



Outcomes of Secondary Compared to Primary Autogenous Haemodialysis Arteriovenous Fistulae, a Five Year Survey

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ABSTRACT

Aims: We examined the outcome and patency rates of secondary in comparison to primary arteriovenous fistulae (AVF) in a cohort of haemodialysis (HD) patients.

Study design: A retrospective review of native AVFs formed in a five year period.

Place and Duration of Study: Department of Renal and Vascular Medicine Hull and East Yorkshire Hospitals NHS Trust, East Yorkshire between December 2000 to December 2005.

Methodology: HD patients who had autogenous AVF created in a single centre over a 5 year period. 346 patients (mean age 61±16 years, 35.8% females, 29.2% diabetics) were included. Data on type of AVF, demographics, co-morbidities, immediate outcome and subsequent vascular access (VA) patency were collected.

Results: 463 AVF were created (304 radiocephalic (RC) and 159 brachiocephalic (BC)), of which 160 (34.6%) were secondary procedures. There was no significant difference in the primary failure rate (PFR) of primary and secondary AVFs (38.9 vs. 37.5% respectively). Primary RC fistulae had a higher failure rate in comparison to BC fistulae (42.6 and 21.3%, respectively, $p = 0.002$, OR 2.7; CI: 1.4-5.3). There was a higher PFR of AVF among females (primary access: 47 vs. 33% in males, $p = 0.028$; OR 1.7; 95% CI: 1.1-2.8; secondary access: 53 vs. 27%, $p = 0.002$; OR 3.1; 95% CI: 1.5-6). There was no difference in PFR of primary and secondary fistulae among

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diabetics and non-diabetics.

Conclusion: The primary success rate of secondary autogenous AVFs is similar to primary fistulae. Females have a higher rate of fistula failure.

Keywords: Arteriovenous; brachiocephalic; fistula; haemodialysis; radiocephalic.

1. INTRODUCTION

Autogenous arteriovenous fistulae (AVFs) are preferred to artificial grafts given their potential better patency and lower complication rates. Type of dialysis access affects survival of patients commencing dialysis, with a 50% increase in mortality when central venous catheters are used compared to AVFs (Aston et al., 2005). Various clinical practice guidelines have emphasized the significance of timely creation and maintenance of autogenous haemodialysis vascular access (VA) (Renal Assoc, 2007; KDOQI 2001), a goal which continues to be hampered by late referral and presentation of end stage renal disease (ESRD) patients to the renal service, the rising prevalence of diabetes among new ESRD patients, and the dialysis of more elderly patients. Even when AVFs are created before patients have started dialysis, their success is still affected by other variables including patient co-morbidity, quality of blood vessels, expertise of the surgeon and post-operative care (Allon and Robbin, 2002). Previous studies have reported variable primary failure rates (PFRs) for AVF from 18-53% (Bunalimi et al., 1982; Wolowczyk et al., 2000; Revanur et al., 2000; Winsett and Wolma, 1985; Rocco et al., 1996; Dixon et al., 2002). The natural loss of autogenous VA means that many ESRD patients, who are surviving longer on dialysis, will require more than one VA during their haemodialysis career. Failure of any autogenous AVF or graft may limit the sites available for subsequent AVF and a small number of patients will have repeated failures of AVF which may not be explained by obvious known risk factors. Whilst the KDOQI guidelines recommend that patients are considered for autogenous AVF after each failure of their VA (KDOQI, 2001), some patients may be reluctant to try again for the creation of autogenous AVF for fear of a further failure. In the current retrospective cohort study our research question consisted of investigating the outcome of secondary autogenous VA in comparison to primary AVFs to determine if the presence of a failed or many failed AVFs affects patency of subsequent autogenous access.

2. MATERIALS AND METHODS

We reviewed all patients who had autogenous AVFs in a single centre over the five years to December 2005. A list of all VA procedures was obtained from the operating theatre register; information was then extracted from case notes, dialysis files, and clinic letters. Data was collected about patient demographics, previous history of VA creation, co-morbidities, type of VA created and immediate outcome of surgery. Subsequently, information about events relating to VA use, complications, imaging, intervention and length of follow up was extracted from the case notes. We studied the risk factors for primary and subsequent failure of initial and repeat autogenous haemodialysis VA, durability and complications of creation. Initial AVF was defined as the patient's first autogenous haemodialysis AVF. The definition of repeat AVF was a fistula that was created after a pre-existing autogenous AVF or prosthetic arteriovenous graft (AVG). The primary end point was any AVF dysfunction preventing its use and requiring an intervention; e.g., thrombosis, poor VA flow requiring either insertion of dialysis catheter or imaging with or without endovascular intervention. Primary AVF failure

was defined as immediate non-function, failure prior to discharge from hospital after AVF creation, or failure of AVF to adequately develop to allow successful use. Patency rates are reported using the intent to treat rule (Sidawy et al., 2002). Primary (unassisted) patency is the intervention free period following AVF creation. Cumulative AVF patency is time from access creation to permanent failure.

Patients were referred to an experienced vascular surgeon for clinical assessment of the venous and arterial tree in the upper limbs, as soon as the patient had chosen haemodialysis as the future dialysis modality. During an assessment, palpation of pulses and Allen's test was used to determine arterial adequacy. Venous adequacy was confirmed, with tourniquet applied, by the presence of a compressible vein with estimated diameter of 2 or more mm, of sufficient length to allow needling and with patency confirmed using a transmitted "tap test". Pre-operative vessel mapping (venogram or duplex scan) was used only in selected patients for whom physical examination could not identify suitable vessels. Initial autogenous AVFs were created in the non-dominant arm by choice, initially at the RC followed by BC site, and moving to the contra-lateral side after that if required. In the case of repeat AVF, an existing draining vein of a previous AVF is used to create a new AVF, if available, and in its absence the same sequence is used as for the initial AVF, based on the clinical assessment by experienced vascular surgeon and pre-operative vessel mapping as indicated above. We routinely started to needle new AVF after 6 weeks from creation.

2.1 Statistics

Continuous variables are expressed as mean with standard deviation or as median with 95% confidence intervals. Comparison between groups was by student's t-Test for continuous variables and Fisher's exact test for categorical variables. Survival of VA was analysed using Kaplan-Meier technique and the log rank test used for comparison of the data points. A Cox model of regression was used to study predictors of VA survival. A multiple regression model was used to study the effect of various predictor variables on VA outcome.

3. RESULTS AND DISCUSSION

Five hundred and eighteen non-catheter VA procedures were performed in 346 patients (124 females (35.8%), mean age 61±16 years (range 21- 88), 29.2% diabetic).

Table 1: Details of primary and secondary arteriovenous fistulae

Particulars	Primary AVF n= 303 (%)	Secondary AVF n=160 (%)	p value
Gender (%)			
Female	114 (37.6)	55 (34.4)	NS
Male	189 (62.4)	105 (65.6)	NS
Mean age (± SD) years	61 (16)	58 (16)	NS
Diabetics (%)	93 (30.7)	40 (25)	NS
Type of AVF			
Radiocephalic (%)	242 (80)	62 (39)	0.0001
Brachiocephalic (%)	61 (20)	98 (61)	0.0001
Primary AVF failure	118 (38.9)	60 (37.5)	NS

NS: non-significant.

This included 304 RC AVFs, 159 BC, 35 thigh PTFE grafts, 16 leg to arm saphenous vein grafts, 3 basilic vein transpositions, and one thigh Autogenous AVF. Only the results of autogenous RC and BC AVFs will be discussed further. One-hundred and fifty-five procedures (34%) were performed prior to patients starting dialysis (pre-dialysis). Seventy-one procedures (15%) were preceded by pre-operative vessel mapping. Primary AVFs constituted 65 % of procedures (303 out of 463 procedures); the remaining 160 were secondary AV fistulas (Table 1).

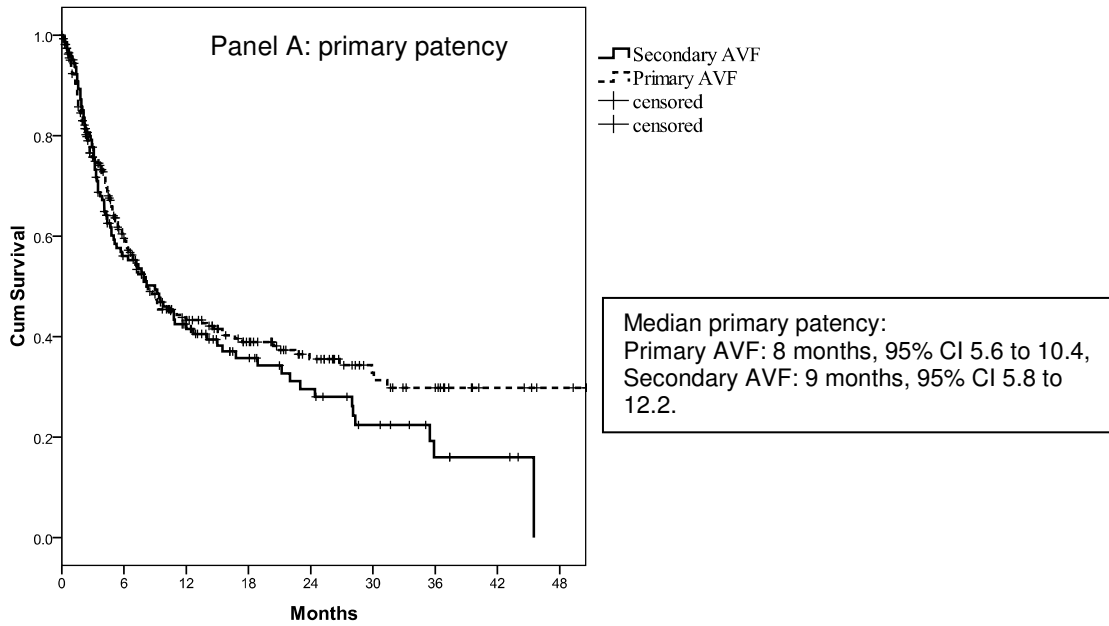
There was no significant difference in the overall PFR of AVFs between primary (38.9%) and secondary (37.5%) procedures ($p = 0.84$). In the primary AVF group, the PFR was 42.6% in RC vs. 21.3% in BC fistulae ($p = 0.002$, OR 2.7; 95% CI: 1.4-5.3), vs. 37 % and 35 %, respectively ($p = 0.87$), in the secondary access group (Tables 2, 3). The PFR of fistulae created in females was 47 % vs. 33 % in males in the primary access group ($p = 0.028$, OR 1.7; 95% CI: 1.1-2.8) vs. 53 % and 27 %, respectively in the secondary access group ($p = 0.002$, OR 3.1; 95% CI: 1.5-6). There was no difference in PFR of fistulae among diabetics and non-diabetics in the primary and secondary access groups (38% and 35% vs. 38% and 39% respectively). In the secondary access group, patients over the 75th percentile of age (over 73 years of age) had a higher PFR compared to those patients below the 75th percentile of age; 61.8% vs. 31%, $p = 0.001$; OR 3.6, 95% CI 1.6-7.9. There was no significant difference in PFR of fistulae between these two age groups in the primary access group. Our over-all PFR of RC AVFs was 41 % vs. 30 % in the case of BC AVFs ($p = 0.015$, OR 1.7; CI: 1.1-2.5). In cases where AVF creation was preceded by preoperative vessel mapping the primary failure rate was 44% (31 out of 71).

Table 2: Primary failure rates of Primary AV fistulae (%)

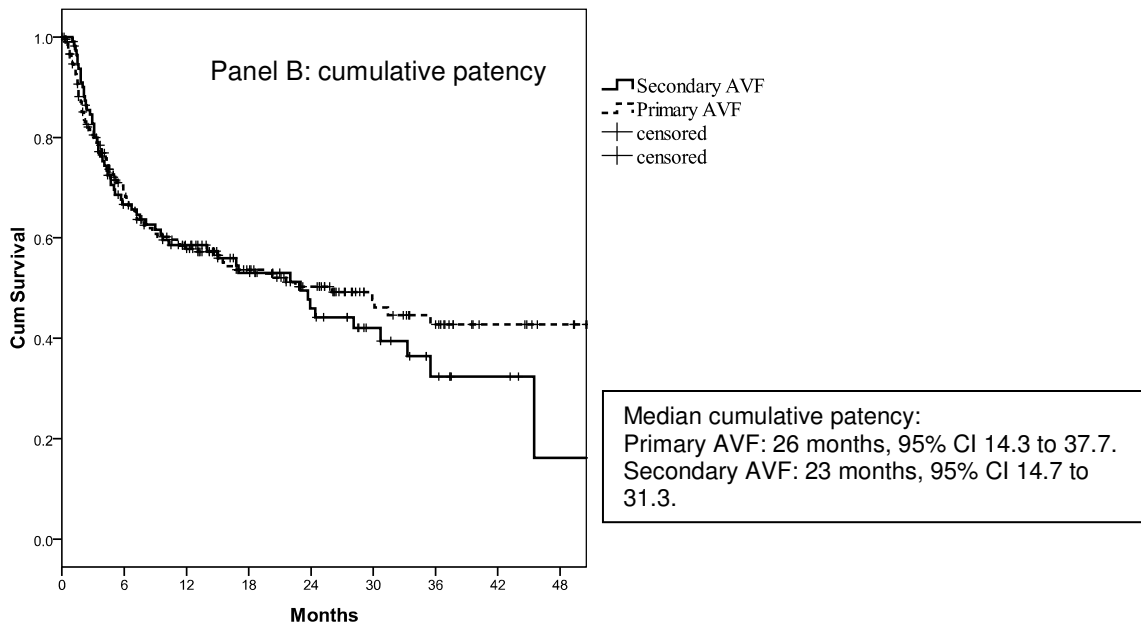
Particulars	Comparator	p	OR	95% CI
Radiocephalic (n= 242) 103 (42.6)	Brachiocephalic (n= 61) 13 (21.3)	0.002	2.71	1.4 to 5.3
Female (n= 114) 53 (46.5)	Male (n= 189) 63 (33.3)	0.028	1.7	1.1 to 2.8
Diabetics (n= 93) 35 (37.6)	Non-diabetics (n= 210) 81 (38.6)	NS	NS	
Age: Over 75 th percentile (n=78) 36 (46.2)	Below 75 th percentile (n= 225) 82 (36.4)	NS	NS	

Table 3: Primary failure rates of Secondary AV fistulae (%)

Particulars	Comparator	p	OR	95% CI
Radiocephalic (n= 62) 23 (37.1)	Brachiocephalic (n= 98) 34 (34.7)	NS		
Female (n= 55) 29 (52.7)	Male (n= 105) 28 (26.7)	0.002	3.1	1.5 to 6
Diabetics (n= 40) 15 (37.5)	Non-diabetics (n= 120) 42 (35)	NS		
Age: Over 7 th percentile (n=34) 21 (61.8)	Below 75 th percentile (n= 126) 39 (31)	0.001	3.6	1.6 to 7.9



Primary	303	128	79	54	38	21	13	7	4
Secondary	160	68	44	26	19	11	5	3	0



Primary	303	139	00	72	54	31	20	12	8
Secondary	160	73	54	35	26	16	7	4	1

Fig. 1: Kaplan Meier graph of AVF patency, primary vs. secondary

There was a trend towards better primary and cumulative patency in favour of primary fistulas after 10 and 20 months, respectively, but this did not reach statistical significance (Figure 1). The six and twelve month cumulative patency of primary fistulae was 50.4% and 37.5% vs. 51.4% and 36.2% respectively in the secondary fistulae. There were 154 VA events during a cumulative patency period of 411 patient years (event rate 0.37 events per patient year of follow up). There were 54 episodes of fistula thrombosis (0.13 episodes per patient year of follow up).

In a multiple logistic regression analysis, male gender and BC fistula site had significant contributions to predicting the likelihood of AVF primary success ($p = 0.0001$ and 0.004 respectively). In the same model, patient age and diabetic status did not affect outcome. In a Cox proportional hazard model, and out of the several predictors entered in the model (type of VA, age, and diabetic status), male gender was the only significant predictor of access patency ($p = 0.01$, 95% CI 1.1-2.1).

3.1 DISCUSSION

In addition to a relatively high initial failure rate of autogenous AVFs (Gibson et al., 2001; Sedlacek et al., 2001; Oliver et al., 2001; Rodriguez et al., 2000; Hodges et al., 1997), the reported annual thrombosis rate (15%) (Schwab et al., 1989), and the prolonged wait on the renal transplant list, indicate that a significant proportion of dialysis patients may be expected to require more than one VA procedure. The KDOQI recommendation is for patients to be referred for further autogenous access creation after each failure of their existing VA (KDOQI 2001). With every VA failure, however, the options available for placing a new VA are considerably reduced. Sustained effort is needed on the part of the treating nephrologist to convince long standing dialysis patients to have further native VA created in preference to arteriovenous grafts of dialysis catheters. Recent studies have addressed the outcome of secondary autogenous AVF created mostly after failure of AVG (Slayden et al., 2008; Salman et al., 2009).

The primary question of this comparative retrospective cohort study found no significant difference in the overall PFR of primary and secondary fistulae (38.9% vs. 37.5%, respectively). This is similar to studies of similar vintage. Indeed Allon et al. reported similar PFR for primary and secondary fistulas (47 vs. 46% respectively) (Allon et al., 2001). On the other hand Miller et al. reported a lower PFR in secondary compared to primary AVFs (36% vs. 59% respectively) (Miller et al., 1999). In our study and the previous two studies there were more upper arm than forearm secondary fistulas (61% vs. 20% in our study, 76% vs. 39% in Miller's and 71% vs. 30% in Allon's). Among our study patients, there were more females and diabetics in the primary compared to the secondary access group, but these difference did not reach statistical significance.

Only 11/160 (7%) of our patients had a secondary AVF created using an existing draining vein from a previous AVF or AV graft (type 1 secondary AVF) (Slayden et al., 2008), the rest were created in a fresh ipsi-lateral or contra-lateral site (type 2). In the study by Salman et al., 35 out of 62 secondary AVFs, were created using a draining vein (type 1) of an existing AVF (4) or graft (31), and 27 using vessels identified during pre-operative vessel mapping (type 2) (Salman et al., 2009). Despite pre-operative vessel identification there was significant early failure rate 31% (type 1) and 41% (type 2).

The cumulative 6 and 12 month patency of secondary AVFs in our group of patients was rather low at 51.4% and 36.2% compared to 100% at 12 and 24 months in Salman's study. The difference in the definition of primary failure and in defining indications for intervention in dysfunctional secondary AVF, may account for the reported differences in outcome of secondary AVF (Sidawy et al., 2002). Further analysis of the data revealed that 45 AVF underwent imaging, 14 were ligated and a further 9 had an episode of infection at the AVF site. These would all increase the failure rates in our study. The relatively low one year survival of fistulas in our study (Figure 1) can in part be due to the inclusion in the analysis of fistulas that failed immediately and before the patient was discharged from hospital. Oliver et al. showed that the difference in cumulative AVF patency depended on whether primary fistula failure was included in the analysis (Oliver et al., 2001).

In our study more RC fistulae failed before use compared to BC fistulae 41.4 vs. 29.6%, OR 1.69, 95% CI 1.1 to 2.5, $p = 0.015$. Miller et al. (1999) reported a substantially lower adequacy rate for forearm versus upper arm fistulas (34 vs. 58.9%). We detected no difference in fistula outcome in diabetics and non-diabetic patients 37.6 vs. 37.2%. Higher PFR has been reported among diabetics in previous studies (Miller et al., 1999; Hakaim et al., 1998). We can only speculate and propose several theories on this finding of the lack of effect of diabetes. It may be that the effect was not seen due to statistical under powering to detect a difference as the data-set examined had 30% of patients with diabetes. Also the overall older age of the population and other cardiovascular co-morbidities may have negated any increased risk attributed to diabetes. However the significance of diabetes as an adverse risk factor is unclear in the literature. Sedlacek et al. (2001) reported that despite increased arterial calcification, vessels diameters and arterial peak systolic volume were not significantly different between diabetic and non-diabetic patients in their population (Sedlacek et al., 2001). Subsequent AVF formation in their diabetic patients was effective and outcomes were similar regardless of the presence of diabetes. Konner et al. (2003) reported increased use of proximal fistulas in diabetic patients, but with primary access survival similar to that of non-diabetic patients.

Our reliance on physical examination alone in the pre-operative vessel assessment could have filtered out patients with more challenging vessels either to not have native access attempted or to be the only group of patients referred for vessel mapping. It is also likely, but not examined in this study, that those patients who underwent vessel mapping were already deemed to be more challenging and therefore the potential failure rate was likely to be higher rather than the investigation aiding the process. Perhaps if all patients had undergone vessel mapping in a non-selected fashion the success rates may have been better. Physical examination may underestimate the suitability of vessels for an AVF creation (Malovrh, 2002). Only a minority of patients in our study had formal preoperative vessel imaging 71/463 (15.3%), which did not significantly influence their fistula PFR (44%). Patel et al. (2003) demonstrated that the adoption of a preoperative imaging protocol resulted in an increased fistula creation rate from 61 to 73% in all haemodialysis patients. This, however, was associated with a significant drop in fistula maturation rate 73 to 57%, $p < 0.05$. Several studies have observed improvement in rates of AVF placement and maturation rates after adapting a preoperative imaging (duplex ultrasound or venography) before AVF creation. (Ascher et al., 2000; Mihmanli et al., 2001; Asif et al., 2007). Allon et al. (2001) showed trends towards improvement in primary AVF adequacy after using preoperative vessel mapping in RC (34 vs. 54% $p = 0.06$), but not in BC fistulae (59 vs. 56%).

Site of AVF, female gender, diabetes and age over 65 years are factors which have previously been reported to be associated with increased risk of primary failure of newly formed fistulae (Wong et al., 1996). Creating more fistulas in incident patients will probably mean taking on more patients with marginal vessels (more elderly and diabetics with multiple co-morbidities). In one study PFR of newly formed AVF increased from 14 to 36% when fistulae were attempted increased from 38 to 72% of new dialysis patients (Sands et al., 1997). This increased PFR is likely to be due to attempting AVF creation in patients with more co-morbidities and similar findings were also reported by Patel et al. (2003). The results from our data somewhat contrasts that of the literature. Our estimation of fistula related events may have been hindered by the unstructured clinical follow up in places at the time, hence our reliance on patient notes and dialysis files instead of a prospective access data base. Other possible explanations to account for this may include the population which has high cardiovascular co-morbidities and low socio-economic status, a high proportion of smokers, the variable use of anti-platelet agents such as aspirin, and potentially surgical operator during a period of skilling in the procedure and other unaccounted factors such as lipids and homocysteine, Indeed it is well recognized that there is a higher incidence of early and late fistula failure in those patients who are cigarette smokers (Erkut et al., 2006; Gheith et al., 2008). Finally evidence indicates that post-operative blood flow through an AVF is reduced with increasing age leading to a higher failure rate compared with younger subjects (Abularrage et al., 2004).

Experience of surgeon may also influence the primary success of a new AVF One hundred and five (22.7%) AVFs were created by a vascular surgeon in training, (65 RC and 40 BC). Consultant surgeons created 358 AVF in our study (240 RC and 118 BC). The overall primary failure rate was similar for AVFs created by trainee surgeons compared to those created by consultant surgeons, 38.1% vs. 39.1% respectively. The primary failure rate after fistula creation was 40% in RC fistulae and 35% for BC fistulae for trainees vs. 43.3% and 30.5% respectively in the cases where the operator was a consultant surgeon. There was no significant difference in age of patients operated upon by trainee or consultant surgeon (mean age 63.7±13.6 years vs. 59.5±16.8 years, respectively) or in the prevalence of diabetes in the two groups (27.6% vs. 27.9%, respectively). Secondary access constituted 31/105 (29.5%) in the trainee group vs. 129/360 (35.8%) in the consultant surgeon group. The consultant surgeon would decide preoperatively following the clinical examination of the patient if the AVF was suitable to be created by a trainee surgeon. A number of consultant vascular surgeons at various stages of their careers created the AVFs during the study period, and we could not rule out an inter-operator effect on the outcome of fistulas created. A previous UK study demonstrated that senior surgeons had higher success rates for both primary and secondary fistulae (Fassiadis et al., 2007). This data have been replicated in the US by dedicated vascular access surgeons with patency rates over 98% versus 71% (Cho et al., 2008).

The high incidence of fistula failure in women seems to concur with the literature. In the HEMO study female gender was identified as a significant predictor of graft rather than AVF use but there is little specific evidence for AVF patency between sexes (Allon et al., 2000). Women tend to have smaller calibre arteries and may therefore be expected to have lower AVF patency rates (Lockhart et al., 2004), however, Caplin et al. (2003) showed that arterial and venous diameters were not significantly different between men and women. The high failure rate in women may in part also be due to obesity leading AVF primary non function due to the deeper location of the veins necessitating a need for vein transposition. As there were few vein transposition procedures this may perhaps account for this. Interestingly in more recent years there has been an increase in the number of vein transpositions and

reduced failure rate in women (unpublished data) which would seem to support this notion. Ideally data on Body mass Index (BMI) in this historical cohort would strengthen the argument but a comprehensive data-set is unavailable for analysis and therefore is a further limitation of the study. However the published data is somewhat conflicting. In a trial comparing AVF outcomes in BMI >27 to those with BMI <27 no difference in rates of obtaining a AVF suitable for haemodialysis was seen (Vassalotti et al., 2002). Furthermore, Chan et al. examined AVF outcomes for 1,486 haemodialysis patients and compared those with BMI <30 to those with BMI >30 but were unable to confirm BMI as a factor in predicting AVF revision or failure (Chan et al., 2008).

3.1.1 Limitations of study

Despite the retrospective nature of our study, it confirms previous findings of comparable outcomes for primary and secondary AVF in a UK cohort of patients. We, however, realize that there is possibly bias by induction in the analysis of primary versus secondary fistula due to the choice of site of creation. This bias would require prospective studies. Due to the retrospective nature of the study, preoperative details about vessels used were not available in the minority of patients who had preoperative vessel mapping. Our study did not differentiate between two different entities of secondary AVF created using patent draining vein or a dysfunctional fistula from those created in a new site.

4. CONCLUSION

The study found that the primary success rate of secondary autogenous AVFs is similar to primary fistulae. Failure rates for both were high. Male gender was the strongest predictors contributing to the likelihood of AVF primary success. In the same model, patient age and diabetic status did not affect outcome. Further larger randomized studies are required to verify these findings.

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