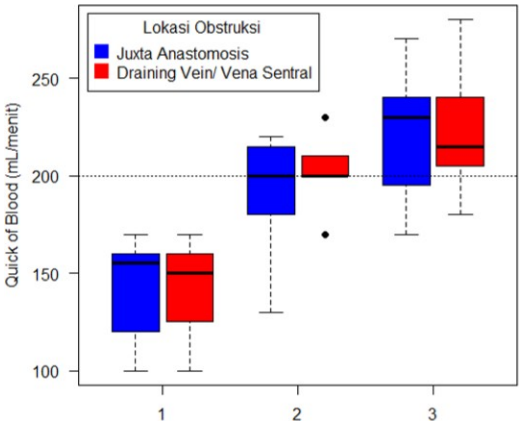


Figure 3. Quick of Blood values by location of stenosis measured before, immediately after, and three months after venoplasty

increase of 221,3−196,7 mL / min or about 25 mL / min in the 3-month period after venoplasty with significant results (p = 0.044). The next two graphs provide a description of the changes in Qb that are stratified according to AVF (Figure 2) and the location of stenosis (Figure 3). Figure 2 shows the difference in quantity Qb with respect to measurement time; the median distribution of the two case groups both those with brachiocephalic and radiocephalic fistula were almost no different and their distribution overlapped at all three time measurements. The change in Qb value according to the location of stenosis in Figure 3 shows a relatively similar picture, with the exception of the last measurement in which the difference in the mean values of the case groups with juxtaanastomosis stenosis and stenosis in central vein/venous draining is clearer.

Factors affecting venoplasty failure to maintain optimal Qb values were analyzed through logistic regression modeling (Table 2). Regardless of other factors (univariable model), the location of stenosis and the presence of DM comorbidities are 2 main factors that have the potential to increase the chance of venoplasty failure. After controlling for one of these variables (multivariable model), it was seen that cases with juxta anastomosis stenosis had a 14 times greater chance of venoplasty failure (p = 0.037) than stenosis in draining veins or central veins. The presence of DM increased the odds of failure of venoplasty 12 times greater (p = 0.038) than when cases did not have this comorbid. The location of AVF had no effect on venoplasty results (p = 0.570).

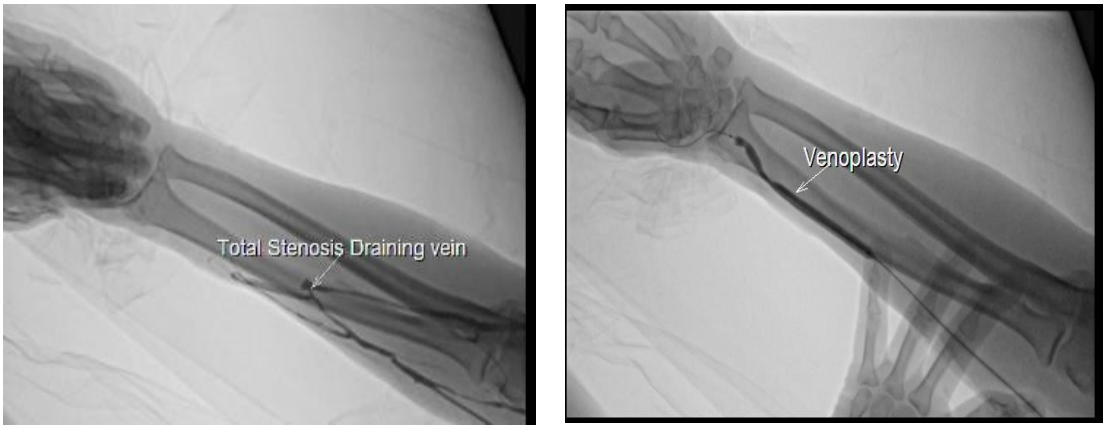
DISCUSSION

This study found the average age of patients over 60 years, which looks the same as the study of Jordan et al (2003), but different from Batieha et al. Where age 40-59 years became the largest age group by 36.2% followed by the age group ≥ 60 years by 33 , 2% and research by Sodavi et al in the age group 31-60 years as much as 46.28% followed by the age group > 61 years as much as 42.45% .[17.18] The number of cases in women is higher than men (56%). The results of this study are similar to those of Allon in which approximately 51.4% of hemodialysis patients are female.[19] Several studies report that female patients appear more likely than men to be dialyzed with fistulas.[20] Batieha et al and Sodavi et al get different results where male patients appear more undergo hemodialysis. However, most of these results were not statistically significant.[18] Hypertension, atherosclerosis, and DM were the most common causes of chronic kidney disease.[21] In this study hypertension was 72% followed by DM 48% and heart disease 8%. Hyperglycemia causes toxic products that damage cells such as TGF-β. Reactive oxygen species (ROS) are thought to be a key factor in the progression of diabetic nephropathy.[22] Atherosclerosis is an indolent fibroproliferative condition driven by

Table 2. Logistic Regression Model of failure to maintain Qb ≥200 mL / min post venoplasty

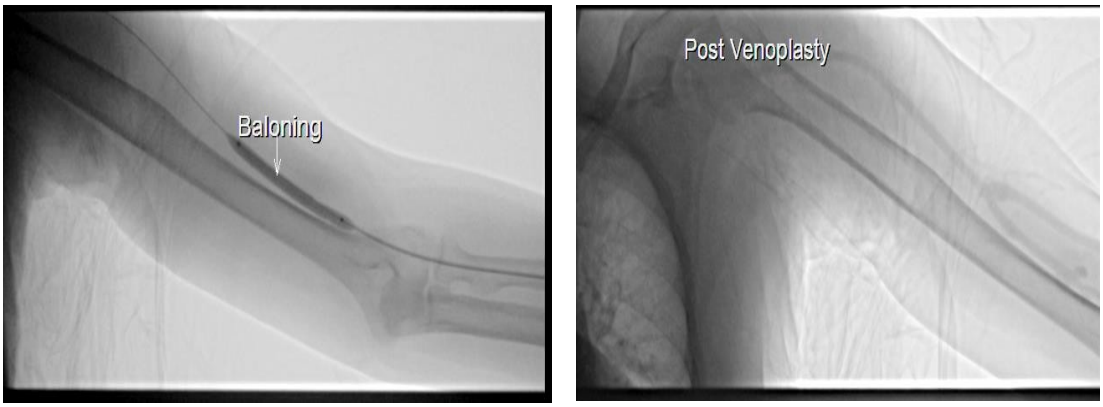
	Univariable Model		Multivariable Model	
Variable	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Age	1.06 (0.97− 1.16)	0.195	*	
Female vs Male	3.15 (0.61−16.31)	0.171	*	
History of Heart Disease	0.92 (0.05−16.49)	0.953	*	
Hypertension	1.67 (0.29− 9.71)	0.570	*	
Diabetes	6.75 (1.16−39.20)	0.033	1.,95 (1.15−123.97)	0.038
AVF: RC vs BC	0.60 (0.10− 3.50)	0.570	*	
Location of Stenosis				
Draining Vein / Central Vein (ref.)				
Juxta Anastomosis	7.70 (1.16−51.17)	0.035	13.86 (1.18−163.50)	0.037

NOTE: OR odds ratio, CI confidence interval, AVF arteriovenous fistula, RC radiocephalic, BC brachiocephalic.



(a) Radiocephalic AVF draining vein stenosis and venoplasty

(b) Stenosis anastomosis juxta braciocephalic AVF



(c) Venoplasty is performed

Figure 4. Procedure of venography and venoplasty. AVF venography and venoplasty in Cath Lab Prof. RD Kandou Hospital

chronic inflammation. Various cytokines, chemokines and growth factors cause imbalance of matrix formation and degradation leading to accumulation of extracellular matrix and glomerulosclerosis and interstitial fibrosis. [23] KDOQI's recommendation is that radiocephalic fistulas are the first choice in making fistulas based on the low stealing syndrome rate in radiocephalic fistulas compared to other fistulas and there are other options that are more proximal if the fistula fails. However, radiocephalic fistulas have poor maturation rates. Brachiocephalic fistulas are generally made if radiocephalic fistulas fail or when

preoperative mapping, radiocephalic fistulas are not suitable to be made. [24] This study 72% of cases found AVF in the brachiocephalic region and the remaining radiocephalic fistula. Women dominate brachiocephalic fistula cases while men dominate radiocephalic fistulae. Studies from the Dialysis Outcomes and Practice Patterns Study (DOPPS) almost all AVFs are at the location of the upper arm (> 96%) while in Japan tend to be more dominant location of the AV fistula at the location of the forearm (89%). In the analysis of the subgroup of the study, it was found that the location of AVF in the forearm was more frequent in men than women in each age group.[25] Women appear to have smaller caliber arteries so that it is estimated to have a lower AVF patency rate than men.[26]

The Aktas et al study totaled 330 stenosis, of which 73 stenosis in the anastomosis segment, 25 stenosis in feeding artery, 78 stenosis in venous draining, and 149 stenosis in juxta anastomosis.[27] Similar to this study, both in brachiocephalic and radiocephalic AVF, the location of stenosis appears more visible in the area of juxta anastomosis than in venous or central venous draining at 64%. The mechanism of stenosis juxta anastomosis there are various hypotheses, including loss of vasa venosum during skeletonization for mobilization of most peripheral venous parts, shear stress is low and fluctuates at that location, twisting, increased downstream venous turbulence from anastomosis, and torsional stress. The combination of some or all of the stress in these venous segments causes intimal trauma with the proinflammatory cascade, including hypoxia inducible factor-1α (HIF-1α), vascular endothelial growth factor-A (VEGF-A), matrix metalloproteinases (MMPs), and platelets- derived growth factor (PDGF) .[28] Proinflammatory cytokines cause migration of fibroblasts and smooth muscle from adventisia and media to the intima, proliferation of smooth muscle cells, myofibroblasts, and extracellular matrix resulting in neointima hyperplasia and stenosis. Stenosis of the cephalic arch is thought to involve extrinsic compression of the clavipectoral fascia, sharp turns of the cephalic arch cause turbulent flow, and high concentrations of valves that experience hypertrophy or cause turbulent flow and higher blood flow in the brachiocephalic fistula.[24,29] Qb is one of the factors that can influence the urea clearance. According to IRR, 2017 in Indonesia an increase in the proportion of Qb to 52% (Qb 200 - 249 ml / min). [6,8] The recommendation given is that Qb should be adjusted to the predialysis body weight, while the optimal Qb at 200 ml / min corresponds to 4 times average predialysis body weight.[8] AVF dysfunction most commonly results from stenosis and venoplasty being a modality for treatment.[4] PTA as the gold standard for stenosis lumens more than 50% occlusion. Of all percutaneous interventions performed on AV access, balloon venoplasty is the most common.[15,30]

From this study, venoplasty was successful in 12 cases, while failure in 13 cases. Even though the results were not statistically significant (p = 0.673), if seen from the number of cases in the study sample it was relatively balanced ie 12 (48%) and 13 (52%) cases, this was because there were 4 cases categorized failed because of death before being evaluated in the third month which was not excluded because other data variables were still needed. The increase in Qb in this study can be seen in the difference in the quantity of Qb related to the time of measurement, which obtained significant results (p = 0.044). Mean Qb in the brachiocephalic and radiocephalic AVF groups, obtained in 3 examination times did not show statistical differences. The same thing is seen in venoplasty results after 3 months, where the proportions of success and failure are relatively balanced in cases with brachiocephalic or radiocephalic AVF. Venoplasty is still an effective modality for treating stenosis in AVF but monitoring for the risk of restenosis is needed.[27] Retrospective cohort studies conducted by Patrianef were performed on patients with immature AVF who underwent EFS procedures during the January-December 2016 period. There were 125 stenosis, a total of 66 stenosis which is noted in juxta anastomosis. Age, DM, length of stenosis and many stenosis are found as factors that influence primary patency. The overall primary patency in 6 months and 12 months was 69.3% and 38.6%, respectively. In his research, it was concluded that the EFS procedure on immature AVF could be applied as the first-choice method, compared to making a new AVF or surgical revision.[7] In this study it was found that the location of stenosis factors and the presence of DM became 2 main factors that have the potential to increase the chance of venoplasty failure. Age, sex, history of heart disease and hypertension, and type of AVF did not affect venoplasty results statistically. The location of stenosis in juxta anastomosis has a 14 times greater chance of venoplasty failure and DM increases the chance of venoplasty failure by 12 times greater. Aktas et al revealed the same thing where the location of juxta anastomosis stenosis and DM was related to failure of angioplasty by univariate analysis.[27] Age factors could increase the risk of venoplasty or AVF failure by increasing the incidence of comorbidities such as DM and peripheral vascular disease. A meta-analysis of 13 studies found that radiocephalic AVF has an increased primary failure rate and decreased patency in elderly patients ranging from 50-70 years. The sex factor is still controversial, because there is an opinion which says that the AVF patency rate in women is lower due to lower arterial caliber but Caplin et al get the diameter of arteries and veins between men and women are not significantly different. Patients with DM are more prone to experience arterial calcification and steal syndrome. Atherosclerosis appears to increase the risk of failure of AVF and venoplasty and the process of atherosclerosis is more common in people with DM.[26]

CONCLUSION

This study proves the increase in Qb of hemodialysis patients after venoplasty for AVF dysfunction. Juxta anastomosis stenosis and the presence of DM are 2 main factors that have the potential to increase the chance of venoplasty failure with statistically significant results

CONFLICT OF INTEREST

The author states the original work, and there is no conflict of interest in doing this research.

ORCID ID OF AUTHORS

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