ORIGINAL ARTICLE

Predictive vascular diameter of cephalic vein and radial artery affecting the patency of radiocephalic arteriovenous fistula

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Abstract:
Objectives: To find out the cut-off values of vascular arterial and venous diameters effecting the patency of arteriovenous fistula (AVF) at wrist.
Study Design: Cross sectional qualitative study with non-purposive consecutive sampling.
Place and duration: Combined Military Hospital Lahore for 2 years.
Materials and Methods: All consecutive patients fulfilling the inclusion criteria and undergoing radiocephalic arteriovenous fistula (RC-AVF) were included. Log Rank test was used to find the cut-off points and Kaplan-Meier survival analysis was done to analyze the effect of vascular diameters on cumulative patency of radiocephalic arteriovenous fistula at 2 years.
Results: A total of 150 radiocephalic arteriovenous fistula (RC-AVF) were analyzed. Mean age at presentation was 53.5 (SD±4.76, Range 46-64) yearswith male to female ratio of 1.5:1. Coronary artery disease (P-value: 0.000) and peripheral vascular arterial disease (P-value: 0.004) had a strong negative association with long term patency of access. Dichotomized cut-off point for radial artery was 2mm and cephalic vein was 2.5mm. Radial artery diameter of less than 2mm (SE 1.155; CI: 5.66-525.2; P value: 0.001) and cephalic vein diameter of 2.5mm (SE 1.155; CI: 5.66-525.2; P value: 0.001) are strongly associated with poor long-term patency of radiocephalic arteriovenous fistula.
Conclusion: Cephalic vein of <2.5mm and radial artery of <2mm diameter is associated with statistically significant failure rates of radiocephalic arteriovenous fistula.

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Introduction:
Arteriovenous Fistula (AVF) has fewer complications, better access patency, and lower mortality risk compared to HD catheters and arteriovenous grafts.[1-3] Hence native arteriovenous fistula is a preferred method for vascular access in patients needing hemodialysis. Although radiocephalic arteriovenous fistula (RC-AVF) is the preferred vascular access method and allows more proximal future access placement options if needed, they have a higher risk of failure compared to more proximal arteriovenous fistula.[4] Many factors including comorbidities and vessel diameters are responsible for loss of AV access.[1,3] Clinicians use physical examination and pre-operative ultrasound vascular mapping to assess suitability of veins and arteries for arteriovenous fistula creation.[5-7] Disturbed shear areas near the anastomosis of the radial artery and cephalic vein trigger intimal hyperplasia leading to hyperplasia-induced stenosis and thrombosis being the primary causes of radiocephalic arteriovenous fistula dysfunction.[8]

Many studies have assessed the effect of vessel diameter on long term patency of radiocephalic arteriovenous fistula (RC-AVF)[6,7] and results are variable. Since there are no local studies in our population addressing the effect of vessel diameter on patency, we designed this study to see the effect of arterial and venous diameter on long term patency of RC-AVF in our setting.

Materials and Methods:

This qualitative cross-sectional study was approved by the institutional Ethical Review Committee and study protocols were followed according to Declaration of Helsinki. The sample size (n) was calculated using the formula n= (Z1-α/2)2 x p(1-p)/e2. Here Z1-α/2 was standard normal variate (at 5% type 1 error (P<0.05) it is 1.96). Absolute error (e) was 0.08 (8%) and prevalence (p) is expected proportion of population derived from a previously conducted study.[9] The calculated sample size was 120. All consecutive patients referred to Vascular Surgery Out Patient Department for creation of an arteriovenous fistula from January 2021 to January 2022 were included in the study. Patients with previously failed arteriovenous fistula at wrists, patients requesting more proximal access and patients who did not consent to be included in study, were excluded. Furthermore, those patients who did not maintain the recommended follow up schedule or those who did not complete a minimum of 2-years follow up were also excluded. Vascular mapping was performed by trained Vascular Surgeon in the Out Patient Department using 10MHz linear vascular probe (LOGIQ Book, GE Medical Systems, Milwaukee, WI, USA). All patients had vascular mapping done in sitting position. The cephalic vein was mapped from wrist to its termination in clavipectoral fascia for any stenosis or thrombosis. If found clear, a tourniquet was applied just above the elbow and internal diameter of the vein was measured from snuffbox to at least 10cm proximally towards forearm at 1cm intervals. For radial artery, the internal diameter of the artery was measured from wrist crease to 5cm proximally at 1cm interval. Mean Arterial Diameter (MAD) and Mean Venous Diameter (MVD) were then calculated. This mapping was done on both arms and the arm with greater mean diameters was selected for the creation of arteriovenous fistula.

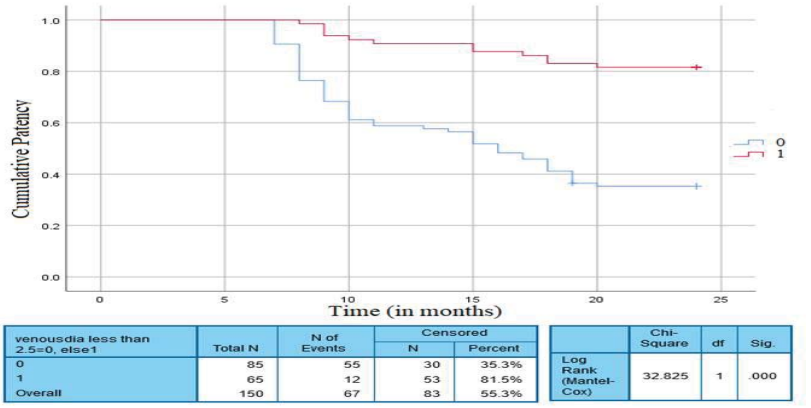
Arteriovenous fistula was created under local anesthesia using plain Lignocaine by a trained Vascular Surgeon with at least 5 years of experience. All patients received 2500 units of intravenous un-fractioned heparin before application of arterial clamps. A standard end to side anastomosis was made using continuous Prolene 7/0 suture. Any tributaries of the vein within the operative field if found, were ligated to prevent diversion of flow. All patients were provided written post-operative instructions about the care of AVF. AVF was considered mature for hemodialysis when it met the KDOQI criteria.[10] All patients were followed up regularly and underwent Doppler scan to assess patency of the access at monthly intervals. All patients in which there was any inability to cannulate, significant flow rate reduction or elevated outflow pressures during hemodialysis; underwent venography. All patients with a stenoticlesion of more than 50% underwent Venoplasty to salvage the access.

The outcome of the study was measured in terms of primary patency, secondary patency and access failure. Primary and secondary patency was defined as per Society of Vascular Surgery guidelines.[11] Primary patency was defined as patency from the time of fistula creation until its thrombosis or ligation or any intervention done to maintain/restore patency. Secondary patency was defined as time from access placement until the time of its abandonment. Access failure is defined according to American Society of Nephrology Kidney Heath Initiative as inability of arteriovenous fistula to be used for successful dialysis for a period of 1 month.[12]

The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 22.0 software (SPSS Inc., Chicago, IL, USA) and R version 3.5.1 (R Foundation; Statistical Comp: Vienna, Austria). All continuous variables were expressed as means and standard deviations (SD), whereas categorical variables were expressed as frequency and percentage. In order to find out the relative influence of diameter of brachial artery and cephalic vein on fistula maturation and patency, dichotomized cutoff points were determined using the log rank test to find out the strongest predictive outcome of continuous variables. The generated dichotomized cutoff point for secondary patency was considered most predictive of fistula maturation over time hence used for assessing long term paten-

Table 1: Effect of demographic variables on long term patency of AVF

Variable	Standard Error	95% Confidence Interval (CI)		p-value
		Lower	Upper	
Age	0.054	1.024	1.263	0.017
Gender	0.330	0.265	0.966	0.039
Diabetes Mellitus	0.394	0.197	0.925	0.031
Hypertension	0.351	0.641	0.322	0.205
Smoking	0.614	0.508	5.636	0.391
Hyperlipidemia	0.682	1.055	15.310	0.042
Coronary Artery Disease	0.869	3.920	118.071	0.000
Congestive Cardiac Failure	0.873	0.102	3.110	0.509
Peripheral Vascular Disease	1.084	0.005	0.371	0.004



venousdia less than 2.5=0, else1	Total N	N of Events	Censored	
			N	Percent
0	85	55	30	35.3%
1	65	12	53	81.5%
Overall	150	67	83	55.3%

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	32.825	1	.000

Figure I : Kaplan-Meier Analysis showing cumulative patency stratified by vein diameter.

cy of the arteriovenous fistula. Cox regression analysis was performed to assess the association of demographic variables with failure of fistula. Time-to-event estimations for primary and secondary patency were done using Kaplan-Meier survival analysis. P-value (two-tailed) was calculated using Bonferroni method and a value of ≤0.05 was considered to be statistically significant.

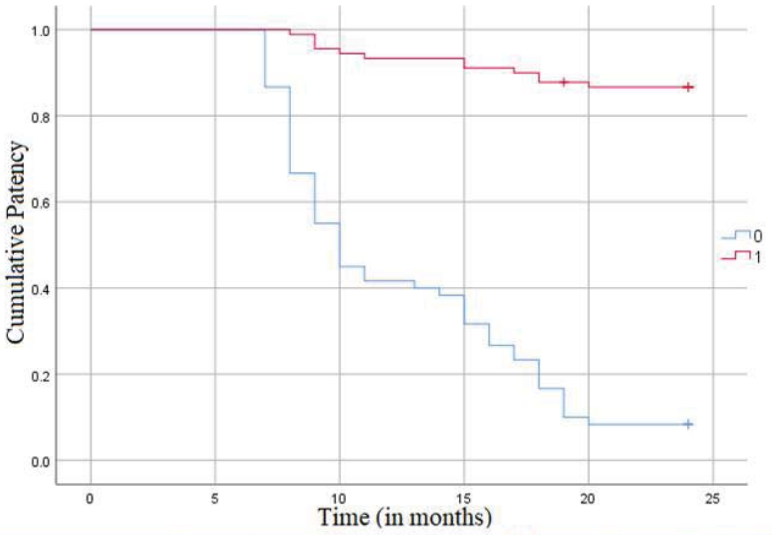
Results:

There was total 230 cases: 25.2% (n=58) patients expired from systemic illness unrelated to any complication of arteriovenous fistula while 9.5% (n=22) did not complete the mandatory follow-up of 2 years; hence they were excluded. Therefore, the total number of patients completing the studywere 150. Mean age of the patients at the time of operation was 53.5 (SD±4.76, Range 46-64) years. There were 90 males with a male to female ratio of 1.5:1. Out of 150, 70% (n=105) arteriovenous fistula were made in left and 30% (n=45) in right wrist. In terms ofmajor atherosclerotic risk factors; 70% (n=105) had diabetes mellitus, followed by hypertension in 23% (n=35) cases, smoking in 20% (n=30) and hyperlipidemia in 13% (n=20) patients. However, there were 10% (n=15) patients with no major atherosclerotic risk factor. There were 16.6% (n=25)patients who had congestive cardiac failure and 10% (n=15) had ischemic heart disease. Peripheral vascular arterial disease was present in 13.3% (n=20)cases. Cox regression shows that coronary artery disease (P value: 0.000) and peripheral vascular arterial disease (P value: 0.004) has a strong negative correlation with long term patency of radiocephalic AVFs (Table I).

At the time of surgery, 80% (n=120) cases were already on hemodialysis. In terms of dialysis access, 73.3% (n=110) had non tunneled double lumen dialysis catheter in neck veins and 6.7% (n=10) had tunneled catheter (PermCath®) in place.

All arteriovenous fistula was patent at 6 months (100%). Primary patency rate dropped to 54.7% at 1 year (n=82). However, 91.1% (n=62/68) patients with failed fistula underwent successful Venoplasty as a salvage procedure. Thus, the cumulative patency raterose to 75.3% (n=113) at 1 year. Over further course of time, more arteriovenous fistula failed thus the final cumulative patency dropped down to 55.3% (n=83) by the end of the study period of 2 years.

Mean venous diameter at wrist was 2.6mm (SD±0.29, Range 2.3-3.1). Dichotomized cut-off point [calculated by Log Rank (Mantel Cox) test] for venous diameter at wrist was 2.5mm. Cox Regression Analysis revealed that 64.7% (n=55/85) patients with venous diameter of less than 2.5mm failed to survive (SE 1.216, CI: 13.1-17.9) by the end of 2 years. However, when the diameter of the vein was >=2.5mm, only 18.4% (n=12/65) failed to survive (SE: 0.69, CI: 17.5-22.2). The difference in the survival



radial art dia less than 2.1=0, else 1	Total N	N of Events	Censored	
			N	Percent
0	60	55	5	8.3%
1	90	12	78	86.7%
Overall	150	67	83	55.3%

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	115.595	1	.000

Figure II : Kaplan-Meier Analysis showing cumulative patency stratified by arterial diameter

between the two groups based on the diameter of vein is statistically significant (SE 1.155; CI: 5.66-525.2; P value: 0.001). When the diameter of vein was less than 2.5mm, the drop in the cumulative survival was sharp within 1st year (from 7th month to 11th month). In this time period almost 2/3 (65.4%, n=36/55)arteriovenous fistula failed despite having salvage procedures (blue line – Figure I), making this as the most vulnerable period for the loss of arteriovenous fistula. In contrast there was a gradual loss of patency starting after 6 months when vein diameter was >=2.5mm (red line – Figure I).

Mean radial artery diameter at wrist was 2.1mm (SD±0.22, Range 1.9-2.6). Dichotomized cutoff point [calculated by Log Rank (Mantel Cox) test] for radial artery diameter at wrist was 2mm. Cox Regression Analysis revealed that 91.6% (n=55/60) patients with arterial diameter of <=2mm failed to survive (SE 1.216, CI: 13.1-17.9) by the end of 2 years. However, when the diameter of the artery was >2mm, only 13.3% (n=12/90) failed to survive (SE: 0.69, CI: 17.5-22.2). The difference in the survival between the two groups based on the diameter of artery is statistically significant (SE 1.155; CI: 5.66-525.2; P value: 0.001). Similar to vein, there was steep loss of AVFs within 1st year (from 7th month to 11th month) when the diameter of the radial artery was <=2mm (blue line – Figure II).

Discussion:

The dimensions of pre-operative veins and arteries significantly impact the maturation process and long-term viability of autologous arteriovenous fistula. Despite knowing that vascular anatomy affects arteriovenous fistula outcomes, the impact of vein and artery diameter on AVF maturation and long-term patency varies greatly.[13-19] These differences occur due to variations in the way patients are chosen for studies, measurements are taken, patients are followed up and results are reported. Some studies only look at people getting their first arteriovenous fistula,[15,18] while others don't include people who already had one on the same side.[20] Additionally, most studies include radiocephalic and/or brachiocephalic arteriovenous fistula, while some focus exclusively on radiocephalic arteriovenous fistula.[15-17] We exclusively enrolled patients with initial radiocephalic arteriovenous fistula (RC-AVF), irrespective of their anatomical placement. This decision was made because individuals with secondary arteriovenous fistula on the same side might present with altered anatomy that could affect vascular diameters. For this reason, patients with prior unsuccessful arteriovenous fistula (AVF) in their wrists or those seeking more proximal access were excluded from our study, although it may be labelled as selection bias.

Studies examining vein and artery diameter reveal significant variability in findings. In the prospective haemodialysis fistula maturation study by Misskey at el findings revealed that early thrombosis incidences were less frequent in arteriovenous fistula (AVF) formed using vein diameters exceeding 3mm.[17] Nevertheless, rates of access success displayed a bimodal distribution, with a greater proportion of failures observed in the 2 to 3mm category and a decreased failure rate noted among patients with cephalic vein diameters below 2mm or exceeding 3mm. Some

investigators employ MVD as a metric, indicating that an MVD < 2.7 mm is associated with Failure to Mature (FTM) within six months.[1,3] Similarly, an MVD < 3 mm is linked to early thrombosis or FTM in 5% and 26% of cases.[14,17] Moreover, FTM rates range from 19.8% to 45% when vein diameter measures 2–3 mm.[13-17] Notably, successful outcomes are observed when vein diameter measures up to 4 mm, with reported success rates ranging between 76-89%.[19] According to Wong et al, AVFs featuring a vein with a diameter of 1.6mm or less would inevitably fail.[21] Additionally, Ferring et al. noted a significantly higher rate of maturation success (76% vs. 16%) in arteriovenous fistula (AVFs) constructed using veins larger than 2mm compared to those with diameters of 2 mm or less.[22] Similarly, Kordzadeh et al suggested a higher FTM rate when vein diameter exceeded 1.5mm, reaching 86% compared to 38%.[19] The result of our study is comparative to this literature. We calculated the dichotomised cutoff point for MVD as 2.5mm and 64.7% (n=55/85) patients with MVD of less than 2.5mm failed when compared to only 18.4% (n=12/65) failure rate when MVD was 2.5mm or more.

Currently few guidelines regarding the impact of vessel diameter on fistula maturation are available. The European Society for Vascular Surgery recommends a vessel diameter of 2mm in the forearm and 3 mm in the upper arm,[6] while the KDOQI 2019 Update suggests the luminal diameter of the artery is at least 2mm and of the vein is at least 2.5mm.[10] Our study reveals similar outcome with significant differences observed in terms of survival based on arterial diameter of 2mm and venous diameter of 2.5mm. A recent metanalysis by Feng et al (80 articles) recommended that venous diameter of less than 2 mm is a strong negative predictor for fistula patency however they found no difference between the primary and secondary patency rates over a period of 1 year.[14]

Recommending the strategy of utilising larger arterial and venous vessels (over 2mm) to improve fistula success might constrain options, especially for younger patients requiring long-term renal support. Embracing smaller veins in younger patients, along with vigilant monitoring, could broaden native options, particularly if patients are referred promptly and arteriovenous fistula (AVF) creation precedes dialysis commencement. Conversely, for elderly patients already undergoing dialysis with limited life expectancy, selecting elbow options with adequate vein and arterial size might provide a more predictable success rate and fewer complications.

Although we found similar cutoff values of vascular diameters in our population when compared across the world, yet we acknowledge the limitations of our study. We did not assess other anatomical factors, such as venous compliance and artery calcification, and there is a risk of patient selection bias due to referral patterns and favourable anatomy. For those reasons we recommend further multicentre studies with larger patient pool to adequately assess the effect of vascular diameters on long term patency of radiocephalic arteriovenous fistula in our population.

Conclusions:
Radial artery of <2mm and vein of <2.5mm diameter at the wrist is associated with statistically significant loss of patency of radiocephalic arteriovenous fistula.

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Role and contribution of authors:
Rashid Usman, collected the data, references, discussion writing and did the initial write up.

Rabail Fatima, collected the data, and helped in interpretation of data.

Minahil Mazhar, critically review the article and made final changes.

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