

ORIGINAL ARTICLE

PREDICTIVE PARAMETERS FOR SUCCESSFUL FUNCTIONAL MATURATION OF NATIVE ARTERIOVENOUS FISTULA

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Background: Successful arteriovenous fistula (AVF) significantly reduces both the morbidity as well as mortality of the patients who have end stage renal disease, and significantly improve their survival rate. The objective of the study was to high light the role of various parameters in the functional maturation of arteriovenous fistula (AVF). **Methods:** This descriptive analytical study conducted at Department of Vascular Surgery, Combined Military Hospital Lahore from January 2014 to January 2015. All consecutive patients who underwent creation of AVF and had pre and post-operative Duplex scan to assess the arteries and veins of the upper limbs, were included. The AVFs were created at wrist, forearm and arm under local anaesthesia. The data was collected from radiology department and dialysis centre and correlated with the data from operation theatre. **Results:** A total of 127 patients (89 males and 38 females) were included in this study. Only 57.5% (n=73) patients showed functional maturation of their AVFs. Of these, only 14 (36.8%) were females. Arterial and venous diameters of more than 2.5 mm ($p=0.0001$ and 0.001 respectively), fistulae created at elbow ($p=0.001$), presence of on-table thrill ($p=0.003$), presence of on-table bruit ($p=0.001$), patients having their AVFs created before the start of dialysis ($p=0.0037$) and kidney transplant ($p=0.0042$) were all positive predictors for successful functional maturation of AVFs. Female gender was a negative predictor and was responsible for non-maturation (p -value 0.003). **Conclusion:** Maturation of AVFs is a complex process influenced by a lot of factors. Although in our study various parameters proved to have positive impact on AVFs maturation, large prospective multi-centre studies are needed to provide well defined outcome.

Keywords: Arteriovenous fistula, artery, vein, fistula maturation

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INTRODUCTION

The first autogenous arteriovenous (AVF) was created in 1966 by Camino for haemodialysis.¹ This was a brachiocephalic fistula. Later on, in 1979 Barnett *et al.* created first brachiobasilic fistula². Successful AVF significantly reduces both the morbidity as well as mortality of the patients who have end stage renal disease, and significantly improve their survival rate.^{3,4} Therefore there is an increasing trend to have a vascular access placement for haemodialysis (HD).^{5,6} Recent studies show that 20–50% of AVF do not get functionally matured for the purpose of hemodialysis.⁷⁻⁹ According to international guidelines of KDOQI (Kidney Disease Outcome Quality Initiative), native AVFs are the first choice for vascular access followed by arteriovenous grafts (AVG) both in pre dialysis as well as post dialysis patients.^{8,10,11} AVGs and central vein catheters have better primary patency rates compared to AVF^{8,12,13}, however native AVFs last longer. The use of arteries and veins of larger diameter in creation of AVFs, is found to be associated with high success rate in many series.^{14,15}

There is conflicting evidence about the impact of various demographic characteristics of the patients on the functional maturation of the native AVFs. Certain characteristics such as diabetes mellitus, female gender and thrombophilia are historically associated with higher failure rates.^{16,17} On the other hand according to

certain studies, diabetes and age show no effect on the functional maturation of the AVFs.¹⁸⁻²²

In light of conflicting results of association of various predictors with maturation of AVF, we decided to conduct a study in our population. The objective was to test the hypothesis that certain patients characteristics like gender, age, comorbid conditions effect the functional maturation of AVF. Also we wanted to assess the impact of certain operative and anatomical factors like vascular diameters, presence of palpable thrill, audible bruit, and anatomical site of fistula; on functional maturation. We also aimed to test the impact of certain haematological factors like platelet count and haemoglobin levels on functional maturation of arteriovenous fistulae.

MATERIAL AND METHODS

In this descriptive study, we selected all those consecutive patients who had their AVFs access created between January 2014 and January 2015 and they had a duplex scan before and after the creation of AVFs. With the help of duplex scan, we noted the preoperative diameters and patency of the arteries and superficial veins of upper limbs. The patency of the subclavian vein was also noted. Patients with stenosis of subclavian vein were excluded from the study.

Patients were regularly followed in dialysis unit. The data included patient's demographics, underlying medical conditions, any previous AVF

access, the anatomical site as well as type of current AVF, operative procedure details, time to become functionally mature, central vein catheter placement at time of fistula creation, transplanted kidney, haemoglobin levels, morbidity and mortality.

Patients were advised to undergo elective surgery for AVF once their renal Glomerular Filtration Rate Estimated (eGFR) was less than 15 ml/min. Patients who needed haemodialysis (HD) on urgent basis before the maturation of fistula, had a HD catheter inserted in their jugular or subclavian veins.

Non dominant upper limb was preferred and saved. Patients were given written instructions. They were advised not to apply blood pressure cuffs on that arm, no venous blood sampling and intravenous access on saved arm and active hand and elbow exercises. AVFs were created at wrist, forearm and arm in both male and female patients under local anaesthesia.

Patients were discharged home same day. Printed instruction cards about the home care of fistula were provided to all the patients on discharge. These instructions included advice such as avoiding the operated arm veins for any blood sampling, avoid taking blood pressure from that arm, not to wear clothes with constrictive sleeves, avoid heavy or tight jewellery, avoid circumferential dressings on wound and avoid sleeping on the operated arm. Patient was taught how to feel for the thrill. They were advised to contact us if they note any numbness in hand, discoloration of fingertips or coldness. All patients were taught active hand ball exercises before discharge from hospital.

The patients then had clinical and radiological assessment till the AVFs became functionally mature. A functionally mature AVF is defined as per Kidney Disease Outcome Quality Initiative (KDOQI) guidelines as one that can be easily cannulated and has at least six successful consecutive dialysis sessions. The association of various factors with functional maturation of AVFs was noted and compared with results of various international studies.

The data was analysed using SPSS-20. The numerical outcomes e.g. age was calculated as mean. Gender was recorded as frequency and percentage. Chi Square test was applied to assess the association of various parameters. The results were considered statistically significant if the *p*-value was found to be less than or equal to 0.05.

RESULTS

In this study, 127 patients were included. The minimum age of patients was 24 years and maximum age was 69 years, with mean age of 43.8 years. Out of 127 cases, 89 (70.1%) were male and 38 (29.9%) were female patients. Male to female ratio was 2.3:1 (Table-1). The minimum follow up was 6 months and maximum follow up was 16 months.

Out of 127 operated cases, 57.5% (n=73) became functionally mature. In these, 80.8% (n=59) were males and 19.1% (n=14) were females. The difference in gender is statistically significant (*p*=0.003) hence suggesting that female gender is associated with a poor functional maturation of the AVF. All these patients were hypertensive. Out of a total of 60 patients who had diabetes, only 37 became functionally mature. 25/60 (41.67%) diabetic patients became functionally mature when compared to 35/67 (52.24%) non diabetics. However the difference between these two groups was statistically insignificant (*p*=0.391).

From a total of 127 fistulae, 70 were created at the elbow, 41 at wrist and 16 in the forearm. 101 were created on the left and 26 on the right side. We found that in patients who had fistula created at elbow had a statistically significant maturation rate when compared to distal forearm fistulae (*p*-value of 0.001).

In terms of arterial diameter; 71 had a diameter of more than 2.5 mm, 37 had 2–2.5 mm and 18 had less than 2mm. The diameter of the anastomotic vein was more than 2.5 mm in 52, 2–2.5 mm in 20 and less than 2mm in 55 patients respectively. Hence arterial diameter of more than 2.5mm (*p*-value 0.0001) and venous diameter of more than 2.5 mm diameter (*p*-value 0.001) is associated with successful maturation of AVF.

Per-operatively, on-table palpable thrill was present in 82.6% (n=105) cases and on-table bruit was audible in 89.7% (n=114) patients. These two parameters were also noted to be statistically significant factors in the successful maturation of AVF. The *p*-value for on-table thrill was 0.003 and for on-table bruit was 0.001 respectively.

Platelet count was also noted in all patients; it was less than 100 10⁹/L in 31.5% (n=40), 100–300 10⁹/L/mm³ in 13.3% (n=29) and more than 300 10⁹/L in 45.6% (n=58) cases. Of the matured fistulae, 76.7% (n=56) patients had a platelet count of less than 100 10⁹/L. Furthermore, haemoglobin levels was less than 8g/dl in 37.7% (n=48), 8–10g/dl in 37.7% (n=48) and more than 10g/dl in 24.4% (n=31) patients. Of these, 63% (n=46) patients having functionally mature AVFs, the haemoglobin count was less than 8 g/dl.

The maturation rate was higher in patients who had AVFs created before the start of HD (73.9%, n=54) when compared with post HD group (20%, n=19). The result was significant with a *p*-value of 0.0037. Similarly, patients with transplanted kidney showed a maturation rate of 75% (n=3) which is also statistically significant (*p*=0.0042). Furthermore, maturation rate was higher in patients who had AVF created as a first procedure (72.6%, n=53) when compared to those patients who had a central vein catheter placed at the time of fistula procedure, however the results were not significant (*p*=0.214).

Causes of 54 failed fistulae included idiopathic (n=41), hypotension (n=8), injury (n=2) and thrombosis (n=3).

Table-1: Baseline demographics of the patients

Number of AVFs created (n)	127
Matured AVFs (Successful)	73 (57.5%)
Age (in years)	43.8 (24–69)
Male gender	89 (70.1%)
Female gender	38 (29.9%)
Diabetes mellitus	60 (47.2%)
Hypertension	106 (83.5%)
First procedure for AVF	88 (69.2%)
Already on Haemodialysis	37 (29.1%)
Presence of central venous catheter	62 (48.8%)
Kidney transplant	04 (3.1%)

DISCUSSION

AVFs provide the best conduit for vascular access placement in patients on haemodialysis.^{5,6} Initially the patency rates are better in arteriovenous grafts and central vein catheters but AVFs last longer.^{4,5} AVFs once created; need time to mature, before their use for HD.^{7,8} According to KDOQI guidelines, 60–80% patients in the world, have haemodialysis through AVFs.¹⁰ Although demand for AVFs creation is increasing, its failure rate still is high (20–50%).^{8,9} In our study functional failure rate was 42.5% (n=54). This percentage is similar to the failure rate being reported in already published literature.⁷⁻⁹

The maturation of AVF is a complex procedure and many factors influencing it are yet to be fully understood. Certain factors such as secondary procedures to maintain patency, hospital admissions, infection and thrombosis are unlikely to be related to a functionally mature AVF access.^{23,24} In our study, certain factors influenced maturation of AVF such as arterial and venous diameters ($p=0.0001$ and 0.001 respectively), female gender ($p=0.003$), kidney transplant ($p=0.0042$), patients having their AVFs created before the dialysis was started ($p=0.0037$), platelet count and haemoglobin levels. Functional non-maturation is high in female gender and high haemoglobin levels. On the contrary; a previous history of renal transplant, larger diameter of vessels used in AVF creation are associated with a successful maturation.

Conte *et al* followed up for 24 weeks a total of 31 diabetic patients who had AVFs created; and found that such patients had lower patency rates when compared with nondiabetics.¹⁶ Similarly Salmela *et al* reported that diabetes mellitus, female gender and thrombophilia were positive predictors for high failure rates of native AVFs.¹⁷ On the contrary, Sedlacek *et al* reported in his study of 195 patients that diabetes mellitus had no effect on AVF.¹⁸ Similar results were also reported by other studies who found no effect of both age and diabetes on AVF maturation rate.¹⁹

Conflicting results regarding association of female gender with functional non maturation had been reported.²⁰⁻²² In our study 25/60 (41.67%) diabetic patients became functionally mature when compared to 35/67 (52.24%) non diabetics. However the difference between these two groups was statistically insignificant ($p=0.391$). We also found that the female gender is associated with a poor functional maturation of the AVF ($p=0.003$).

The American Institute of Ultrasound in Medicine (AIUM) published their practice guidelines in 2010 with respect to diameter of anastomosing vessels. According to these guidelines, an arterial and venous diameter of less than 2 mm and 2.5 mm respectively are associated with high failure rates of native AVFs.²⁵ Sahasrabudhe *et al* also demonstrated that arterial and venous diameter of less than 2 mm is associated with higher failure rates with a p -value of 0.028 and 0.0001 respectively.²⁶ In our study, arterial and venous diameters of less than 2.5 mm each are associated with significantly high failure rates. Our results are statistically significant (p -values of 0.0001 and 0.001 respectively) and comparable to international literature and guidelines.

It is hypothesized that a lower haemoglobin and platelet levels have a better functional maturation.²⁷ Association of lower haemoglobin levels with better fistula maturation rate can be explained from production of Nitric oxide synthetase at newly formed conduit resulting in vasodilation and decreased cellular proliferation, platelet aggregation, and vasospasm.^{27,28} Khavanin *et al* in his study reported a higher maturation rate of AVFs in patients with haemoglobin levels of less than 8 g/dl.²⁹ In our study 63% (n=46) patients having functionally mature AVFs, the haemoglobin count was less than 8 g/dl. Salmela *et al* reported that thrombophilia was positive predictor for high failure rates of native AVFs.¹⁷ We also found that a platelet count of less than $100 \times 10^9/L$ is associated with a higher success rate. In our study 76.7% (n=56) of functionally matured fistula patients had a platelet count of less than $100 \times 10^9/L$. These results are comparable to international studies.

There were certain limitations in our study like the retrospective nature of collection of the date from the dialysis unit and operation theatre. It is worth mentioning that some of the fistulae which were considered non-mature (as per our study criteria) may still be patent on Doppler scan. Also the variation of the expertise of the dialysis staff should be kept in mind which may have influenced the maturation rate.

CONCLUSION

Fistula maturation rate is affected by many factors. Arterial and venous diameter of more than 2.5 mm, palpable thrill, audible bruit, AVFs created before the

start of haemodialysis, kidney transplant, low platelets and haemoglobin levels of less than 8 g/dl were all positive predictors for successful functional maturation of AVFs. This paper should serve as a guide for further studies, as well as an up-to-date review of published evidence. In light of conflicting evidence and lack of studies with large volume of patient, we recommend multicentre randomised control trials to see the impact of various factors in the maturation of arteriovenous fistulae.

AUTHOR'S CONTRIBUTION

MJ: Conception of idea, Manuscript writing, manuscript guarantor. RU: Manuscript editing, data analysis, reference checking.

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