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master thesis

The Determinants of Successful Development of Native Arteriovenous Fistulae in a Prospective Cohort of Incident ESRD Patients

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Abstract

Background

To accomplish hemodialysis, an access to the patients' circulation is required. The optimal access is a fistula (see operational definition on page 37). With increasing vascular co morbidity; fistulae often fail to develop satisfactorily. We sought to determine the factors associated with primary success of a fistula.

Methods

We studied the determinants of primary success of first fistulae (see definition, page 37) in a prospective cohort of 205 incident hemodialysis subjects in Southern Alberta from July 1999 until October 2001. We collected demographic and co morbid variables at commencement of hemodialysis, classifying co morbid variables according to the Charlson index. Surgeons were classified into two groups, based on whether or not they used an algorithm that included operative determination of vessel lumen diameter prior to placement of a fistula. Fistulae were categorized based on location into forearm or upper arm. The primary success or failure of fistula was determined through careful review of hemodialysis records.

We examined univariate and multivariate associations between the independent variables (surgical group, age, sex, fistula location and co morbidity index) and the dependent variable of primary success. We employed chi^2 tests and two sample t tests to examine for univariate associations, and logistic regression to examine for multivariate associations.

Results

Sixty four percent of primary fistulae were successful. There were no statistically significant predictors of primary success based on univariate analysis. Upper arm fistula location (OR 6.91, p=0.006) and male gender (OR 3.13, p=0.016) predicted success in a multivariate

logistic model when sex/fistula location and surgical approach/fistula location were added as interaction terms. Given these interactions, we constructed separate models looking at primary success in forearm and upper arm fistulae respectively. Male gender predicted primary success in forearm fistulae only ($p = 0.016$).

We also examined the determinants of upper arm fistula selection and found female gender and surgical group independently predicted this choice. Subjects with grafts as their first access were older, more often female or diabetic and had greater co morbidity, compared to fistula subjects. Hemodialysis subjects who never had access surgery were more often female, older and had greater co morbidity than fistula subjects.

Conclusions

Male gender significantly predicted primary success in forearm fistula. We found evidence of selection of higher risk subjects to upper arm (as opposed to forearm) fistula surgery and evidence of selection of higher risk subjects to non-fistula groups. This rational selection may account for the unexpected homogeneity of success among fistula sub groups. Type II error may have been an additional factor in accounting for the paucity of risk factor identification.

Introduction

End Stage Renal Disease {ESRD} occurs when a patient's renal insufficiency requires long-term support with hemodialysis, peritoneal dialysis or renal transplantation. In the United States there were 326,217 patients with ESRD on the 31st of December 1998[1]. The majority of this group were on hemodialysis {196,803}. This translates into a point prevalence of 731 subjects per million population. In Canada, the point prevalence of hemodialysis at the end of 1998 was 440 per million[2]. In the Southern Alberta Renal Program {SARP} at the end of 2002 there were 590 patients {454 per million} receiving hemodialysis. The prevalence of hemodialysis is increasing at 10% and 5% annually in Canada and the US respectively over the last five years[1-2].

This increase in prevalence of hemodialysis in North America has been accompanied by an increase in the proportion of patients with diabetes and vascular disease[1]. It is estimated that two thirds of the American hemodialysis population have diabetes or vascular disease as a cause for ESRD[1]. In Canada in 1998, 30% of incident ESRD patients had diabetes as the cause and another 10% had incidental diabetes.[2] New hemodialysis patients are also older each year. The SARP has seen similar increases in co morbidities.

Types of Vascular Accesses

To perform hemodialysis, an access to the circulation is required. This can be a central line, an arterio-venous fistula or a synthetic graft. The preferred access to the patients' vasculature for hemodialysis, traditionally, has been the distal forearm native radio-cephalic fistula. Brescia and Cimino {BC} described the innovative surgical technique of anastomosing the side of the radial artery, above the snuffbox at the wrist, to the conveniently proximate cephalic vein in their seminal New England Journal of Medicine paper in 1966[3]. The BC fistula was a huge improvement over previous access types; the ability to create such fistulae was facilitated by the fact that in those early days of hemodialysis, most subjects were young and did not have diabetes or atherosclerosis. Moreover, their forearm cephalic veins had not developed sclerosed segments at the sites of venesections or canulations.

After surgical creation of a radio-cephalic fistula in these otherwise healthy subjects, the flow in the radial artery increases to a plateau of 700 - 1000 mls per minute, as the healthy cephalic vein dilates and arterializes its' walls. Successful maturation of BC fistulae occurred (usually within 4 months) in over 90 % of surgeries as reported in case series from the early 1980s[4]. Arterial steal or neuropathy (due to inadequate blood supply) were rare complications due to the distal location of the anastomosis and the healthy vasculature of the subjects. They generally went on to provide excellent complication free dialysis for many years. Finally, if they failed, a more proximal (upper arm) arterio-venous fistula was usually an option.

With these benefits, the BC radio cephalic fistula became the gold standard hemodialysis access throughout the world. It remains the recommended first hemodialysis access option in both the National Kidney Foundation {NKF} Kidney Dialysis Quality Initiative {K/DOQI} 2000 and in the Canadian Clinical Practice Guidelines for Vascular Access 1999[5-6]. Recognizing the high primary failure rates for BC fistulae (i.e. the failure of the fistula to develop sufficiently to sustain dialysis) and often the impossibility of establishing a BC fistula in certain subjects, the guidelines proceed to prioritize subsequent access selection. If the BC fistula fails to mature sufficiently the guidelines recommend placing a more proximal radio-cephalic or elbow brachio-cephalic fistula. If it is not possible to establish any of these types of fistulae, it recommends that an arteriovenous graft (see definition; page 37), a vascular conduit of synthetic material, or a transposed (upper arm) brachial-basilic fistula be attempted. (Because of the perceived excess risk of complications, the brachial basilic fistula is rarely performed in our center). The last access option is the cuffed subcutaneously tunnelled central (internal jugular) venous catheters. Thus, there are three types of permanent hemodialysis access, namely fistulae (the favoured option), synthetic grafts and tunnelled central lines.

Prevalence of fistulae

There are many cross-sectional and retrospective studies, which record the prevalence of A-V fistulae in different geographic locations. The point prevalence of patients with native fistulae as a proportion of all hemodialysis patients varies enormously. In the US, the prevalence ranges from 20 % in the South East to as high as 70% in the NorthEast[1]. Nova Scotia boasts the highest proportion in Canada with 66% of hemodialysis patients using native fistulae[7]. This result is partly attributable to selecting poorer fistula candidates for peritoneal dialysis, where one-half of all dialysis patients receive peritoneal dialysis. This contrasts to the average Canadian and US peritoneal dialysis proportion of all dialysis subjects of 18 and 10 % respectively [1, 2]. In the SARP, 82% of the total dialysis population receive hemodialysis and of those 50% dialyse with a fistula, 30% with central catheters and 20% with synthetic grafts. In Catalunya Spain and Piedmont in Northern Italy, 83-85 % of hemodialysis subjects have a fistula [8, 9]. As is the case in Nova Scotia, both of these populations have a high proportion of dialysis patients treated with peritoneal dialysis. This discrepancy in prevalence of fistula use between Europe {60%} and the US {23%} is mirrored in their differential-approach to fistula creation[1] as well as their differential propensities to choose peritoneal dialysis. Windus has recommended synthetic graft accesses for as many as 80% of US diabetic subjects[10]. He does not inform us on how to select those candidates suitable for fistula creation. Leapman (another US author) concluded that the "arterio-venous fistula is not a panacea for vascular access" and that other access types should be considered for older patients and diabetics[11]. Besarab in the Midwestern area, on the other hand, has succeeded in increasing the proportion of his centers' dialysis subjects with a fistula to over 40 %[12]. Miller in Birmingham Alabama has achieved similar results[14]. The disagreement between these American authors is more about who should have a fistula attempted rather than whether a functioning fistula is the best access option, on which they agree. The K DOQI guidelines recommend that over 50 % of subjects should have a fistula attempted as their first hemodialysis access type and that at least 40% of US hemodialysis should have fistulae. The guidelines do not provide patient tailored selection criteria, for choosing the type and/or site where the first access should be attempted. Often, the rigid implementation of guidelines, by attempting a forearm fistula in high-risk subgroups, leads to an unacceptable failure occurrence.

Primary failure of fistulae

An important consideration when choosing the appropriate vascular access for an individual patient is the likelihood of primary failure of the access (see definitions, page 37). The probability of primary failure is reported to be highest for fistula, though the magnitude of this risk, as discussed below, differs based on patient characteristics.

Konner describes a series of 748 consecutive A-V fistulae created in a single center in Koln, Germany from 1993 to 1998[13]. He performed all the surgeries himself and retrospectively reviewed the outcomes of primary {unassisted} and secondary {assisted} survival by phone calls to the dialysis centers. He reports results of primary and secondary fistula survival (see operational definitions, page 38) between 75% and 94% respectively, at 2 years. He reported 80 complete surgical failures. He documented access survival at one and two years. He reported access survival on only 450 subjects, representing significant loss to follow-up. It seems likely that the majority of subjects unaccounted for were true primary failures of fistula development. It seems more likely that, at least 450 of 748 subjects or 60% of fistula surgeries were primary successes. He defines primary fistula failure as occurring if subjects require a secondary access surgery and not as their ability to sustain dialysis. This lack of clarity as to what constitutes primary fistula failure and the lack of a meaningful definition, is common in other studies and thereby makes the appraisal of the determinants of this important outcome of primary fistula failure very difficult [14, 15, 16]. Konner does not outline the process of selecting subjects for fistula surgery and does not provide baseline vascular co morbidities. Thus, it is difficult to conclude anything about risk factors for primary failure of fistulae from this study, but we can appreciate that once fistulae mature sufficiently, they continue providing access for dialysis in 94 % of subjects at 2 years. Even if a clear, clinically relevant definition of primary fistula failure had been given, Konners' study design could be faulted on the likelihood of selection and misclassification bias as well as confounding. Selection bias could occur because of significant loss to follow up, and non-random and random miss-classification of the outcome could easily occur, given the retrospective phone call method of outcome ascertainment. The absence of baseline vascular co-morbidity data would create the potential for important confounding.

It is unclear why successful fistula maturation occurs more frequently in Europe than the US, but some of the differences are likely associated with greater vascular co morbidity, diabetes and obesity in the US as well as alternative surgical approaches and perhaps different selection criteria for surgical candidates. The frequent absence of any clear definition of adequate fistula maturation (primary success) makes it virtually impossible to appreciate the determinants of this critical outcome.

As mentioned, studies conducted in the US record higher primary failure rates, particularly in fistulae. Miller reported the primary failure of 54 out of 101 consecutive fistulae, in a prevalent population of predominantly (80%) African American hemodialysis patients, over a two-year period ending in 1998[17]. Only 47 fistulae were the first hemodialysis access attempted. Wrist fistulae failed to develop adequately (i.e. primary failure) in 79% of patients with diabetes, 88% of patients over 65 years old and 93% of females (1 out of 13). In contrast, upper arm fistulae developed adequately in 48% of patients with diabetes, 54% of patients over 65 years old and 56% of females. Non-diabetic men under the age of 65 were the only subset of patients in whom adequate development of BC wrist fistulae occurred in a significant proportion {55%}. In contrast to other literature, these findings were strengthened by the study's use of a clear and clinically meaningful definition of primary failure (similar to the definition used in our study) of adequate fistula development. If six hemodialysis sessions occurred, at a pump speed of 350 mls per minute, over a one-month period, within six months of fistula creation, the surgery was classified as a success. The authors, however, did not have complete data on vascular co morbidities and duration of ESRD, at the time of surgery. This coupled with small numbers of subjects (most notably for first fistulae) were deficiencies which prevented the assessment of the independent and relative impact of potential risk factors for adequate fistula development such as diabetes, age, gender and weight. Finally, the high proportion of African American subjects makes generalization of the results of this descriptive, non-analytic study to a Canadian population questionable.

Benefits of fistulae

The importance of determining the factors that predict primary success of a fistula is highlighted by evidence suggesting an association between having a functioning fistula and improved survival, reduced morbidity and economic costs. For instance, Dhingra et al analyzed data on a random sample of 5,507 prevalent {including an adequate sample of incident (25% of total)} United States Renal System {USRDS} patients with 2 year follow up from 1993 to 1995[18]. The primary outcome was time to death from commencement of hemodialysis. The occurrence of a significant interaction between vascular access type and diabetes was observed when a Cox survival analysis was conducted on combined prevalent and incident patients. Thus, separate models were used for diabetic and non-diabetic subgroups for the total {prevalent and incident} and incident-only, groups. The models were adjusted for age, gender, race, body mass index, coronary vascular disease, peripheral vascular disease, cerebrovascular disease, ability to ambulate and education level. The adjusted relative risks for mortality in the total diabetic group were 1.41 for grafts {$p<.003$} and 1.54 {$p<.002$} for central venous catheters compared to fistulae. The adjusted relative risks of mortality in the non-diabetic group were significantly higher in patients with central catheters {RR 1.7} and non-significantly higher in grafts compared to native fistulae. The trends were similar in the incident group, though statistical significance was not reached, possibly due to inadequate power. Thus, fistulae, once they develop satisfactorily, are associated with improved survival, independent of other risk factors.

The Canadian hemodialysis morbidity observational study recorded a higher bacteremia occurrence in patients dialyzing with grafts compared to AV fistulae {19.7 vs. 4.5 %} over a one-year period [19]. Access thrombosis was 2.5 fold higher and hospital admissions were 50% more frequent in subjects with grafts compared to those with fistulae. Central venous catheters portended the highest risk of bacteremia, with an estimated 16 fold higher probability than fistulae. This study was a non-analytic, observational study. Some of the benefits ascribed to patients with fistulae may have been due to confounding i.e. fistula patients may have been healthier and independently less prone to infection and thrombosis. The very high risk ratios, however, are suggestive of an independent benefit of fistulae.

The morbidity associated with vascular access is matched by the concomitant economic burden. Vascular access complications account for 16 to 25% of hospital admissions in the US and cost over 1 billion dollars annually according to USRDS estimates in the mid 1990s[20]. Moreover, in an unadjusted comparison of costs related to vascular access, in a prevalent hemodialysis Canadian population, Lee et al found the yearly access-related cost to be significantly higher for catheters and grafts when compared to fistulae ($4,000 difference)[21]. Lee's study may have favoured fistulae, however, by underestimating the cost of early, failed fistula surgery. On the other hand, complications related to synthetic grafts and central lines may have been more common in the early months of dialysis. A similar study design in incident hemodialysis subjects would have accounted for early access related costs.

Rationale for proposed study

So in conclusion, even though there are no randomized comparisons of native fistulae to grafts (or central lines), there is an abundance of evidence favouring fistulae, from complication, cost, longevity and patient survival advantage perspectives. The main drawback with fistulae is their high primary failure rate. Once they develop sufficiently to provide reliable hemodialysis access, they continue doing so for long periods with all their attendant benefits. A better understanding of the determinants of successful fistula development should lead to an increase in the prevalence of fistula. Specifically, knowledge of these factors and their interrelationships should facilitate improved selection of the optimal fistula type(s) for patients with a particular set of favourable characteristics and avoidance of attempting a fistula in those with a very high probability of failure or complications. Lastly, given the lack of differential survival between peritoneal and hemodialysis(s), peritoneal dialysis could then be promoted as a preferable option (when feasible) to hemodialysis, when a central dialysis catheter or graft is the only remaining access choice.

The objective of this study therefore, is to identify the determinants of successful development of native arteriovenous fistulae in a prospective cohort of incident ESRD patients in Southern Alberta in whom a fistula was attempted.

Objectives

Primary: To identify the important determinants and their interrelationships, in predicting the success {see definition in method section} of development of the first native arteriovenous fistula, in a prospective cohort of Southern Albertan, incident end-stage renal disease patients in whom a fistula was attempted.

Secondary: In those patients whose first fistula fails, to identify the important determinants and their interrelationships in predicting the success {see definition} of the second native arteriovenous fistula. (See comment in results section on why this secondary objective was not feasible.)

Methods

Patient cohort

This cohort includes all SARP patients who commenced dialysis between July 1, 1999 and November 1, 2001. Patients were identified from the SARP computer database, a database that collects demographic, clinical and laboratory data for all ESRD patients in Southern Alberta [22]. A research nurse collected data on patient co-morbidity in a standardized manner within 6 weeks of starting dialysis. Cause of ESRD was determined from physicians' notes and co-morbid baseline variables were collected according to the original Charlson definitions (Appendix 1). Each of the 14 scales was answered categorically as a yes or no, according to the definitions appearing in the attached questionnaire. The research nurse marked a score of one for each affirmative answer, and summated all scores based on relative weight, to derive the final score (ref Charlson et al). The research nurse used patients' written inpatient and outpatient records, sometimes supplemented by patient interviews to complete the baseline co-morbidity categorization. The Charlson index has been validated as predictive of hospitalizations and survival, in both non-renal and ESRD populations [23, 24].

Data on patients in the SARP database were linked to an electronic surgical record that captures data for all hemodialysis access surgeries done from January 1st 1997 onwards. At the end of each access surgery, the responsible surgeon entered an electronic standardized record of the particular artery and vein used, and whether it was a graft or fistula, and whether any complication occurred. Other data recorded include a unique surgery number, patient identification number, the date of the surgery, and the contemporary dialysis modality. Serial complications are entered into the surgical electronic record, by the access coordinator as they occur with the date of occurrence (Appendix 2).

Surgeons were classified into group 1 or group 2 depending on their method of determining vessel suitability. The author interviewed surgeons to obtain this categorization.

Group 1 surgeons adhered to the algorithm described in detail in the ensuing paragraph. If the physical examination of the subjects' non-dominant arm revealed an "adequate" radial and ulnar artery pulsation at the wrist, they went on to surgically explore the distal cephalic vein. If this vein was present and allowed the insertion of a 3 mm diameter garret dilator 10 centimetres proximally, followed by the insertion of an umbilical catheter 30 centimetres proximally they proceeded to explore the distal radial artery. They carried out exactly the same sequence of catheter insertion in the artery. If the artery was of sufficient internal diameter to allow comfortable catheter insertion, they proceeded to create an end to side radio-cephalic anastomosis. If any of these steps failed, they abandoned forearm fistula surgery and commenced a similar process with the cephalic vein at the elbow. Between the time of determination of a suitable vein and before arterial exploration, the subject was usually given 3000 to 5000 units of heparin intravenously. If a suitable cephalic vein at the elbow was discovered (based on the above criteria), a brachio-cephalic (upper arm) fistula was created, and if not a brachio-basilic graft fistula was created. This algorithm depended on vessel size predominantly, rather than based on any demographic or co morbid variable, though in "better" surgical candidates, borderline vessel size might not contraindicate a forearm fistula attempt, whereas it might in "poorer" surgical candidates.

The other surgical approach (group 2) relied on the peri-operative appraisal of the suitability of vessels without the aid of dilators or catheters. This approach has broader inclusion criteria with acceptance of patients for forearm fistula who have smaller veins.

The research nurse reviewed the subsequent relevant hemodialysis run sheets to determine if the surgery met the defined criteria of “success”. The attached “access results” paper form was completed (Appendix 3). Generally, the outcome of successful fistula development was unambiguous but in a minority of subjects, the result was indeterminate and the surgical database was reviewed for clarification by the author. This step was necessary in forty-two subjects. If the result was still uncertain, the author communicated with the dialysis center by telephone. This final step was required in seven subjects. In only three subjects was it impossible to determine the outcome. These subjects were not included in the study. Selection bias due to inability to determine outcome was thus not a significant factor.

Three subjects died within six weeks of their access surgery. They had insufficient time for outcome ascertainment. (It was not possible to elucidate in two of these, whether the fistula surgery played any role in their deaths but considering the time lag of several weeks from surgery to hospital admission this was felt to be unlikely. One subject died within 24 hours of fistula surgery and the cause of death was attributed to the surgery.) Because of the possibility of the deaths being related to the fistula surgery, I classified all three as outcome failures.

The primary outcome of interest is whether the first fistula develops sufficiently to satisfy the pre hoc definition of success (agreed upon prior to ascertainment). Successful use of a fistula is defined as affording an extracorporeal blood flow of at least 300 mls per minute, for at least 3 hours, using an arterial and venous needle placed in the fistula, for a minimum of three consecutive dialysis sessions. This same definition of success applies to the outcome of the second fistula, given that the first fistula fails.

Analysis

Two sample t tests and two sample tests of proportions were used to compare differences in continuous variables and categorical variables respectively. The association between five explanatory variables, namely, age, gender, surgical approach (1 or 2), fistula location (upper arm or forearm) and the Charlson index with the dependent variable of primary first fistula success was explored. Firstly, univariate associations between individual independent and the dependent variable, using chi^2 tests of two independent proportions were assessed. Next, I categorized age and Charlson index as greater or less than the mean. (As age was normally distributed and many subjects had the median Charleson score, I chose the mean rather than the median to dichotomize these two variables.)

As the Charlson index contains several related variables, I also examined in its' place, diabetes, ischemic heart disease, peripheral vascular disease, congestive heart failure and cerebrovascular disease as separate categorical independent variables, and examined their univariate (and multivariate) associations with first fistula success.

As I was predominantly interested in whether the fistula functions, and not when the fistula functions (since most fistulas that succeed do so within a narrow timeframe) I performed a multiple logistic regression (using Stata 7.0) with success as the dependent variable.

As described above, in the logistic model, age, gender, location of fistula (upper arm or forearm), surgical approach (1 or 2), and Charlson index were used as the independent variables. The Charlson index was then replaced with the five component variables listed above to determine if there was much loss in explained deviance. There was no significant co-linearity between the four vascular variables, so there was no need for elimination of redundant variables. Two-way interaction terms (as decided upon a priori) between fistula location and age, fistula location and diabetes, fistula location and gender and finally, fistula location and surgical approach were included. Miller[17] reported much higher failure proportions in subjects older than 65 years, in diabetics and in females when they had a forearm as opposed to an upper arm fistula constructed. This provided a clinical rationale for choosing the first three interaction terms. Surgical expertise is challenged to a greater degree with the smaller forearm than with the larger sized upper arm fistula vessels. In addition, surgical approach 1 might improve success in upper arm fistulae through more appropriate selection of adequate sized vessels. These two factors provided the rationale for choosing the surgical approach/fistula location interaction term. I checked the models for evidence of violation of the assumptions of linearity.

Results

Three hundred and fifty six subjects commenced ESRD treatment with dialysis in the SARP between July 1999 and October 2001. Of these, 297 were initiated on hemodialysis. In turn, 205 of these had an attempt at a fistula as their first access, 41 an attempt at a graft as first access and 51 had neither procedure attempted. Thus, 51 subjects dialysed solely with a central line and never had an access attempted. Of the 205 fistula subjects, 69 had their access created prior to initiation of hemodialysis. Three subjects died within 6 weeks of their surgery. In only one subject (who died within 24 hrs of surgery) did the surgery definitely affect survival.

Of all first arterio-venous accesses created, 80 % were fistulae. Of all first fistulae, 55% were forearm fistulae. One hundred and thirty three (65%) first fistulae were created using surgical approach 1. The remaining 72 fistulae were created using surgical approach 2.

There were only 36 subjects who had a second fistula attempted. Nineteen of these met the definition of success. This unexpectedly small number of second fistula surgeries precluded risk factor determination in this group, as originally planned. Of interest, 24 of these second fistula subjects had a forearm fistula as their first access.

Using the definition as established within this study, primary success for first fistulae occurred 64% of the time. The primary success proportion was identical, at 64%, in both, forearm and upper arm fistulae. There was no statistically significant predictor of success of first fistulae (forearm and upper arm combined) on univariate analysis.

Table 1 shows differences in proportions of age, gender, and diabetes, mean Charlson co morbidity scores, ischemic heart disease, congestive heart failure, peripheral vascular disease and cardiovascular disease, in forearm fistula, upper arm fistula, grafts, and lines only, groups. Fifty-one subjects never underwent any kind of access surgery and constituted the lines only group.

This group was significantly older (mean age 70) and had a non-significantly higher mean Charlson co morbidity score (5.3), than subjects who underwent first fistula access surgery (mean age 65, p = 0.0018; mean Charlson Index score 4.76, p =0.2) (Table 1). Differences in age and sex between lines only and fistula groups reached statistical significance (Table1). The line only group had the shortest survival of all groups. Twenty (39%), of these subjects died within 6 months of starting hemodialysis. (Information was not collected as to why these subjects had no access surgery. I suspect in some cases the nephrologist decided not to refer for access surgery. Some subjects may have died while waiting for surgery after referral. Whatever the reason for no surgery, this group is clearly different from the fistula group and non-selection for access surgery is likely related to these differences.)

Those subjects (n=41) who had grafts created, had the highest prevalence of diabetes (60%) and of female gender (61%). Differences in the proportion of diabetic subjects in first fistula compared to graft subjects approached statistical significance (chi^2 3.0, p = .08). Differences in female proportions between these two groups reached statistical significance (chi^2 3.6, p=0.03). Graft subjects had a clinically significant higher Charlson score than those with fistulae.

In the fistula group, 80 % were Caucasian, 47 % diabetic and their mean age was 65 years. Demographic variables and baseline co morbidities are shown in Table 2. Of note is the high proportion of subjects with diabetes (47%), ischemic heart disease (41 %) and congestive heart failure (37 %). Surgical group 1 performed 133, and group 2 performed 72 of first fistulae surgeries. There were 113 forearm fistulae created compared to 92 upper arm fistulae.

Table 3 outlines the distribution of demographic and co morbid variable(s) in upper arm and forearm fistula groups. Surgical group 1 more frequently placed an upper arm fistula (univariate chi^2; p<0.0001). Forty five % and 74% of all fistula surgeries performed by group 1 and 2 surgeons were forearm, respectively. Females had upper arm fistulae performed more frequently than forearm surgeries (chi^2 2.93, p=.087). Diabetes, ischemic heart disease and congestive heart failure (table 3) were all more prevalent (non-significantly) in upper arm compared to forearm fistula subjects. Mean age and mean Charlson index score were also greater in patients who had upper arm fistulae (Table 3).

Table 4 shows proportional and percentage success (unadjusted) in all fistulae, upper arm, and forearm groups (in several sub-categories) respectively. The marked similarity between success proportions in divergent subgroups is noteworthy. Male gender is the only statistically significant association (univariate: chi^2 3.6, p=0.045) with success and this was only noted with forearm fistulae.

As planned, a logistic regression model with success as the dependent variable and sex, age, charlson score, timing of surgical placement (predialysis vs. postdialysis), surgical approach and surgery location (upper arm versus forearm) as the dependent variables, with interaction terms involving each of the dependent variables and surgery location, was constructed. Since the interaction of sex with surgery location and surgical approach with surgery location were significant interaction terms (table 5), separate models were constructed for success of forearm, and upper arm fistulae. Of importance, this overall models' ability to predict success is statistically significantly better than chance (p=0.029) but the proportion of deviance explained by the model is low (Model Log Likelihood ratio = 17.52, Total Log Likelihood = - 125.5). Males faired better than females overall and subjects with upper arm fistula surgeries achieved statistically significant higher success proportions than forearm fistula subjects. As discussed, the effect of male gender on success depended on whether the fistula was upper arm or forearm.

Males had (statistically) significantly more success than females in forearm fistulae but not in upper arm fistulae. Moreover, this difference (in success between males and females) was significantly different between forearm and upper arm fistulae groups. It would therefore be illogical to group male (or female) upper arm with forearm fistula subjects. Similarly, the differences in success between surgeons depended on fistula location. These two interactions were the rationale for using separate models for forearm and upper arm groups. These models are shown in Tables 6 and 7.

Table 6 shows the results of a logistic regression with success in forearm fistulae as the dependent variable and sex, age<65, surgical group 1 or 2 and Charlson score as the independent variables. The odds of success of males was 2.6 times that of females. This reached statistical significance as indicated by a confidence interval of 1.3 to 6.9 and a p =0.025. ((This means that males achieved more success than females even when adjusted for co morbidities, age and surgical approach. Thus, sex is an independent (statistically significant) predictor of success in forearm fistulae in our cohort of incident HD patients.)) Age, co morbidity score and surgical approach had no significant (statistical or clinical) impact on success. There was a non-significant trend for subjects less than 65 years to have more success than those over 65. (Females and older subjects' forearm vessels status may explain these differences. This effect would likely be greater if preferential selection of females and/or older subjects to upper arm fistulae location did not take place.). This models' prediction of success was significantly better than the null model but explained only a small proportion of the overall deviance.

Table 7 represents the results of a similar logistic regression in upper arm fistula subjects. Age less than 65 and female gender showed non-significant trends of greater success. Surgical approach 1 odds of success was over three times that of approach 2 (p=0.019.). Of note, only 19 upper arm fistula surgeries were performed using surgical approach 2. This small number is reflected by the imprecise wide confidence interval. The overall models' prediction was not significantly better than chance (P = 0.169).

Finally, the Charlson co morbidity variable, as planned, was replaced with diabetes, ischemic heart disease, congestive heart failure, peripheral vascular disease and cerebrovascular disease. These models are shown in tables 8 and 9. These models fail to show any additional significant predictor of success. (Timing of fistula placement before initiation of hemodialysis was not associated with greater success than placement after commencement of hemodialysis on unadjusted or adjusted analysis.)

A final logistic regression model (table 10), was constructed, using location of fistula (upper arm versus forearm fistula) as the dependent variable with the same explanatory variables as before. The purpose of this model was to detect criteria that may have been used by the surgeons in selecting patients for upper arm fistula selection. Female gender (odds ratio 1.8, p=0.038) and surgical approach 1(odds ratio 3.4, p<0.001) independently predicted upper arm fistula selection in a statistically significant manner. Female gender was a statistically significant predictor only within surgical approach group 1 (not shown). Subjects with diabetes and those with higher co morbidity scores had greater odds (non-significant) of upper arm fistula selection (Table 10). In addition, subjects with ischemic heart disease, congestive heart failure (outlined in table 2) or mean age > 65 (Table 1) were all more prevalent in upper arm compared to forearm fistula groups. Thus, factors associated with poor forearm vessels appear to predict upper arm fistula choice. Likewise, surgical approach 1 should have increased awareness of those subjects with poor forearm vessels, thereby explaining the marked difference in selection between the two surgical groups. The overall models' prediction was statistically significantly better than chance.

Compliance of Regression Models with Assumptions of Logistic Regression Models

The only continuous variable was age. This continuous variable was divided into quartiles of 20 to 50, 51 to 60, 61 to 70 and > or equal to 71. The logit of success in these groups were 0.55, 1.2, 0.6 and 0.3. As this does not conform to a linear distribution, we categorized age categorically as greater than or less than the mean for each of the regression models. The interval variable of Charlson score was also classified categorically as greater than or less than the mean. The confinement of fistula study subjects to first fistulae only, assured independence. Thus no underlying assumption for a logistic model, other than independence, was made.

Interpretation

Of all first arterio-venous accesses created, 205 of 246 (80 %) were fistulae. This superseded the goal of 50% recommended in the DOQI guidelines. Of all first fistulae, 55% were forearm fistulae. This is consistent with Canadian and American guidelines, which recommend radio-cephalic fistula as the preferred first option. One subject died because of fistula surgery. This translates into a mortality risk of less than 0.5%. Thus, fistula surgery was relatively safe.

Significant differences in demographic and co morbid variables between subjects who had different accesses (grafts, forearm or upper arm fistulae, or no access) provided evidence of occurrence of selection. Line only subjects had the highest co morbidity and this was likely the major factor in determining their non-selection for access surgery.

The surgeon's determination of the state of the subjects' vessels intra-operatively influenced the selection of access type. The vessel size in turn correlated with co morbidity. The increase in co morbidity, age and diabetic proportions from forearm through upper arm fistulae to graft subjects (Table 1) is a consequence of patient selection by the surgeon. The order of risk factor progression in these three access groups is testament to the rationality of the surgeons' selection.

This rational selection may explain the homogeneity of fistula success results within divergent risk groups, as exemplified by the models' (Table 5) small contribution to overall deviancy. If no selection process took place in upper arm versus forearm fistula choice, and surgeons blindly created forearm fistulae in all first accesses, it is likely that we would have seen significant risk factors emerge, in accordance with their association with diseased vasculature.

Our study suggests that female gender is probably (chance is another potential explanation) an independent risk factor for forearm fistula failure. This occurred despite females having proportionally (compared to men) significantly fewer fistulae overall and significantly less forearm fistulae (compared to upper arm) in the minority that had fistulae.

Surgical approach 1 may have improved success for upper arm fistulae at the expense of fewer forearm fistulae being created.

Paradoxically, patients with diabetes had greater success in forearm fistulae when compared to non-diabetics, although this did not reach statistical significance when adjusted for other risk factors (Table 6). This anomaly may have been due to over selection, (only choosing diabetics for forearm fistulae when their vasculature was superior to non- diabetic forearm fistula subjects), or alternatively due to chance.

Study Strengths

There were several strengths to this study. This study had the second largest number of subjects with first fistula results available for evaluation of determinants of successful development in the literature. A clinically meaningful definition of successful fistula development was used. Baseline co-morbid and demographic variables, collected in a comprehensive, detailed, validated manner were available for analysis of their role in determining the outcome, as well as for standardized comparisons. Contrasting numbers of subjects and their aggregate co-morbidities amongst incident hemodialysis subjects with fistulae and those without, educated us as to our centers' selection criteria for attempting fistula surgery. We were also able to determine selection criteria used by surgeons in choosing upper arm fistulae in addition to showing differences between surgical approach groups. Almost complete follow-up as well as the inclusion of all incident hemodialysis patients undergoing fistula surgery minimized any potential for selection bias. Any misclassification of baseline data was most likely of the non-differential variety as the outcome was unknown at the time of collection. Similarly, differential misclassification of the outcome was unlikely, as the exposures were unknown by the research nurse at the time of the outcome collection. Thus, the misclassification of outcome or exposure was not likely dependent on the exposure or outcome, respectively. Random misclassification of the outcome should also be uncommon because of the clear, easy to ascertain nature of a relatively "hard", pre-defined, outcome measure. Any difficulties with outcome classification by the research nurse were referred to the author for resolution, who in turn referred to the surgical database and when necessary telephoned the relevant dialysis center. This resulted in determination of outcomes in all but two subjects. These subjects were not included in the study. We classified the three subjects who died within 6 weeks of their access surgery (who had insufficient time for outcome ascertainment) as fistula failures. Excluding these subjects would not have resulted in any important alteration in the results.

Sixty-five subjects had their fistula surgery prior to commencing hemodialysis, but there was a minimum of 6 months observation on hemodialysis allowing adequate time for success outcome ascertainment in this group. Over 70 % of subjects had already started dialysis at the time of fistula surgery and the remainder commenced dialysis during the course of the study. Thus, selection bias due to inadequate follow up or to non-inclusion was not a factor in our study.

Study limitations

There were several notable limitations to our study. The size of our study population may have been too small to appreciate significant differences between groups. The outcome data were collected some time after their occurrence, using a secondary data source, i.e. dialysis record sheets that were not designed for the study purpose. As this is an observational study, unidentified confounders may have distorted the exposure(s) outcome effect measure. Thus, several factors could have contributed to our inability to detect any significant risk factors for success of fistula development (Type II error).

Furthermore, the identification of female gender as a statistically significant predictor of forearm fistula success may have been a Type 1 error. Considering I looked at multiple (16 risk factor/fistula success outcome) effect measures, this result may have been due to chance, although the association makes clinical sense. If I used a correction for these multiple comparisons, female gender would no longer be statistically significant at the 5% level of significance. Likewise, Type 1 error is a potential explanation for greater success by surgical group 1 approach amongst upper arm fistulae subjects. Another explanation for this greater success could be that surgeon 2 was less skillful at upper arm fistula surgery than the three surgeons in surgical approach 1, independent of the surgeon's assessment of vein size. In this prospective cohort design, we cannot disentangle the effect of surgical skill from surgical approach on fistula success. (Observational studies, by virtue of unidentified confounders and inseparably linked risk factors are useful in generating cause-effect hypotheses that can be further studied in suitably designed randomized controlled trials.)

Conceivably, some subjects were referred for access surgery, but died before the surgery date. I do not, unfortunately, have data to identify this group (referred for surgery), or those in whom it was decided not to refer for access surgery. (Furthermore, I do not have data on whether the cause of death, was related to a complication of their central line access.) If a significant number of subjects died while awaiting access surgery this could introduce a survival bias, i.e. only healthier subjects survived from referral to access surgery. Exclusion of these subjects could have introduced a selection bias if their central line caused their deaths and their risk factor

/success relationships were potentially different to the study groups'. This omission could have potentially falsely inflated the success proportion.

Statistical Considerations

We chose as our primary regression model a logistic model. The rationale for selecting a logistic as opposed to a survival model is described below.

The dichotomous nature of the outcome variable made a logistic model suitable. The disadvantage of the logistic model for this study was that subjects who died prior to the fistula having time to develop, or subjects who had fistula surgery but had not yet started dialysis, could not be included in the study. A survival model that censors these subjects (assuming stochastic curtailment) would partially overcome this problem. Using an outcome of time to success, however, would not clearly capture the complement of success (i.e. failure). Definite failures and subjects censored would all be classified as having the same outcome. This lack of outcome differentiation makes a survival model unsuitable. As the fistula has only two possible (mutually exclusive) outcomes (either of which occurs within a few months of surgery), and these outcomes constitute the entire distribution probability i.e. success or failure must occur, the logistic model solely has the ideal dependent variable.

Interpretation in light of other studies

The overall fistula primary success proportion of 64 % compares favourably to Miller's study result of 47% success in a prevalent population of mixed first and subsequent fistulae surgeries. In our study, 36 subjects went on to have a second fistula attempted and 19 of these were successful which gives an overall success proportion of first and second fistulae of 61 %.

This result is similar to Konners' proportion of 60 %. In our study, forearm fistula success proportions in diabetics and in those aged greater than 65 were both over 60 %, contrasting with Millers' 21% and 12% success proportions in the same respective groups [17]. It should be noted that an advantage of our study is that, unlike the above two studies, we had comprehensive demographic and co morbidity baseline data, including separation of fistulae into upper arm and forearm locations. This allowed for an appreciation of the independent effect of sex on success of forearm fistulae.

Huber[25] studied predictors of fistula success in 139 surgeries. These subjects constituted the 82 % of prospective surgery candidates who had satisfactory vessels on Doppler ultrasound. Sixty % of these subjects had diabetes. Seventy one % of his subjects proceeded to undergo a first needling. Using this unsatisfactory definition of successful maturation, female gender and forearm fistula location statistically significantly predicted failure in a multivariable logistic regression analysis. This result concurs with our study (Table 5).

Feldman[25] recently published a prospective cohort study in 348 first hemodialysis fistulae subjects. He looked at demographic and co morbid determinants of fistula maturation success. Their study participants differed to those in our study in having a lower mean age of 58 years, a lesser proportion of Caucasians (44%) and only 12 % (compared to 43% in our study) with diabetes as the cause of ESRD. In addition, there was a higher proportion of subjects with a history of ischemic heart disease in our study. Success was defined in a similar manner to that used in our study, as successful needling in six (instead of three) consecutive hemodialysis runs. Unlike our study, data was also collected at the time of surgery and included variables like dose of heparin, mean arterial blood pressure and diameter of fistula veins. Logistic regression analysis was conducted using independent variables from demographic and baseline co morbidity variables (similar to our study) with the success of fistula development, as the outcome dependent variable. They performed a second logistic regression, which combined surgical, independent variables with the aforementioned risk factors. Cardiovascular disease (previous myocardial infarction/Coronary artery bypass grafting), mean arterial blood pressure < 85 mm hg, and dialysis dependency at the time of surgery were found to be independent, statistically significant, predictors of access failure in the first analysis, and vein diameter, age, and dose of heparin, were additional significant predictors in the combined model. Younger age, larger upstream vein diameter and larger doses of heparin independently predicted success in the combined model. Interestingly, age only became significant when adjusted for vessel size. I interpret this, as evidence that the larger vessels used in older subjects may have compensated for lower vessel quality. Like our study, they did not find sex or diabetes to be significant predictors of overall first fistula success. They did not include a sex/fistula location interaction term in their model so they did not investigate if sex was predictive of success in forearm fistulae. As 70 % of their subjects had a forearm fistula compared to 55 % in our study and they had a similar proportion of females they could have easily investigated this association.

They identified a history of cardiovascular disease as a significant risk factor, whereas we did not. This may have been due to differences in definition of cardiovascular disease, as the Charlson index does not use CABG history as a criterion. It was unlikely due to type 2 error in our study, as we had 81 subjects classified as having cardiovascular disease compared to 56 in Feldman's study. Alternatively, more appropriate subject selection criteria for fistula surgery choice or in selecting upper arm over forearm location may have occurred in our study.

The overall success in Feldman's study was 56 %, which was lower than the success proportion of 64% noted among our cohort, despite the greater prevalence of diabetes and vascular co morbidities amongst our subjects.

There was much more variability in success within groups, compared to our study. This may have been due to less appropriate selection of surgery subjects or alternatively to random variation or greater variation in surgical skill in their study. Insufficient selection for upper arm fistula location in Feldman's subjects may explain the larger differences in success within subgroups between the two studies.

Feldman's study excluded 86 subjects, based on patient refusal to participate, or inability to obtain surgical data. This may have lead to the introduction of selection bias, if success in this group related to predictor variables in a different manner to the study group. Moreover, the success proportion, in ineligible and eligible subjects combined may be different to the study group alone. No results on baseline covariates or success outcomes were provided on ineligible subjects, making it impossible to conclude if selection bias occurred, or if this group had a different success proportion. Our study included almost all subjects who had a first fistula created and thus was relatively immune from this source of potential selection bias or distortion of success proportion. Loss to follow up was not a factor in either study.

Feldman's group did not provide differences in demographic and baseline co morbidities between hemodialysis subjects who had grafts, or who had lines only. This makes it impossible to appreciate differences in selection criteria employed, in choosing these accesses.

Despite these misgivings, Feldman et al's conclusion that timing of fistula creation before initiation of hemodialysis, dose of heparin, size of fistula vein and intra-operative hypotension were significant predictors of success in the group studied appears to be a valid and clinically relevant conclusion. Feldman's study is the only other study in the literature, besides our own, that looks at determinants of success of first fistula development in a prospective cohort of incident hemodialysis subjects, using a clinically meaningful definition of success.

While we did not have information on specific vessel size pre or intra operatively, we did note that surgeons in our study who followed an algorithm of vessel size measurement by using catheters had better results in upper arm fistulae. Thus, vessel size determination by this means may facilitate improved selection of upper arm fistulae subjects.

It was of interest that timing of fistula placement before initiation of HD was associated with primary success in Feldman's study. This could be explained given that fistula placement before initiation of hemodialysis would obviate the need for central line access use, if the fistula were useable at the time of dialysis initiation. Central lines predispose to central venous stenosis. Thus, venous return through an ipsi-laterally placed fistula could, conceivably be compromised sufficiently to impair adequate maturation. Furthermore intra-dialytic, or central line related bacteremia induced-hypotension, could result in fistula thrombosis.

Small forearm veins in female fistula subjects, low mean arterial blood pressure, and finally low dose of heparin could all predispose to fistula failure by virtue of diminishing blood flow. Thus, the requirement of fistula blood flow, to attain and maintain a minimum threshold value may be the final common pathway through which all risk factors act, in determining success of fistula development.

Recommendations for future research

This prospective cohort study could be enlarged by including SARP subjects who commenced hemodialysis since November 2001. The risk of Type 11 error would be reduced with the increased number of study subjects. If gender remained a significant predictor of forearm fistula success with narrower confidence intervals, one would attach greater credence to this result. It is also possible that other risk factors would emerge.

A prospective clinical trial could be undertaken to assess for an association between primary success of fistulae and venous internal diameters (as measured by Doppler ultrasound pre and perioperatively), and to determine if there is a threshold below which the success rate becomes unacceptable. (It would be interesting to determine whether gender remained an independent statistically significant predictor of successful forearm fistula development. I would predict that the effect of gender would disappear on adjusting for vein size.) The effect of arterial internal diameter (as well as perioperative blood flow through the fistula) on successful fistula development could also be studied. Age, diabetes and co morbidity score might become significant predictors of successful fistula development after adjustment for vessel diameter and/or flow.

Conclusions and Recommendations

We were not successful in identifying subject risk factor profiles that could clearly differentiate those in whom a fistula would work from those in whom it would not. We did demonstrate that rational selection of fistula feasibility and location choice occurred. Male gender was the only significant predictor of (forearm) fistula success. Upper arm fistulae were significantly more likely to be successful than forearm fistulae in an adjusted interaction model (Table 5). Appropriate selection, however, resulted in identical success proportions for both fistula locations.

Our results surpassed the DOQI recommended objectives in fistula creation. Older age, diabetes, ischemic heart disease and other vascular co morbidities do not contraindicate attempting a fistula or even a forearm fistula if the vessels are adequate. The algorithm of catheter vessel measurement used by surgical group 1 may also help fistula feasibility choices and location selection.

Operational Definitions of Terms Used Within This Thesis

- End-stage renal disease (ESRD): a state of irreversible kidney failure, which if left untreated will result in severe symptoms and death. The treatments comprise peritoneal dialysis or hemodialysis or kidney transplantation.
- Peritoneal dialysis: a form of dialysis that is accomplished by instilling a special glucose in water solution through a permanent tube (the placement of which requires a short surgery) into the abdominal cavity and leaving the fluid in place for a period of 1 to 6 hours before it is drained out. The drainage immediately followed by instillation of fresh fluid is a procedure performed manually by the patient or automatically by a machine (usually in the patients' home) and needs to be repeated, several times per day.
- Hemodialysis: a form of dialysis that is performed in hospital or in an 'outpatient dialysis unit or at the patients' home. It involves sitting in a chair for three to four hours while the patients' blood is circulated through tubing and through a special membrane for cleansing. The patients' blood circulates from a vein in the patients arm or neck, through the membrane, and back to the vein repetitively during the course of a dialysis session. The hemodialysis nurse has to access the patients' venous blood by placing two needles in an arm vein or arm graft. Alternatively, the nurse accesses the internal jugular neck vein through a double lumen plastic catheter previously placed by a doctor.
- Fistula: a large vein that has been attached (anastomosed) to a nearby artery. Because it carries arterial blood under high pressure its' walls thicken (arterialize) and its' lumen dilates to accommodate the increased blood flow. This process takes several weeks before the vein (or fistula) can have two needles inserted to provide an exit and return conduit for blood flow during dialysis.

- Graft: a hollow cylindrical synthetic tube that the surgeon attaches between an artery and a vein, and superficially places under the skin of the upper arm or forearm. The hemodialysis nurse at the start of each dialysis session accesses the blood flowing through it. The “arterial” needle is attached to an extracorporeal plastic tube through which the patients’ blood flows and passes onto the dialysis membrane and then returns through another plastic tube to the patient via the “venous” needle.
- Primary success of fistula: Successful use of a fistula is defined as affording an extracorporeal blood flow of at least 300 mls per minute, for at least 3 hours, using an arterial and venous needle placed in the fistula, for a minimum of three consecutive dialysis sessions.
- Primary failure: this is the complement of primary success and is defined as the proportion of fistulae that do not develop satisfactorily for hemodialysis use, divided by the number of fistulae surgically created over a calendar period. The fistula may thrombose immediately or within the first 6-8 weeks, before ever being used. The fistula may fail to develop adequately and be judged by a nephrologist to be chronically unusable. Lastly, the fistula may primarily fail to provide dialysis after several initial attempts and end up being abandoned.
- Primary (unassisted) patency is the time from fistula creation until first thrombosis
- Secondary (assisted) patency is the time from fistula creation until its abandonment (i.e. the day of last use)

Table 1: Comparison of Demographic and Co-Morbid Variables in Fistulae, Upper Arm Fistulae, Forearm Fistulae, Grafts and Lines

Characteristic	Any Fistula (n = 205)	Forearm AVF (n = 113)	Upper Arm AVF (n = 92)	Grafts (n = 41)	Lines (n = 51)
Diabetes	47%	42%	53%	62%	35%
Female Sex	29%	24%	34%	61% [a]	45% [b]
Mean Age, Years	62.5	61.9	63.2	66.5	70 [c]
Mean Charlson Score	4.7	4.58	4.99	5.2	5.3
IHD [d]	40%	35%	46%	44%	40%
CHF [e]	37%	34%	40%	37%	47%
PVD [f]	20%	19%	22%	17%	27%
CVD [g]	17%	17%	16%	22%	16%

[a] p=0.0001, Chi2 test of two sample proportions comparing grafts with all fistulae

[b] p=0.006, Chi2 test of two sample proportions comparing lines with all fistulae

[c] p=0.0018, Two sample T Test comparing lines with all fistulas

[d] Ischemic heart disease

[e] Congestive heart failure

[f] Peripheral vascular disease

[g] Cerebrovascular disease

Table 2: Baseline Demographic and Co-Morbid Variables for Patients in Whom First Fistulae Were Placed (n = 205)

Characteristic	Proportion
Age	
< 65 yrs	51%
65 - 75 yrs	26%
> 75 yrs	23%
Male Sex	71%
Ethnic Group	
Caucasian	80%
Other	20%
Diabetes	53%
Surgical Approach	
1	65%
2	35%
Fistula Location	
Forearm	55%
Upperarm	45%
Ischemic Heart Disease	40%
Hypertension	87%
Peripheral Vascular Disease	20%
Congestive Heart Failure	37%
Cerebrovascular Disease	17%

Table 3 Baseline Demographic and Co-Morbid Variables for patients with Forearm and Upper Arm Fistula

Characteristic	Forearm Fistula (n = 113)	Upper Arm Fistula (n = 92)
Diabetes	42%	53%
Surgical Approach		
1	45%	55%
2	74%	26%
Hypertension	88%	86%
Peripheral Vascular Disease	19%	22%
Congestive Heart Failure	34%	40%
Cerebrovascular Disease	17%	16%

Table 4 Comparison of Success in Forearm and Upper Arm Fistulae Sub-Groups (Unadjusted)

Characteristic	Primary Success in Forearm Fistula		Primary Success in Upper Arm Fistula	
	Proportion	%	Proportion	%
Age				
< 65 yrs	40/57	70%	30/44	68%
> or = 65	32/56	57%	29/48	60%
Sex				
Female	12/27 [a]	44%	21/32	66%
Male	60/86	70%	36/60	63%
Diabetes				
Absent	38/65	58%	29/43	67%
Present	34/48	71%	30/49	61%
Surgical Approach				
1	37/60	62%	51/73 [b]	70%
2	35/53	66%	8/19	42%
Ischemic Heart Disease				
Absent	46/74	62%	35/50	70%
Present	26/39	67%	24/42	57%
Hypertension				
Absent	12/14	86%	8/13	62%
Present	60/99	61%	51/79	65%
Peripheral Vascular Disease				
Absent	60/92	65%	47/72	65%
Present	12/21	57%	12/20	60%
Congestive Heart Failure				
Absent	48/75	64%	35/55	64%
Present	24/38	63%	24/37	65%
Cerebrovascular Disease				
Absent				
Present	59/94	63%	48/77	62%
	13/19	68%	11/15	73%

[a] P = .017: Chi^2 two-sample test of proportions (Comparing proportion of females' successes to male successes in forearm fistula subjects).

[b] P = .025: Chi2 two-sample test of proportions (Comparing surgical approach 1 to 2 in upper arm fistulae success proportions).

Table 5 Logistic Regression of Fistulae Success and Its Association with Sex, Surgical Approach, Diabetes, Age and Fistulae Location Interaction Terms (n = 205)

	Odds Ratio	Probability	Confidence Interval
Sex (Male compared with female)	3.13	0.016	(1.04, 6.42)
Surgical Approach 2 (Compared with Approach 1)	1.25	NS	
Diabetes	1.94	NS	
Age < 65	1.67	NS	
Upper Arm Fistula (Compared with Forearm Fistula)	6.91	0.006	(1.74, 27.3)
Surgical App. X Surg. Location Interaction Term	0.21	0.024	(0.055, 0.81)
Sex X Surgery Location Interaction Term	0.26	0.047	(0.07, 0.98)
Diabetes X Surgery Location Interaction Term	0.32	0.073	(0.09, 0.73)

Table 6 Logistic Regression of Primary Success in Forearm Fistulae Considering Sex, Surgical Approach, Age and Charlson Score (n = 113)

Independent Variable	Odds Ratio	Probability	95% Confidence Interval
Sex (Male compared with female)	2.84	0.025	(1.23, 6.90)
Surgical Approach 2 (Compared with Approach 1)	1.29	0.529	NS
Age < 65	1.65	0.223	NS
Charlson Score	1.01	0.894	NS

Table 7 Logistic Regression of Upper Arm Fistulae Success Considering Sex, Surgical Approach, Age and Charlson Score (n = 92)

Independent Variable	Odds Ratio	Probability	95% Confidence Interval
Sex (Male compared with female)	0.78	0.618	NS
Surgical Approach 2 (Compared with Approach 1)	0.29	0.023	(0.1, 0.84)
Age < 65	1.51	0.36	NS
Charlson Score	1.02	0.68	NS

Table 8 Logistic Regression of Forearm Fistulae Success Considering Sex, Surgical Approach, Age, Diabetes, IHD, CHF, CVD and PVD (n = 113)

	Odds Ratio	Probability	Confidence Interval
Sex (Male compared with female)	3.57	0.012	(1.36, 9.38)
Surgical Approach 2 (Compared with Approach 1)	1.18	NS	
Age < 65	1.69	NS	
Diabetes	1.91	NS	
Ischemic Heart Disease	1.31	NS	
Congestive Heart Failure	1.21	NS	
Peripheral Vascular Disease	1.86	NS	
Cerebrovascular Disease	0.41	NS	

Table 9 Logistic Regression of Upper Arm Fistula Success and its Association with Sex, Surgical Approach, Age, Diabetes, IHD, CHF, CVD and PVD (n = 113)

	Odds Ratio	Probability	Confidence Interval
Sex (Male compared with female)	0.79	NS	NS
Surgical Approach 2 (Compared with Approach 1)	0.25	0.016	(0.08, 0.7)
Age < 65	1.63	NS	NS
Diabetes	0.79	NS	NS
Ischemic Heart Disease	0.58	NS	NS
Congestive Heart Failure	1.57	NS	NS
Peripheral Vascular Disease	2.31	NS	NS
Cerebrovascular Disease	0.62	NS	NS

Table 10 The determinants of Choosing Upper Arm Over Forearm Fistula Location Considering Sex, Surgical Approach, Diabetes, Age and Charlson Score

	Odds Ratio	Probability	Confidence Interval
Sex (Male compared with female)	0.56	0.038	(0.26, 0.96)
Surgical Approach 2 (Compared with Approach 1)	0.29	0.0001	(0.15, 0.55)
Diabetes	1.31	0.47	NS
Age > 65	1.05	0.88	NS
Charlson Index Score > Mean (Compared with < Mean)	1.25	0.55	NS

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Appendix 1: The weighted scoring system for the Charlson co morbidity index

Assigned Weights for Diseases	Conditions
1	Myocardial infarct
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease
	Diabetes
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end organ damage
	Any tumor
	Leukemia
	Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor
	AIDS

Assigned weights for each condition that a patient has. The total equals the score.
Example: chronic pulmonary (1), severe renal disease (2) and myocardial infarct (1) = total score (4)

Appendix 2:

Appendix 3: Access Information Abstraction Form

1. Name (Last name, first name) ___________________
2. Surgery number ___________________
3. First access date (YILMAZ) ___________________ (yy/mm/dd)
4. Access used >once
   YES
   NO (Access malfunction)
   NO (not enough time has elapsed)
   NO (death)
   NO (changed to PD)
   NO (transplant)
   NO (other reason _________________________________)
   UNKNOWN
   ____
5. First date of using permanent access (2needles) _______________________(yy/mm/dd)
6. First date of using access 3 consecutive times (2 needles, Qb >300)? _____________ (y/m/dd)
7. Used at 3 months (GORETEX)
   YES
   NO (Access malfunction)
   NO (not 3 months yet)
   NO (death)
   NO (changed to PD)
   NO (transplant)
   NO (other reason __________________________________)
   UNKNOWN
   ____

8. Used at 6 months (AVF)

YES

NO (Access malfunction)

NO (not 6 months yet)

NO (death)

NO (changed to PD)

NO (transplant)

NO (other reason ________________________)

UNKNOWN

____

9. Confirmed access failure YES / NO (Total abandonment)

10. Date of access failure _________________________ (month/day/year)

11. Reason for access failure

a) Thrombosis
b) Infection
c) Never fully matured
d) Other _______________________