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# FACTORS PREDICTIVE OF FAILURE OF ARTERIOVENOUS FISTULAS: OUR EXPERIENCE AND REVIEW OF LITERATURE

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## ABSTRACT

**Objective**: Evaluation of the patency rates of Arteriovenous Fistula with correlation of factors associated with failure of Arteriovenous Fistula. **Materials and Methods**: 150 successive patients (mean age 57years, range 19–76) on whom 156 primary Arteriovenous Fistulas were created during the period of 1 year between January 2009–December 2009 and who were followed up for 1 year. **Results**: The primary patency rate was 88% at 3 months. 7 distinct factors were significantly associated with both early and late failure of the fistula. Association of factors such as age>40years, uncontrolled diabetes, hypotension, smoking, pre Arteriovenous Fistula dialysis through central venous catheters, hypercholesterolemia and poor quality of artery and vein resulted in higher failure rates. **Conclusion**: The major determinants for a successfully created Arteriovenous Fistula were creation of the fistula before the start of dialysis and good quality of both, the artery and the vein. This argues in favour of timely creation of such fistulas in patients with end-stage renal disease, avoidance of hypotension, strict glycemic control and accurate preoperative Doppler examination to establish the quality of the vessels.

**Keywords**: AVF, Patency Rates, Prognostic Factor

## INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem with a stressful life for the patient and the family. In the year 2000, in the United States (US) alone, about 30 million people were diagnosed with CKD. It was estimated that by 2010, six million people worldwide would need renal replacement therapy (RRT) costing 28 billion dollar [(1)]. Most of the patients with CKD progress to End Stage Renal Disease (ESRD) and are dependent on lifelong RRT until kidney transplantation is possible. Its impact in developing countries like India is well documented as studies based in Delhi revealed a prevalence of CKD (serum creatinine more than 1.8 mg %) at 7852 pmp and studies from Bhopal, revealed an incidence of 151 pmp suffering from ESRD [(2)]. A further increase in the number of patients on dialysis is expected as a result of longevity of population. The number of CKD patients requiring haemodialysis is progressively increasing over the years in other countries also.

The most common and the best site for access for haemodialysis is through the creation of a distal autogenous ArterioVenous fistula (AVF) **[(3)]**. Originally described by Brescia et al, it allows for easy repeated access to the circulation using the native vessels without the need for prosthetic material once the AVF is created **[(4)]**. Its advantages are easiness to cannulate with good flow rates and

its limited restrictions of AVF arm mobility [5]. Yet, various postoperative complications tend to occur in the lifetime of an AVF. Failure due to thrombosis and local infection being the most common as per many studies [6,7]. The major predisposing factor for thrombosis of the fistula is stenosis, which occurs as a result of myointimal hyperplasia at the anastomotic site, accounting for 80% to 85% of thromboses [7]. Thrombosis also occurs due to dissection and haematoma during punctures, excessive compression of the fistula after dialysis, hypotension, hypovolaemia and hypercoagulable states. The primary reported failure rate is 12% to 24% and rises upto 50-70% after 6months [8,9,10]. Variations in the failure rates by different groups indicate the use of different criteria for selection of patients [11].

This study was undertaken to study the various factors and their contribution in the AVF failure.

## MATERIAL AND METHODS

Patients with Primary arteriovenous fistula created for haemodialysis between January 2009 and December 2009 were followed up for 1 year. Total of 156 such fistulas were created in 150 CKD patients at M.S. Ramaiah Medical College and Hospital, Bangalore, India. There were 108 male and 42 female patients with a mean age of 57years (range 19 to 76). The most frequent co morbid factors included hypertension (*n* = 128, 85%), diabetes mellitus (*n* = 110, 73%), smoking (*n* = 75, 50%), Hypotension (n=21, 14%) obesity (n=56) and dyslipidemia (*n* = 56) and bronchial asthma (n=26) (Table I).

**Preoperative procedure:** Patients needing haemodialysis were referred from the Department of Nephrology, M. S. Ramaiah Medical College and Hospital, Bangalore, India for AVF creation. Consent was obtained for the procedure and anaesthesia with the advantages, disadvantages, risks involved in the procedure, complications of the procedure including the failure, the need for repeated AVF creation in case of failure or usage of graft in dominant or in nondominant hand, the need for Kidney Transplantations as and when required and the associated morbidity and mortality being explained in patient's language. Non-dominant hand was examined mostly to assess the cephalic vein on the radial side of the wrist for its visibility and sufficiency of outflow. The patency of the palmar arch and its contributes were also tested by Allen's test (by occlusion of the ulnar and radial arteries). Duplex Scan assessment of the limb vessels was sought for certain cases (n=42) where the size of the vessel on physical examination was doubtful. A patent radial and ulnar artery and a venous diameter of 2.5 mm during proximal venous occlusion were regarded as sufficient.

**Surgical procedure:** Over 99% of the cases were operated under Local anaesthesia with a mixture of 2% Xylocaine and 0.25% Bupivacaine (5:1 ratio) amounting to 5-10ml per AVF. Brachial plexus block or General anaesthesia were used in highly uncooperative patients (n=3). 70 radiocephalic and 86 brachiocephalic AVFs were created, mostly on the nondominant hand (70%, 75%respectively)(Table - II). Through a longitudinal incision on the radial side of the wrist, the cephalic vein and radial artery were dissected and secured. Through a transcubital incision brachial artery and cephalic veins were taken into control for brachiocephalic AVF. The cephalic vein was transected, dilated and patency maintained with intermittent flushing using heparinised saline in all cases. None of the patients experienced spasm of the vein during the procedure. Intraoperative heparin bolus 2000–5000 IU was used intravenously in all cases. An arteriotomy was made on the radial artery or brachial artery and an end to side AVF anastomosis was created with 6/0 or 7/0 polypropylene running sutures. The mean operating time was 35 minutes.

The patency of anastomosis was assessed perioperatively by palpation, auscultation, and by hand-held Doppler. The fistula was allowed to mature for a period of about 6 weeks, by which time the cephalic vein would be mature enough to be accessed for haemodialysis and sustain an adequate blood flow. Personal outpatient, inpatient, telephonic interviews were performed monthly to know the status of the fistula. All the AVFs were examined at regular interval of 1 month for the following outcomes : complete failure (either early or late failure, including insufficient maturation at 6 weeks), inability to use access site for dialysis due to poor flow, patient's death (either with a functioning or a non-functioning fistula), AVF complications and normally functioning fistula.

Various preoperative, operative, and postoperative variables were analyzed and correlated with the AVF failures (Table - III). Variables included were age, sex, smoking history (non-smoker or smoker), preoperative serum creatinine (mg/dL), serum cholesterol concentration (normocholesterolaemia or hypercholesterolemia), diabetes mellitus (nondiabetic or diabetic), preAVF dialysis (patients who had not been dialysed at the time of creation of the fistula or patients in whom dialysis began before the operation), side of the fistula (left or right), calibre of the artery and vein.

## RESULTS

Most of the failures occurred during the first three months after surgery. One of the 156 primary fistulas occluded within the first 24 hours. 10 fistulas had weak thrill, but only 6 of them failed by 6 weeks. 11 fistulas which were patent at 6 weeks, did not develop sufficiently to be used for access for haemodialysis, and hence were classified as failures. The primary patency rate at 3 months was 88%. In addition to the 156 primary procedures, 14 revisions to the primary repair were made to salvage the fistula and consisted of 12 thrombectomies using Fogarty balloon catheter no. 3 introduced through a venotomy, 1 repair of a pseudoaneurysm and 1 thrombectomy plus vein patch revision. In 11 patients, the salvage procedure took place on the same day as the primary operation (not intraoperative revision of the anastomosis). The other revisions were made at a mean of 7 months after the first operation. 10 revisions were successful. Completely newer anastomosis at a site more proximal than the previous were performed without a vein patch in 24 cases. 11 patients died during the 2-year follow-up, all of them with a functioning fistula at the time of death. The causes of death were cardiac ($n$ = 8), pulmonary ($n$ = 2) or unknown ($n$ = 1). There were no deaths directly related to the surgery.

**Prognostic factors**

The following factors were compared between the failure and functioning AVF groups: age, sex, side, poorly controlled diabetic status (HbA1c>8), hypertension and hypotension, smoking, preAVF dialysis, moderate or poor quality of the artery, moderate or poor quality of the vein, S.Creatinine and S.cholesterol levels.

The first group includes failures within 3 months (early failure, $n$ = 18) and the second group includes the failures at 3 months or later (late failure, $n$ = 6). (Table - IV)

Significant predictors for early failure were: age >40yrs, uncontrolled diabetes, hypotension, smoking, start of dialysis before formation of the fistula, moderate or poor quality of the artery and vein and high S. creatinine.

Significant predictors for late failure were: age, smoking, moderate or poor quality of the vein and hypercholesterolemia.

## DISCUSSION

Early AVF failure is known to occur in up to 60% of newly created AVFs. Most of them are due to thrombosis or marked in-flow stenosis, leading to non-maturation of AVF.[12,13] Several studies

predict several modifiable variables during initial surgery which have been linked to greater AVF maturation, including use of high-dose intraoperative heparin, utilization of large-diameter veins, and a mean arterial pressure of 85mmHg or greater.[14]

Apart from clinical examination, Duplex ultrasound of the AVF is a useful armamentarium in the assessment for AVF. A vein diameter ≥4mm or the blood flow rate >500ml/min are highly lucrative with more than 84% of fistulas maturing within four months of AVF creation. According to a study if both the criteria are met, a 95% likelihood of maturation of the fistula for dialysis is observed, whereas if neither criterion is met, only 33% of AVF successfully mature [15] .

The venous stenosis and the presence of multiple accessory veins are the other contributors for early failure [16,17]. In 78% of non-maturing AVFs, Venous stenosis was mostly adjacent to the anastomotic area. In a documented study, 88% of AVFs matured following the Percutaneous ligation of the accessory veins has been documented [18].The accepted standard for the minimal vein diameter associated with successful AVF is 2–2.5mm. at vein diameter <2mm only 16% of AVFs are patent at 3 months, compared to 76% patent at diameter above 2mm [19,20] . Distal AVFs are likely to fail when the arterial diameter is <1.6mm [21]. A study by Silva et al [19] demonstrated a 36% early failure rate compared with 8.3% failure rate after implementation of standard preoperative duplex. In addition, focal atherosclerotic areas can be identified by duplex examination and a percutaneous transluminal angioplasty or a proximal anastomosis can be performed.

Therefore pre-operative vein mapping increases the rate of successful AVF creation. Further, it is advisable to have a central vein imaging using venography or magnetic resonance imaging (MRI)/MR angiography (MRA) in patients with a previous history of Central venous catheter use to look for proximal occlusion.

Perioperative identification of risk factors for failure of AVF is important in view of the large proportion of failures. Complications arising out of the procedure cause significant morbidity and are a major contributor to the cost of long-term haemodialysis [22].

This study shows that seven clinical variables were significant predictors for failure. Older patients have higher failure rates due to collagen degeneration and deposits of plaques in all the vessels [23,24]. Such vascular systems are prone for more vortices and hence high thrombus rates. Similar observations are seen in other vascular reconstruction or anastomosis studies. Uncontrolled diabetics [25] have both acute and chronic prolonged impact on the vessels in the form of microvasculopathy, neuropathy as well as deposition of advanced glycation products in the neurons, vasovasorum and the intima of the microvessels. The higher failure rates in them are due to soft tissue occlusion at the anastomosis, either due to the plaques or thrombosis.

Fistula constructed before the start of dialysis had significantly better patency rates than patients who were already on dialysis at the time of creating AVF. In the latter group of patients, dialysis was often started urgently—for example, after cardiovascular/pulmonary events. In addition, these patients were more likely to have indwelling central venous catheters in subclavian veins which may also have influenced shunt patency, as well as multiple punctures of lower arm veins during their stay in intensive care units [26]. Previous studies have shown that late stenosis or occlusion of the subclavian vein can affect up to 50% of patients who have had indwelling central venous catheters [27,28].This group might be a cohort of patients with poor quality vessels who had periods of hypotension leading to failure, which often happens in convalescence period.

Highly significant predictors of failure in our study were moderate or poor quality of the artery and the cephalic vein. A poor quality vein is more

prone to occlude when its lumen is narrowed or flow is sluggish for reasons unknown. The patency of the fistula during the first month after surgery is particularly affected by these physiological factors [21,29]. Quality of the vein has also been identified as a significant predictor of late failure and is explained by the occurrence of venous neointimal hyperplasia leading to stenosis at the anastomotic site [6,23].

Furthermore, patients, residents, and nursing personnel are instructed not to puncture or cannulate a cephalic vein that might be needed for a future AVF, because this often leads to thrombosis and fibrosis of the vein.

Thrombosis is a cause of early AVF failure. Several studies have sought to determine whether common cardiovascular, antiplatelet, and lipid-lowering agents are associated with greater AVF maturation; however, none have been found to have a beneficial effect on primary AVF failure [30,31].

Overall, percutaneous and surgical techniques remain the only proven methods to promote AVF maturation in a non-maturing AVF [32,33].

## CONCLUSION

In conclusion, we consider creating a AVF at an early stage, preferably before dialysis has started. Creation of AVF atleast 6 months in advance to the predicted time of dialysis may allow sufficient time for the AVF to mature and for tackling any complications that might arise out of it. A strict glycemic control, prevention of hypotension and hypercholestermia, usage of accurate duplex venous mapping, adhering to strict guidelines for AVF creation are the most important factors influencing the patency rate of the fistula.


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| TABLE I – Patient Characteristics | |
|---|---|
| Factors | No of patients n=150(%) |
| **Age** | |
| >40 years | 112(74) |
| <40 years | 38(26) |
| **Sex** | |
| Male | 108(72) |
| Female | 42(28) |
| **Diabetic** | 110(73) |
| Controlled (HbA1c<8) | 87 |
| Uncontrolled(HbA1c>8) | 23 |
| **Hypertension** | 128(85) |
| Controlled | 87 |
| uncontrolled | 41 |
| **Hypotension** | 21(14) |
| **Smoking** | 75(50) |
| **Obesity** | 56(37) |
| **Bronchial asthma** | 26(17) |
| **PreAVF dialysis central line catheters** | 34(22) |
| IJV | 26(76) |
| Femoral vein | 8(44) |
| **No of Central line catheters insertions** | |
| Once | 23(67) |
| >once | 11(33) |
| **S.creatinine** | |
| >7mg/dl | 93(62) |
| <7mg/dl | 57(38) |
| **S.cholesterol** | |
| >200mg/dl | 67(44) |
| <200mg/dl | 83(56) |

| Table – II AVF characteristics | |
|---|---|
| **AVF (n=156)** | 156(%) |
| **Primary AVF** | |
| **Local Anesthesia** | 153(98) |
| **Radio cephalic** | 70(47) |
| Left | 53(70) |
| Right | 17(30) |
| **Brachiocephalic** | 86(53) |
| Left | 66(76) |
| Right | 20(24) |
| **Complications** | |
| **Failures** | 24(15%) |
| <24hrs | 1(<1%) |
| At 6weeks | 6(3.8%) |
| At 3 months | 11(7%) |

| | |
|---|---|
| At 1year | 6(3.8%) |
| **Thrombosis** | 12(7.6%) |
| **Pseudoaneurysm** | 1(<1%) |
| **Deaths** | 11(7%) |
| | |
| **Secondary AVF(all Br-C AVF)** | 24(15%) |
| Left | 20(83) |
| Right | 4(17) |

**Table III– Significant factors in AVF failures**

| Factors | AVF FAILURE(n=24) |
|---|---|
| Age>40yrs:<40yrs | 22:2 |
| Sex: M:F | 13:12 |
| Diabetes – controlled : uncontrolled | 1:23 |
| Hypotension | 21 |
| Smoking | 20 |
| Obesity - | 11 |
| Bronchial asthma | 3 |
| PreAVF dialysis | 22 |
| Moderate to poor quality of vein | 23 |
| Moderate to poor quality of artery | 16 |
| Side left:right | 20:4 |
| S.Creatinine >7:<7 | 24:0 |
| S.cholesterol>200:<200 | 14:10 |

**Table IV – Independent factors in early and late AVF failures.**

| Factors | Early failure(<3months)(n=18) | Late failure(>3months)(n=6) |
|---|---|---|
| Age >40 | **16** | **6** |
| Uncontrolled diabetes | **18** | 5 |
| Hypotension | **17** | 4 |
| Smoking | **16** | **6** |
| Predialysis AVF | **17** | 5 |
| Moderate to poor quality of vein | **15** | **6** |
| Moderate to poor quality of artery | **13** | 3 |
| S.creatinine >7 | 10 | 2 |
| S.cholesterol>200 | 8 | **6** |