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Mr. Bernard O'Brien

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Prospective long-term study of patency and outcomes of 505 arteriovenous fistulas in patients with chronic renal failure: Authors experience and review of literature

Parag Sahasrabudhe, Tushar Dighe¹, Nikhil Panse², Shraddha Deshpande, Amit Jadhav, Sheetal Londhe

Departments of Plastic Surgery and ¹Nephrology Deenanath Mangeshkar Hospital, ²Department of Plastic Surgery, Sassoon Hospitals, Pune, Maharashtra, India

Address for correspondence: Prof. Parag Sahasrabudhe, Plot 82, Lane 2, Natraj Society, Karve Nagar, Pune - 411 052, Maharashtra, India.
E-mail: drparags@gmail.com

ABSTRACT

Background: This study describes our experience of arteriovenous fistula (AVF) creation as vascular access for haemodialysis. **Materials and Methods:** This study has been carried out in our hospital from January 2004 to December 2012. A total of 505 AVFs were created in 443 patients. Maximum follow-up was 8 years, and minimum was 6 months. **Observations and Results:** In this study of 505 cases of AVFs, primary patency rates by Kaplan — Meier analysis showed 78.81% patency of fistulas at the end of 1 year and patency dropped to 14.81% at the end of 5 years. Our primary failure rate was 21.2%. Basilic vein was used in 26.35% cases, cephalic vein in 63.5%, and antecubital vein in 9.75% cases. On table, bruit was present in 459 (90.9%) and thrill in 451 (89.3%) cases. During dialysis, flow rate >250 ml/min was obtained in 150 (29.9%) cases. In complications, 2 (0.4%) patients developed distal oedema, 33 (6.5%) developed steal phenomenon. **Conclusions:** Presence of on table thrill and bruit are indicators of successful AVF. If vein diameter is <2 mm, chances of AVF failure are high. Flow rates in patients with vein diam. >2 mm were significantly higher as compared with patients with vein diam. <2 mm ($P < 0.001$). Flow rates are higher in non-diabetic patients as compared to diabetic patients ($P < 0.001$). Average blood urea and serum creatinine values are significantly lesser in patients undergoing dialysis through successful fistulas as compared to patients with failed fistulas. Correspondingly, incidence of deaths is significantly lesser in patients with successful fistulas. During proximal side-to-side fistula between antecubital/basilic vein and brachial artery, dilating of the first valve toward wrist helps to develop distal veins in the forearm by retrograde flow. This technique avoids requirement of superficialization of basilic vein in the arm.

KEY WORDS

Arteriovenous fistula; chronic kidney disease; haemodialysis; vascular access

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INTRODUCTION

End stage renal disease (ESRD) patients depend on lifelong renal replacement therapy (dialysis or renal transplant) to sustain their lives. After Scribner's shunt in 1960, Brescia *et al.* described the creation of subcutaneous arteriovenous fistula (AVF) constructed

between the radial artery and an adjacent vein in 1966. Cimino fistulas are currently accepted as the best mode of vascular access for haemodialysis (HD).^[1]

This is single-centre, single surgeon observational study comparing pre-operative vein and artery diameters, presence of bruit and thrill on operation table, flow rates, site of the fistula, associated comorbidities for postoperative outcome, and duration of patency by Kaplan–Meier analysis.

MATERIALS AND METHODS

This observation study was carried out in our institute in patients who underwent surgical AVF creation between January 2004 and December 2012.

Patients were advised surgery for AVF when their Modified Diet for Renal Disease estimated Glomerular Filtration Rate^[2] was below 15 ml/min. HD catheter was inserted only in cases who presented late and required HD before maturation of fistula.

History of diabetes mellitus, anticoagulant therapy for coagulation disorder, cardiovascular disease, heart valve disease or prosthesis, previous dialysis access, previous central venous, or peripheral catheter were noted. Physical exam of the arterial system (peripheral pulses, Allen test, and bilateral upper extremity blood pressure) was performed along with physical exam of the venous system (tourniquet venous palpation with vein mapping, examination for previous central or peripheral venous catheters, etc.). Dominance of hand was examined, and preference was given to non-dominant hand for creation of vascular access.

Pre-operative colour Doppler ultrasound (duplex) of upper limb veins and arteries was done in selected patients to look for size and patency. It was done in patients with inadequate clinical examination findings like in cases with obesity, absent or feeble pulses, multiple previous access surgeries, indwelling dialysis catheter on the same side, and history suggestive of thrombophlebitis.

Subclavian vein catheterization was avoided for temporary access in all patients due to the risk of central venous stenosis, which compromises entire ipsilateral arm for vascular access. Arm veins suitable for vascular access placement were preserved, and patients and dialysis staff were instructed not to prick selected arm.

In cases where there was extensive venous thrombosis in a particular limb different limb was selected for fistula.

During this period, AVF was created in 756 patients; but, we could follow-up only 443 patients. Follow-up was obtained in collaboration with dialysis unit staff by telephonic calls and personal visits to the patients. The data extracted from hospital records included patient demographics, comorbidities, details of previous access, location and type of AVF, operative details, patency, morbidity, and mortality.

A total of 505 AVFs were placed in 443 patients as 62 patients required repeat procedure due to failure of the previous fistula. Of the 443 patients 187 (42.2%) patients have died. Average mean survival in dead patients was 1.59 (standard deviation \pm 1.07) years. However, before death they were regularly followed-up on dialysis. Maximum follow-up was 8 years, and minimum follow-up was 6 months.

Surgical technique

All patients were admitted on the day of surgery. All cases were done under local anaesthesia using 10 cc 2% Xylocaine by single surgeon under loupe magnification using microvascular instruments. “S” shape 2.5-3 cm long incision was used. Vein and artery were mobilized adequately. Arteriotomy size in all cases was 6-7 mm. In cases wherein there was extensive atherosclerosis involving the artery best possible segment of exposed artery was selected for anastomosis. Diameter of the vessels were noted using calipre. Anastomosis was done by taking continuous running suture using 7-0 polypropylene or 8-0 ethilon depending upon vessel wall thickness. For distal and mid forearm fistula, end of the cephalic vein to side of radial artery anastomosis was performed [Figure 1].

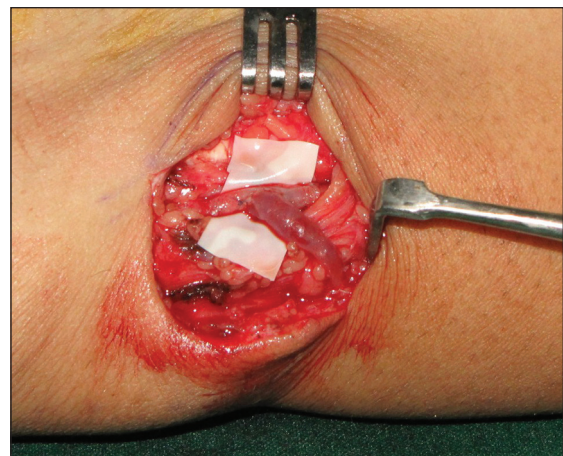


Figure 1: Distal end to side radio-cephalic fistula

For proximal fistula, we performed side — to-side anastomosis between antecubital or basilic vein and brachial artery [Figure 2]. Before anastomosis was completed, we dilated distal vein using venous dilator to break the first valve toward the wrist end to allow retrograde flow into forearm veins [Figures 3 and 4]. This allows forearm veins to develop [Figure 5] which can now be easily assessed for cannulation. This technique avoided requirement of basilic vein transposition in the arm thus avoiding long incisions in arm and reducing morbidity of the procedure. In cases where antecubital vein was used, both cephalic and basilic veins got arterialized and could be cannulated. Skin closure was done with 3-0 ethilon in a single layer. Non-compressive dressing was given. Bruit was heard, and thrill was felt on operation table end of dressing. In cases where bruit and/ or thrill was absent, but there was good venous filling, we started anticoagulation with low molecular weight heparin subcutaneously for 3-5 days, (doses according to creatinine clearance), along with tablet aspirin 75 mg once a day for 3-5 days.

Patient was discharged on the same day or next day. Relevant instructions about care of operated side arm were given to the patients and their relatives. They were told to avoid arm vein blood collection on the operated side, avoid blood pressure cuffs, not to use tight clothing or jewellery, and avoid the prolong pressure on operated arm. Written instructions about how to feel for the thrill were given, and patients were asked to report any coldness, numbness, ulcers, discoloration at fingertips. Handball exercises were taught to patients before discharge.

Fistula maturation and its cannulation for use of dialysis were decided by nephrologists based on visible enlarged vein and well felt thrill, which required 4-6 weeks after construction. We considered 250 ml/min as a flow rate obtained on HD machine during HD, which was sustained for a minimum of 3 h without recirculation as acceptable flow during HD.

We followed the National Kidney Foundation/Disease Outcome Quality Initiative (NKF-K/DOQI) Vascular



Figure 2: Proximal side-to-side brachiobasilic fistula

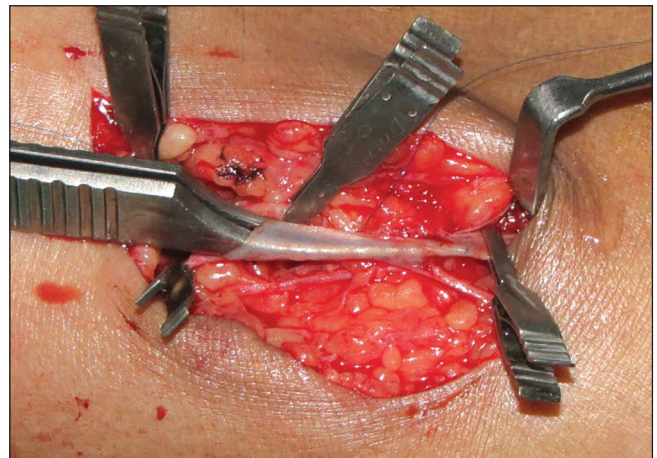


Figure 3: Vessel dilator passed through venotomy to dilate first valve towards wrist end

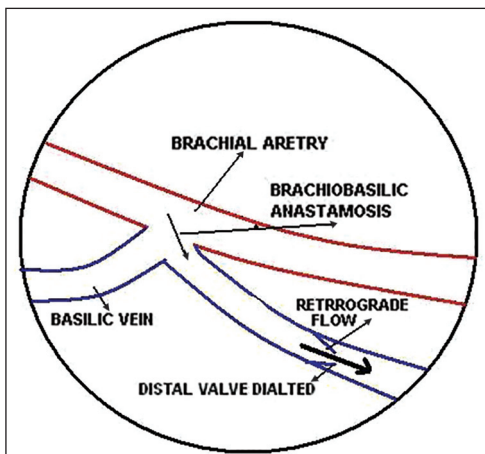


Figure 4: Diagrammatic representation of retrograde flow across dilated valve

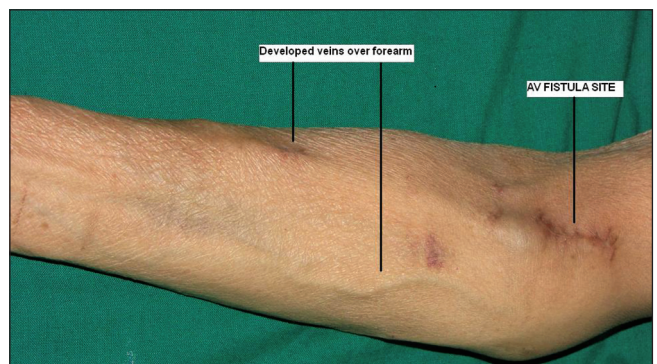


Figure 5: Well-developed forearm veins in proximal arteriovenous fistula

Access Clinical Practice Guidelines 2000.^[3] However, few guidelines could not be followed, for example, early reference, timing of access placement (1-4 months before anticipated HD), Doppler ultrasound in all cases and early intervention in failing fistulas. Above limitations were due to poor patient compliance and affordability in Indian scenario. In none of our patients and interventional or salvage procedure was done. Hence, our patency statistics is of 100% primary patency rates.

The data were analysed using IBM SPSS (statistical package for social sciences) version 20. Student's *t*-test was used to find the differences. Paired *t*-test is not appropriate in our series as it is for pre- and post-comparison. Chi-square test was used to look at the association.

Regression was used to find predictors or risk factors.

RESULTS

In the present series of 505 fistulas (baseline characteristics [Table 1]), 185 (36.6%) were proximal fistulas, 310 (61.4%) were distal fistulas, and 10 (2%) were mid forearm fistulas. Preference was given to non-dominant hand. However- in cases where non-dominant hand was pricked repeatedly or had intracath *in situ* dominant hand was selected. 135 fistulas were done on the right side, and 370 were done on the left side. Basilic vein was used in 133 cases; cephalic vein was used in 321 cases, and antecubital vein was used in 49 cases. Vena comitans and dorsal hand vein were used in 1 case each for anastomosis. Vein anastomosis was done with radial artery in 322 cases and brachial artery in 183 cases. End (vein) to the side (artery) anastomosis was done in 303 cases. Side (vein) to the side (artery) anastomosis was done in 202 cases. Bruit was heard in 459 (90.9%) cases and thrill was felt in 451 (89.3%) cases on the operation table. Both bruit and thrill were present in 448 cases (88.71%).

During HD, flow rate >250 ml/min was obtained in 150 (29.9%) cases. It was sufficient to perform successful HD in these patients as it sustained for a period of at least 3 h during 4 h of HD. The flow rate >250 ml/min was not flow across fistula, as measured by radiological or any other means, but actual flow rate obtained on blood pump during HD.

In complications, 2 (0.4%) patients developed distal oedema, 33 (6.5%) developed steal phenomenon. One patient developed aneurysm. No patients had operative site infection and major bleeding requiring intervention during the follow-up period.

Logistic regression for success and failure

Using logistic regression [Table 2] with success and immediate failure as the dependent variables it was found that:

1. Failure is 5.4 times more among subjects with no bruit heard on operation table ($P < 0.001$) as compared to those with bruit.
2. Similarly, failure is 6.7 times more among subjects with no thrill felt on operation table ($P < 0.001$) as compared to those with thrill.
3. Although risk of failure is more among subjects with art <2 mm as compared to subjects with art >2 mm, it is not statistically significant ($P = 0.114$) in our series.

Table 1: Baseline characteristics

| Senario | Number |
|---------------------------|-----------------|
| Number of AVFs created | 505 |
| Number of patients | 443 |
| Number of successful AVFs | 398 (78.81%) |
| Age | 54.58 (±14.092) |
| Gender | |
| Male | 279 (62.98%) |
| Female | 164 (37.02%) |
| Diabetes | 216 (48.76%) |
| Atherosclerosis | 18 (4.1%) |
| Coagulopathy | 4 (0.9%) |

AVFs: Arteriovenous fistula

Table 2: Logistic regression table

| Variables in the equation | SE | OR | 95% CI for OR | | P value |
|---------------------------|-------|--------|---------------|-------------|---------|
| | | | Lower limit | Upper limit | |
| Bruit | | | | | |
| Yes | | 1 | | | |
| No | 0.320 | 5.464 | 0.098 | 0.342 | 0.001 |
| Thrill | | | | | |
| Yes | | 1 | | | |
| No | 0.303 | 6.6667 | 0.082 | 0.273 | 0.001 |
| Vein <2 mm | | | | | |
| Yes | | 1 | | | |
| No | 0.463 | 5.366 | 2.283 | 12.613 | 0.001 |
| Art <2 mm | | | | | |
| Yes | | 1 | | | |
| No | 0.528 | 2.305 | 0.818 | 6.492 | 0.114 |
| Site of fistula | | | | | |
| Proximal | 0.230 | 1.207 | 0.769 | 1.895 | 0.413 |
| Distal | 1.070 | 0.460 | 0.056 | 3.747 | 0.468 |

SE: Standard error; OR: Odds ratio; CI: Confidence interval

4. Failure is 5.4 times more among patients with vein <2 mm as compared to those with vein >2 mm ($P < 0.001$).
5. Risk of failure was observed to be higher among patients with distal fistula (22.6%) than proximal fistula (19.5%), although not statistically significant ($P = 0.413$).

Of 505 fistulas, 449 patients had both presence of bruit and thrill at end of surgery. The failure rate was 16% ($n = 75$) in such cases at end of 12 weeks. When bruit was present and thrill was absent at the end of the surgery ($n = 11$) the failure rate was 63.6% ($n = 7$). Only 3 patients had a palpable thrill without an audible bruit. Of these three, one fistula failed (33%). When both bruit and thrill were absent at the end of the surgery ($n = 42$) the failure rate was as high as 57% ($n = 24$).

| Scenario | Number of patients | Failures (%) |
|-----------------|--------------------|--------------|
| Bruit+, thrill+ | 449 | 75 (16) |
| Bruit+, thrill- | 011 | 07 (63) |
| Bruit-, thrill+ | 003 | 01 (33) |
| Bruit-, thrill- | 042 | 24 (57) |

Flow rates

Patients with vein diam. >2 mm had higher flow rates (>250 ml/min) as compared with patients with vein diam. <2 mm. The difference was found to be statistically significant ($P = 0.05$).

Diabetes

1. Flow rates across fistula were found significantly higher in non-diabetic patients ($P < 0.001$) compared to diabetics.

Biochemistry

The average blood urea and serum creatinine values in patients with successful fistulas were significantly ($P < 0.001$) lower as compared with failures [Table 3].

Site

1. In proximal fistulas, bruit was heard and thrill was felt in 95.1% cases on operation table. In distal

fistulas, bruit was heard in 88.1% and thrill was felt in 85.5% on operation table. Hence, success rate was more (80.5%) in proximal than in distal (77.4%) fistulas. This difference was however not statistically significant.

2. Of 310 cases of proximal fistulas basilic vein transposition for proximal fistula was done in 1 case only. In rest of the patient's veins over forearm developed within 6 weeks due to retrograde flow across the anastomosis. Distal oedema developed in 2 (0.4%) patients post-operatively.

Mortality

The incidence of deaths was much higher in cases of primary fistula failure (60.7%) as compared with successful fistulas (30.7%). This value had statistical significance ($P < 0.001$).

Patency ($n = 505$) [Table 4]

1. Patency more than 1 year was found in 398 cases (78.81%).
2. Patency more than 2 years was seen in 213 cases (53.63) and
3. Patency more than 3 years was seen in 93 cases (34.39%).
4. Patency more than 4 years was seen in 36 cases (19.05%).
5. Patency of more than 5 years was seen in 21 patients (14.81%).

The data when used for Kaplan — Meier analysis showed the following curve as given in Graph 1.

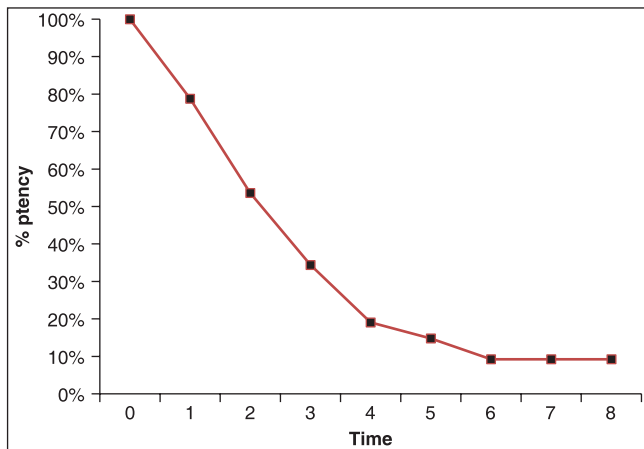
Table 3: Blood urea and serum creatinine values

| Biochemistry | Mean | SD | SEM |
|--------------------------|--------|--------|--------|
| Blood urea level (mg/dl) | | | |
| Successful fistulas | 87.67 | 38.778 | 2.03 |
| Failed fistulas | 112.39 | 38.888 | 4.077 |
| Serum creatinine (mg/dl) | | | |
| Successful fistulas | 6.022 | 2.0449 | 0.1067 |
| Failed fistulas | 8.608 | 1.7728 | 0.1858 |

SD: Standard deviation; SEM: Standard error mean

Table 4: Kaplan–Meier analysis for patency

| Time (in years) | Number of fistulas | Failures | Dropouts | Patency | Probability of patency | Conditional probability of patency |
|-----------------|--------------------|----------|----------|---------|------------------------|------------------------------------|
| 0 | 505 | 0 | | 505 | 1 | 1 |
| 1 | 505 | 107 | | 398 | 0.78812 | 0.78812 |
| 2 | 313 | 100 | 85 | 213 | 0.68051 | 0.53632 |
| 3 | 145 | 52 | 68 | 93 | 0.64138 | 0.34399 |
| 4 | 65 | 29 | 28 | 36 | 0.55385 | 0.19052 |
| 5 | 27 | 6 | 9 | 21 | 0.77778 | 0.14818 |



Graph 1: Graph showing Kaplan–Meier analysis for patency

DISCUSSION

Successful HD depends on creation and maintenance of adequate vascular access. Due to general population aging, median age at onset of ESRD has been progressively increased over last few decades. More than 20% of people have diabetes as a cause of ESRD and average age is 54.5 years.^[4] In our study of 505 cases, average age of presentation was 54.5 years and 48.76% patients had diabetes as a cause of ESRD.

Patients who receive dialysis across a functional AVF have lower complication rates and longer duration of event-free patency than patients with catheter access^[5-8] and arteriovenous grafts (AVGs).^[6,9] Thus, construction of a native AVF on arm or forearm is considered a good practice over prosthetic grafts and central venous catheters. There were no AVGs created in the present series. There is vast data proving that native AVFs are superior to grafts as a form of vascular access for dialysis.^[6] It has been demonstrated that early referral to nephrologists and good collaboration with microvascular surgeon reduce the need for temporary dialysis access for first dialysis and increase the rate of successful AVF placement.^[10] However, central venous catheters are primary method of choice for temporary access in which there is urgent need for HD and no other vascular access is available or has failed.^[8] However, these devices suffer from several complicating factors as infection, thrombosis, venous stenosis, and damage to proximal vessels.^[11] We performed AVF in all our chronic kidney disease patients as first choice of vascular access.

The most common operative procedure was the creation of the distal radio-cephalic fistula, initially described by

Brescia *et al.* in 1966.^[1] This operation is still considered to be the gold standard for vascular access for HD^[12] and it accounted for 310 (61.4%) of our operative procedures. High radio-cephalic (mid forearm) and brachial-basilic AVFs were reserved for patients with previously failed Brescia-Cimino AVFs or where patent adequate size vessels at wrist level were not available for anastomosis. The outcomes of the classic Brescia-Cimino operation were accompanied by acceptable rates of morbidity.^[13,14] In our analysis of 310 (61.4%) distal fistulas, 240 (77.42%) were successful. 2 patients developed distal oedema (0.65%) and 16 patients developed steal phenomenon (5.16%). Mortality among cases with radio-cephalic fistulas was 114 (36.77%).

Most large-volume centres report 15-30% primary failure rates for distal radio-cephalic AVF.^[13,14] The reported incidence of primary failure in the medical literature varies from 9%^[15] to 40%^[16] and our results with 21.2% primary failures were comparable. Primary Failure is defined as Absence of well-developed veins accessible for dialysis at 12 weeks after fistula surgery.^[16] The NKF/DOQI work Group did not recommend the use of primary failure as an index of quality because it would discourage attempts at AVF construction in patients with complex vascular anatomy.^[2]

American Institute of Ultrasound in Medicine Practice Guideline 2011^[17,18] states that arterial diameter <2 mm and venous diameter <2.5 mm were associated with high failure rate. This study also proves that venous diameters <2 mm are associated with significantly high failure rates ($P < 0.001$). However, arterial diameter of <2 mm was not found to be significant in our series.

Arteriovenous fistula creation in all (100%) patients with ESRD in our institution far exceeds the target goals of 50% set forward by the NKF/DOQI^[3] and the Centres for Medicare and Medicaid Services Fistula First Breakthrough Initiative.^[19] This was being achieved with acceptable rates of morbidity (7.2%), no operative mortality and good primary patency (78%). However, early detection of complications by patient education can help to improve long-term patency rates.

Results of Kazemzadeh *et al.*^[20] in 2012, in their case series of 245 patients of primary patency at 6 months, 1, 2, 3, and 4 years for 245 patients were 79.5%, 70%, 65%, 60.5%, and 48%, respectively. This was comparable to our results showing 78.81% patency of fistulas at the end of

1 year. However, in our series patency rates dropped to, 53.63% patency at the end of 2 years, 34.39 patency at the end of 3 years, 19.05 patency at the end of 4 years, 14.81 patency at the end of 5 years. Our primary failure rate was 21.18%.

It is routine practice to transpose basilic vein during proximal brachio-basilic fistulas^[21] In a series of 70 patients with brachio-basilic fistulas in order to gain easy access to veins, Hossny^[22] observed that all dialysis nurses were satisfied with the transposed veins, but only 53.3% were satisfied with the elevated veins; the difference was statistically highly significant ($P < 0.001$). Thus, concluding that among the various procedures, transposition has a lower complication rate and is favoured by the dialysis staff dealing with such fistulas. In our study, during the creation of proximal fistula by side-to-side anastomosis between antecubital/basilic vein and brachial artery, dilatation of distal vein to dysfunction the first valve towards wrist end helps to develop distal veins in the forearm by retrograde flow avoiding need for transposition of basilic vein thus avoiding the additional extensive procedure of transposition. In only one of our patients with proximal fistula superficialization of basilic vein in the arm was needed. Distal oedema was seen only in 2 patients with proximal fistula.

Though the risk of failure was observed to be lower in proximal fistulas in our series, it was not statistically significant. In a study conducted by Sultan *et al.*^[23] it was observed that 4 years primary functional patency was better with proximal fistula as compared with distal fistulas.

We have established direct correlation of bruit heard at end of surgery and thrill felt at the end of the surgery with the final outcome of the fistula. In the majority of our cases, we had both present at the end of the surgery (449 out of 505). In cases where both were absent the failure rate was as high as 57%. Since the failure is defined as the absence of visible veins suitable for cannulation at the end of 12 weeks after surgery, we have to wait for veins to develop until at least 12 weeks. In cases where either bruit or thrill or both were absent at the end of surgery, we started patient on anticoagulative measures as described earlier along with handball exercises. No surgical intervention was done in any of the cases with absent bruit and/or thrill. In India, because of poor socioeconomic status, fistula salvage

by early detection of failing fistula and intervention by exploration, embolectomy, or radiological intervention like percutaneous angioplasty for venous outflow stenosis^[3] is not cost-effective. In our study, no salvage or secondary procedures were done and hence all our statistics reflect primary failures. We prefer to perform new fistula in cases where previous has failed or not sustaining adequate flow rates on HD.

CONCLUSION

We found that

1. Vein diameter < 2 mm. showed very high failure rate ($P < 0.001$). Hence, we recommend either using proximal site or use of the alternative method of access placement such as peritoneal dialysis/permacaths in such patients.
2. Thrill felt on the operation table has a direct relation with success of fistula operation ($P < 0.001$).
3. Similarly, presence of on table bruit was found to be statistically significant in correlation with success of fistula surgery ($P < 0.001$).
4. Flow rates in patients with vein diameter > 2 mm were significantly higher as compared with patients with vein diameter < 2 mm ($P < 0.001$).
5. Flow rates are higher in non-diabetic patients as compared with diabetic patients ($P < 0.001$).
6. Average blood urea and serum creatinine values are significantly lesser in patients undergoing dialysis through successful fistulas as compared with patients with failed fistulas. Correspondingly, incidence of deaths is significantly lesser in patients with successful fistulas ($P < 0.001$).
7. During the creation of proximal fistula by side-to-side anastomosis between antecubital/basilic vein and brachial artery, dilatation of distal vein to dysfunction the first valve towards wrist helps to develop distal veins in the forearm by retrograde flow avoiding need for basilic vein transposition.
8. Primary patency rates by Kaplan–Meier analysis shows 78.81% patency of fistulas at the end of 1 year, 53.63 patency at the end of 2 years, 34.39 patency at the end of 3 years, 19.05% patency at the end of 4 years, 14.81 patency at the end of 5 years.

The presence of Bruit and thrill on the operation table at the end of the surgery are the key indicators of successful fistula. This has not been reported in the literature so far to the best of our knowledge.

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Announcement

6TH AND 10TH OF JULY, 2015

IPRAS 2015 - 18th IPRAS World Congress

Venue: Hofburg Palace, Vienna, Austria

Contact: Mr. Nikos Antonopoulos
Telephone: (+30) 211-1001782
Fax: (+30) 210-6642116
E-mail: n.an@zita-congress.gr
URL: <http://www.ipras2015.com>