Predictors for Failure to Mature of Autogenous Arteriovenous Fistulae: Alor Setar Experience

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INTRODUCTION
Renal replacement therapy in Malaysia has changed dramatically. In 1980 there were only 59 patients on dialysis. Since then the number of patients has increased exponentially from 4,540 in 1998 to almost 15,000 in 2006[1]. Autogenous Arteriovenous Fistula (AVF) provides an excellent long term hemodialysis access with low rates of infection, thrombosis and is cost effective.

Hospital Sultanah Bahiyah is a tertiary hospital situated in the northern region of Peninsular Malaysia. Vascular Access creation is one of the main services provided by our surgical unit; with an average of 100 patients seen in the vascular access clinic per month. The number of AVF operations has increased from 30 cases in 2001 to 328 in 2007.

The reported rates of Primary Fistula Failure (fistula fail to mature) varies from 8% to 53%[2,4]. Immature fistulae will lead to prolonged dependence on dialysis catheters. This phenomenon is well known to be associated with the risk of infective complications, central venous thrombosis or stenosis and patients' inconvenience. Numerous studies have reported the predictors of successful fistulae, but are varied in their design, definitions, end points and clinical factors considered [2,3] Preoperative imaging also has been proposed, but their widespread use is generally limited in most of the centres[4]. Knowing the risk factors for failure will help the surgeon to take the necessary precautions and preventive measures more effectively. The information may help to stratify the patients into various risk groups based on their likelihood to develop fistula failure. Thus, the main objective of this study was to identify clinical risk factors that are related to Failure to Mature (FTM) of autogenous AVF.

MATERIALS AND METHODS
We performed a one year prospective observational study from 1st January 2008 to 31st December 2008 in our institution, Hospital Sultanah Bahiyah, Kedah, Malaysia. Every patient aged between 15 to 80 years during the study period who had been referred to our vascular access clinic were screened and recruited if they fulfilled the criteria and gave informed consent. The patients also had autogenous AVF performed within the study period and complied with the post operative follow up plan. Two operating surgeons were responsible or performing all the AVF throughout the study period. Age in years, gender, type of co-morbidities, site of fistula, the highest intra-operative mean arterial pressure, vessel size, type of anastomosis, degree of atherosclerosis and presence of immediate post operative thrill were recorded.

Co-morbid illnesses are defined as the existing medical diseases associated with these patients such as Hypertension, Diabetes Mellitus, Cerebro-Vascular Accident, Ischemic Heart Disease and Peripheral Arterial Disease. Characteristics of Peripheral Arterial Disease (PAD) were history of claudication, absence of peripheral pulses and history of revascularization or amputation.

The sites of fistula were divided into three groups; distal fistula (distal radio-cephalic fistula-DRCF and Radio-cephalic Fistula- RCF), middle radio-cephalic fistula – MRCF and proximal fistula (Brachio-cephalic Fistula –BCF and Brachio-basilic Fistula- BBF).Size of the vessels was estimated intra-operatively in comparison with the rubber vascular loop. In our institution, we use two mm and three mm rubber loops. Presence and degree of arterial calcification were anticipated by preoperative arterial palpation and eventually confirmed intra-operatively. Degree of arterial calcification was divided into mild, moderate or severe based on surgeons' assessment. Patients were seen at least twice in the post operative follow up period. Premature failure was defined as absence of thrill along the arterialized vein within six weeks postoperatively. All data were entered using SPSS version 12.0[13]. The univariable analyses of continuous variables by independent t test; and of categorical variables by Chi square test were performed to determine which of these risk factors differed significantly between fistula FTM and fistulae that successfully matured. We proceeded to the final model of risk factors using multiple logistic regressions. To select the variables, the backward stepwise method was used. The level of statistical significance was set at p value of < 0.05 (2-sided). The results from multiple logistic regressions were shown as adjusted odds ratio along with their 95 confidence interval. We finally checked the Hosmer-Lemeshow test and its p-value for model fitness, the percentage of correct classification and area under curve from ROC graph.

RESULTS
There was a total of 310 autogenous AVF performed for 282 patients within this study period. Male to female ratio was 1.2 to 1. The mean age was 52.4 years with the majority between the ages of 40 to 60 years. A total of 45% of these patients had

two co-morbid diseases. About two thirds (72.6%) of the procedures were the distal fistulae, followed by middle radio-cephalic fistulae (17.7%) and proximal fistulae were only 9.7%.Overall, 100 AVF performed on 80 patients or 32.3% failed to mature (Table I). The success rate of distal fistulae (DRCF and RCF) was 64% (n=144), followed by middle fistulae 69.1 % (n=38).Proximal fistulae had the best success rate of 93.3% (n=28).Among these 80 patients with FTM, almost a quarter of them or 19 patients (6.1%) were the repeat failures. Only 27 patients of the failure group (8.7%) were successfully revised.

Results from univariable analyses are shown in Table II. Factors such as presence of PAD, site of fistula, low intra operative mean arterial pressure and presence of immediate post operative thrill were found to have association with FTM at univariable level, when the other confounders were not adjusted.

To establish the final model of factors that were associated with failure (Table III), multivariate analysis using multiple logistic regression was used. Presence of established PAD and low intra-operative mean arterial pressure were among the final variables or predictors of FTM, with adjusted OR of 3.53 (95% CI: 1.02, 12.25) and 0.971 (95% CI: 0.96, 0.98). More distally placed fistulae have higher risk of FTM as compared to middle and proximal fistulae, with adjusted OR of 0.57 (95% CI: 0.27, 1.18) and 0.08 (95% CI: 0.02, 0.39). Absence of immediate post operative thrill; with only palpable pulsation has an adjusted OR of 3.41 (95% CI: 1.97, 5.91). The risk of FTM was almost certain if neither post operative thrill nor pulsation was noted with adjusted OR of 43.69 (95% CI: 4.91,388.58).From Hosmer and Lemeshow test, the p value was 0.152 with overall correct classification equals 73.9% and the Area Under the Curve (AUC) equals 0.78.

DISCUSSION

Autogenous Arteriovenous fistula (AVF) is regarded as the first and perhaps the best choice of vascular access in hemodialysis patients. Among the various sites, fistula placed at the wrist is the first choice of access because of its simplicity and fewer complications [7,19,22]. Besides a complete history and examination, several imaging tools have been proposed in order to select the most suitable type and site of the permanent access. Despite all these, the failure rate of autogenous AVF which fail to mature has a wide range and differs from centre to centre. In relation to this, numerous studies have been performed in an attempt to correlate the factors responsible for failure of maturation of autogenous AVF. The rate of Primary Fistula Failure is reported as 8 to 53% [2,3,4,5,9,10].

Ernandez et al found that predictive factors of early failure were distal location with adjusted OR equaled 8.21 (95% CI: 2.63, 25.63, p < 0.001), female gender with adjusted OR equaled 4.04 (95% CI: 1.44, 11.30, p = 0.008), level of surgical expertise adjusted OR of 3.97 (95% CI: 1.39, 11.32, p = 0.010) and diabetes mellitus with adjusted OR equaled 3.19 (95% CI: 1.17, 8.71, p = 0.024). However these results were doubtful since the sample was quite small (n=119). In addition to that, his criteria for acceptable minimum number of fistula

performed by the surgeon per year (5 fistulae) was questionable and generally not accepted [2].

Miller et al. reported higher primary fistula failure rate in older and female patients with diabetes. Feldman et al. published data from his cohort of 348 patients, with to that, his criteria for acceptable minimum number of fistula performed by the surgeon per year (5 fistulae) was questionable and generally not accepted [2].

Miller et al. reported higher primary fistula failure rate in older and female patients with diabetes. Feldman et al. published data from his cohort of 348 patients, with primary success rate of 54%. Preexisting cerebrovascular disease, older age, and commencement of dialysis before access creation were noted to be associated with higher primary fistula failure [3,6,10]. Although diabetes affects the micro- and macro vasculature, we did not find it as predictor of FTM in our model.

Most authors demonstrated that vessel size of less than 2 mm was associated with high failure rate regardless of age, race and gender [3,6,8,11]. For instance, Wenjie W concluded that vessel size is the main determinant of the success [6]. However in our model, the vessel size was not statistically significant to predict FTM.

Charmaine et al have proposed their model of predictors of FTM and is perhaps the simplest and most easily used. From 442 patients in Canada, they found the clinical predictors which were significantly associated with FTM were: Age >65 yr (odds ratio [OR] 2.23; 95% confidence interval [CI] 1.25 to 3.96), peripheral vascular disease (OR 2.97; 95%CI 1.34 to 6.57), coronary artery disease (OR 2.83; 95% CI 1.60 to 5.00), and Caucasian race (OR 0.43; 95% CI 0.24 to 0.75). The resulting scoring system, which was then externally validated in 445 patients, had four risk categories for fistula FTM: low (24%), moderate (34%), high (50%), and very high (69%; trend P < 0.0001) [5].

From our final model (Table III), presence of established PAD and low intra-operative mean arterial pressure were among the final variables or risk factors of FTM, with adjusted OR of 3.53 and 0.971.To clarify this further, patients who have established PAD will have 3.53 higher risk of FTM compared to those who don't have PAD. Besides this, each mmHg increment in their intra operative mean arterial pressure will reduce the risk of FTM by about 3% respectively.

Charmaine et al included PAD as one of the predictors in their model with OR 2.97. Feldman found that MAP less than 85 mm Hg had a higher risk of FTM [3,5]., whereas A.Hassan concluded blood pressure of less than 100/80 mm Hg during dialysis was significantly associated with venous thrombosis [9]. These findings are very important since the majority of the patients are the elderly, diabetic and atherosclerotic. Physicians should alert their patients about this possibility. In addition to that, over vigorous control of the blood pressure indeed may result in FTM if not monitored closely. Similar to previous reports, we found that more distally placed fistulae have a higher risk of FTM as compared to middle and proximal fistulae, with adjusted OR 0.57 and 0.08.In other

Table I: Sites of AVF and Failure Rate

Sites	Successful	Fail	Total
Distal (DRCF and RCF)	144 (68.6%)	81 (81.0%)	225 (72.6%)
Middle (MRCF)	38 (18.1%)	17 (17.0%)	55 (17.7%)
Proximal (BCF and BBF)	28 (13.3%)	2 (2.0%)	30 (9.7%)
Total	210 (67.7%)	100 (32.3%)	310 (100%)

DRCF: distal radio-cephalic fistula   RCF: Radio-cephalic Fistula
MRCF: middle radio-cephalic fistula   BCF: Brachio-cephalic Fistula
BBF: Brachio-basilic Fistula

Table II: Univariate Analysis of the Predictors for Premature Failure of Autogenous AVF

Variables	Status		Crude P-value
	Successful n (%)	Fail n (%)	
Gender			
Male	120 (57.1)	49 (49.0)	0.178
Female	49 (42.9)	51 (51.0)	
Age (years)*	52.6 (11.8)	52.0 (10.8)	0.683
Highest Intra-operative Mean AP*	116.5 (22.2)	107.1(21.1)	<0.001
History of Hypertension			
No	25 (11.9)	15 (15)	0.447
Yes	185 (88.1)	85 (85)	
History of Diabetes Mellitus			
No	81(38.6)	33 (33)	0.342
Yes	129 (61.4)	67 (67)	
History of Ischemic Heart Disease			
No	189 (90)	89 (89)	0.787
Yes	21 (10)	11(11)	
History of Cerebral-Vascular Accident			
No	205(97.6)	99 (99)	0.409
Yes	5 (2.4)	1(1)	
History of Peripheral Arterial Disease			
No	203(96.6)	90 (90)	0.016
Yes	7 (3.3)	10 (10)	
Site of AVF			
Distal	144 (68.6)	81(81)	0.005
Middle	38 (18.1)	17 (17)	
Proximal	28 (13.3)	2 (2)	
Venous size			
2mm	29 (13.8)	25 (25)	0.020
3mm	106 (50.5)	51(51)	
4-5mm	75 (35.7)	24 (24)	
Arterial size			
2mm	18 (8.6)	15 (15)	0.006
3mm	88(41.9)	54 (54)	
4-5mm	104(49.5)	31 (31)	
Arterial calcification			
Yes	71 (33.8)	42 (42)	0.161
No	139 (66.2)	58 (58)	
Immediate Post Operative Thrill			
Strong thrill	152 (72.4)	37 (37)	<0.001
Only pulsation	57 (27.1)	54 (54)	
None	1(0.5)	9 (9)	

*mean (SD)

Table III: The Final Model from Multivariable Analysis of Predictors for Premature Failure of Autogenous AVF

Variable	b(se)	Adj OR (95% CI)	P-value
Iimmediate post operative thrill			
strong thrill	-	1	
only pulsation	1.23(0.280)	3.41(1.97,5.91)	0.005
no pulsation	3.78(1.115)	43.70(4.91,388.58)	0.001
Sites of AVF (Grouped)			
Distal	-		
Middle	-0.56(0.368)	0.57(0.28,1.18)	0.129
Proximal	-2.58(0.832)	0.08(0.02,0.39)	0.002
Intra-operative mean arterial pressure	-0.03(0.01)	0.97(0.96,0.99)	0.005
Presence of Peripheral Arterial Disease (PAD)			
No	-	1	0.047
Yes	1.26(0.635)	3.53(1.2,12.25)	

*Hosmer and Lemeshow test, p value = 0.152 (model is fit if p value is > 0.05)
*Overall correct classification = 73.9%.
*Area Under the Curve (AUC) = 0.78

words, the proximal fistulae have a success rate of 92% which is higher, as compared to distal and middle fistulae. Nevertheless, most people will still attempt the first fistula distally if other factors are feasible as recommended by the guidelines [7].

We also found a new variable (immediate post operative thrill) which has never been assessed in previous studies. Absence of immediate post operative thrill with only palpable pulsation has an adjusted OR of 3.41. The risk of FTM was almost certain if neither post operative thrill nor pulsation was noted with adjusted OR 43.69. This means the risk of FTM is 3.41 higher if only pulsation was felt; and worsens to 43.7 times if even pulsation is absent. However, this may be rather subjective since the vessels size, cardiac output and blood pressure may influence these findings. From Hosmer and Lemeshow test, the p value = 0.152 with overall correct classification = 73.9%. Area Under the Curve (AUC) = 0.78; compared to 0.69 in Feldman's study [3]. This predictor model is currently being validated externally in our institution.

In conclusion, our rate of FTM is comparable to published reports [2,3,4,5,9,10]. From our study, established peripheral arterial disease, distally placed fistulae, lower mean arterial pressure and absence of post operative immediate thrill were significantly associated with premature failure of autogenous AVF (overall correct classification = 73.9%). Factors leading to repeat failures need further evaluation. These simple predictors perhaps can be used to guide clinicians in better managing their renal failure patients.

LIMITATIONS AND RECOMMENDATIONS

Ideally we would like to assess the vessel size preoperatively by both clinical evaluation and ultrasound, but this was not possible due to limited resources. In future, we wish to organize a combined vascular access clinic with nephrologists to discuss the most appropriate access for dialysis for each of these patients, using our predictor model as a guide to decision making.

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