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CLINICAL & BASIC RESEARCH

Factors Affecting the Early Maturation of Arteriovenous Fistulae Created at a Tertiary Centre in Oman

Sheikha Al Hashmi,[1] Shouq Al Hudar,[1] Edwin Stephen,[2] *Dawood Al Riyami,[3] Hanan Al Maawali,[2] Ibrahim Abdelhady,[2] Khalifa Al Wahaibi,[2] Syed Rizvi[4]

abstract: ***Objectives:*** This study aimed to determine the risk factors associated with the failure of arteriovenous fistulae (AVF) maturation. ***Methods:*** This retrospective cohort study was conducted from January 2014 to December 2018 in Sultan Qaboos University Hospital, Muscat, Oman. Patients were followed-up 3 months after surgery, and their electronic medical records were accessed for demographic and clinical data. Univariate analysis was used to determine the risk factors associated with early AVF maturation and multivariant analysis was used to determine the predictive factors for AVF failure. ***Results:*** A total of 269 patients were included. Female gender was a significant factor affecting AVF maturity (P = 0.049), while age (P = 0.626), diabetes (P = 0.954), hypertension (P = 0.378), dyslipidaemia (P = 0.907), coronary artery disease (P = 0.576), cerebrovascular accident (P = 0.864), congestive heart failure (P = 0.685), previous central venous catheterisation (P = 0.05), fistula type (P = 0.863) and fistula site (P = 0.861) did not affect AVF maturation. Binary logistic regression showed that all the risk factors were insignificant. Failure of early AVF maturation affected 11.5% in the cohort. ***Conclusion:*** This study found that the proportion of early AVF maturation at our hospital is at par with that in the international literature. Failure of AVF maturation was significantly associated with the female gender. These findings can help nephrologists and vascular surgeons prognosticate AVF maturation rates. However, a larger study is needed for definitive conclusions.
Keywords: End Stage Renal Disease; Arteriovenous Fistula; Dialysis; Outcome.

Advances in Knowledge

- *The findings of this study will serve as a guide for vascular access teams regarding the proportion of early primary arteriovenous fistulae maturation failure and its predictive factors among Omani patients.*

Application to Patient Care

- *Knowing the risk factors associated with the failure of arteriovenous fistulae to mature will help improve the outcome, success rates of arteriovenous fistulae patency and quality of life of patients with end-stage renal disease in Oman.*

The incidence of end-stage renal disease (ESRD) in Oman was 120 per million population in 2013. It was more prevalent among males (57.1%) than females (42.9%), and the leading risk factor was diabetic nephropathy (46%), followed by hypertensive nephropathy (19%).[1]

An arteriovenous fistula (AVF) is a surgically crafted anastomosis between an artery and a vein at the level of the wrist, elbow, axilla or groin. This connection increases the blood flow through the vein, enlarges it and, over time, makes it thicker, allowing for dialysis needles to be inserted and for haemodialysis (HD) to be performed. This change that the vein undergoes, when combined with a blood flow rate through the vein of at least 300 mL/min, is called 'maturation of the fistula'. This maturation process normally takes 6 weeks from the time the AVF is created. AVFs are the commonest vascular access used for HD, but they are fraught with a high proportion of failure to mature.[2,3]

The literature defines 'failure of maturation' as when a fistula fails to achieve at least one of the following criteria 6 weeks after its creation: (1) blood flow proportion of greater than 600 mL/min, (2) vein diameter of greater than 6 mm and (3) a maximum depth of 6 mm from the skin surface.[4]

Multiple factors are involved in the functional maturation of AVFs and these factors can be demographic (including patient age, gender, race/ethnicity, etc.), clinical (such as the presence of cardiac disease, peripheral arterial disease, pulmonary hypertension, diabetes mellitus and obesity), haemodynamic (including vein size, feeding artery size and blood flow) or technical (such as the training/experience of the surgeon creating the AVF and the care and use of the AVF).[5] A study conducted in South Korea observed 15% failure of AVF maturation in their cohort of 60 patients.[6,7]

The current study aimed to determine the proportion and risk factors associated with early failure of maturation of AVFs created at Sultan Qaboos University Hospital (SQUH).

Departments of [2]Surgery and [3]Internal Medicine, Sultan Qaboos University Hospital and [4]Department of Family Medicine & Public Health, [1]Sultan Qaboos University, Muscat, Oman.
**Corresponding Author's e-mail: dawood@squ.edu.om*

Methods

This retrospective cohort study conducted in SQUH, Muscat, Oman and included all adult Omani patients who underwent AVF creation at the hospital between January 2014 and December 2018 and had their fistula's primary patency assessed at 3 months follow-up. Patients who had either not used the AVF for HD or had succumbed within the 3-month follow-up period were excluded.

For the purpose of the current study, patients were divided into two groups—those below 65 years of age and those 65 years old and above, based on the World Health Organization's definition of the term 'elderly'.

Data were collected from the hospital's electronic medical record system and included patient demographics such as age, gender, weight and height; history of previous tunnelled neck central venous catheter (CVC) insertion or failed AVF creation; and comorbidities including hypertension, diabetes mellitus (DM), dyslipidaemia (DLP), coronary artery disease (CAD), congestive heart failure (CHF) and cerebral vascular accident (CVA). All patients underwent a pre-operative ultrasound mapping and a venogram if there was history of tunnelled catheterisation. AVFs were created by three surgeons. Surgical data collected included anatomical factors such as the type of fistula (radio-cephalic AVF [RCAVF], brachio-cephalic AVF [BCAVF] and brachio-basilic AVF [BBAVF]) and site of fistula (left or right arm).

All patients were placed on 100 mg of acetylsalicylic acid pre- and post-operatively. Anticoagulants were only used in patients with atrial fibrillation. Furthermore, information about the HD sessions, such as blood flow through the dialyser and outcomes of AVF maturation, were obtained.

The collected data were analysed using the Statistical Package for Social Sciences (SPSS), Version 23 (IBM Corp., Armonk, New York, USA). The fistulae were evaluated at 3 months post-creation to check if they successfully withstood at least 6 sessions of HD, with an adequate flow rate and ease of cannulation. An AVF was considered mature if it met the above-mentioned criteria. For continuous variables, mean and standard deviation were used. Body mass index (BMI) was calculated as body weight kg/height in m^2; obesity was defined as BMI >29.9 kg/m^2 and overweight was defined as a BMI between 25–29.9 kg/m^2. A Chi squared test was used to find the association between the proportion of failure of AVF maturation and each studied variable. A P value <0.05 was considered statistically significant. Frequency tables were used to get the frequencies and percentages of demographic variables as well as the prevalence of diseases. Multivariate analysis (binary logistic regression analysis) was also performed to identify the significant independent factors.

Ethical approval was obtained from the Medical Research Ethics Committee at the College of Medicine and Health Sciences in Sultan Qaboos University.

Results

A total of 282 patients underwent AVF creation during the study period. After excluding patients who did not use the AVF for HD during the 3-month follow-up period and those who died before using the fistula (n = 13), 269 patients remained in the study.

There were 161 (59.9%) males and 108 (40.1%) females, with a mean age of 54.8 ± 15.7 years (age range: 18–90 years). BCAVF was the most common type of AVF created (n = 195, 72.5%), followed by BBAVF (n = 64, 23.8%) and RCAVF (n = 10, 3.7%). Failure of early maturation occurred in 11.5% of patients at 3 months post-creation [Table 1].

Of the 269 patients, the AVF of 13 (8%) of the 161 males and 18 (16.7%) of the 108 females failed to mature at 3 months post creation (P = 0.049), showing a significant association between gender and failure and a relative risk of 2.277. Binary logistic regression analysis also resulted in a similar conclusion.

Majority of the patients (72.1%) were elderly, with an early failure of AVF maturation at 9.3%; whereas, in the group of patients aged 65 years and below (27.9%), 12.4% had failure of maturation (P = 0.626).

Approximately 27.1% of the patients in the cohort were obese, 45.7% were overweight and the remaining 27.1% had a normal BMI. The proportion of early failure among the obese, overweight and normal BMI patients was 13.7%, 11.4% and 9.6%, respectively (P = 0.737).

Hypertension was the commonest comorbidity (n = 242, 89.9%), followed by DM (n = 181, 67.2%), CAD (n = 63, 23.4%) and past history of CVA (n = 28, 10.4%). A total of 26 of the 31 patients with failed AVF were hypertensive (P = 0.378). Diabetic patients constituted 66.5% (n = 179) of the cohort, and 11.7% of them had an early failed AVF compared to the non-diabetic patients (11.2%; P = 0.954). Sixty-three (23.4%) patients in the current study had CAD and 9 of them (29.0%) had early failure of AVF maturation (P = 0.576). Furthermore, 10.4% of the cohort had a history of CVA, and 4 of them had failed AVF maturation (P = 0.864).

Of the 31 patients with failed AVF, 26 had hypertension (10.7%; P = 0.378), 21 had DM (11.7%; P = 0.954), 9 had CAD (14.3%; P = 0.576), 4 had a history of CVA (14.3%; P = 0.864), 11 had a previous history

Table 1: Distribution of the study participants among different variabilities (N = 269).

Characteristic	n (%)
Mean age in years ± SD (range)	54.8 ± 15.7 (18–90)
Gender	
Male	161 (59.9)
Female	108 (40.1)
Mean BMI in kg/m² ± SD (range)	28.0 ± 6.3 (13.9–54.9)
Side of AVF	
Right	49 (18.2)
Left	220 (81.8)
Type of AVF	
Radio-cephalic	10 (3.7)
Brachiocephalic	195 (72.5)
Transposed brachio-basilic	64 (23.8)
Comorbidities	
HTN	242 (89.9)
DM	181 (67.2)
DLP	99 (36.8)
CAD	63 (23.4)
CHF	46 (17.1)
CVA	28 (10.4)
PVD	13 (4.8)

SD = standard deviation; BMI = body mass index; AVF = arteriovenous fistula; HTN = hypertension; DM = diabetes mellitus; DLP = dyslipidaemia; CAD = coronary artery disease; CHF = congestive heart failure; CVA = cerebral vascular accident; PVD = peripheral vascular disease.

of DLP (P = 0.907), 4 had a history of CHF (P = 0.685) and 26 (10.7%) had a history of CVC insertion (P = 0.05).

The rate of failure of maturation in each type of fistula is as follows: RCAVF: 1 (10%); BCAVF: 21 (10.7%); and BBAVF: 9 (14%) (P = 0.863). In the 269 AVFs created, 220 were created in the left upper limb and 49 in the right; 25 (11.4%) of the left-sided AVFs and six (12.2%) of the right-sided AVFs failed to mature (P = 0.861) [Table 2].

Univariate analysis showed gender to be the only significant risk factor for failure to mature; the risk of failure in females was found to be 2.277 times higher than that in males. For the binary logistic regression analysis, BMI and hypertension were also added as risk factors, and the analysis found all 3 risk factors to be insignificant [Table 3].

The rate of early failure of AVF maturation was 11.5% in the current study's cohort; i.e. 31 newly created AVF were considered to have failed because they could not adequately support dialysis, be needled or allow more than 300 mL/min of blood flow through them (which is needed for successful dialysis treatment) within the first 3 months of their creation.

Discussion

This study was the first of its kind in Oman, as per the English-language literature. It aimed to assess the prevalence of failure of early maturation of AVFs in Omani adults as well as the risk factors associated with this key performance indicator.

The rate of maturation of AVF created at a single centre in Oman, determined at 3 months post creation, was 88.5%. This study shows a lower proportion of early failure of AVF maturation when compared with other single-centre international studies from North America, Korea and the Netherlands.[6–8] Previous studies used ultrasound to evaluate artery size, venous dimensions and blood flow before subsequently predicting AVF maturation.

This study used a different definition for early failure of AVF maturation: non-matured AVFs comprise those that either fail to be cannulated during HD sessions or fail to achieve blood flow (≥300 mL/min) within 3 months of their creation. The reason for the difference in the proportion of early failure of AVF maturation between this study and previous research could be due to the relatively lower mean age of this study's cohort, the higher proportion of BCAVF in this study, the different definition used for failed AVF and the differences in the number of centres involved, the surgeons' experience, conduction of primary-assisted/secondary interventions and ethnicity. The higher proportion of BCAVF in the current study's cohort reflects the effect of pre-operative vein mapping, likely leading to the avoidance of RCAVF, which is known to have higher proportion of failure. Therefore, sparing the patient from undergoing a second surgery.

There was no significant difference in the proportion of early failure of AVF maturation between the two age groups. This result is inconsistent with a meta-analysis conducted in the USA, which revealed a statistically significantly higher proportion of failure of AVF maturation in elderly patients, with an odds ratio of 1.525. This significant difference is explained by the presence of comorbidities such as diabetes, DLP and cardiovascular disease in elderly patients, which exerts a stronger effect on AVF maturation compared with age alone. Furthermore, elderly patients experience health issues including arteriosclerosis, poor-quality veins and thin skin, which affect the maturation process of the vascular access.[9] The explanation for this difference in results can be the relative significant

Table 2: Analysis of the risk factors associated with failure of AVF maturation (N = 269).

Characteristic	n (%)			*P* value
	Total	Failed AVF (n = 31)	Mature AVF (n = 238)	
Gender				0.049 RR = 2.277
Male	161	13 (8.1)	148 (91.9)	
Female	108	18 (16.7)	89 (83.3)	
BMI				0.737
Normal	73	7 (9.6)	66 (90.4)	
Overweight	123	14 (11.4)	109 (88.6)	
Obese	73	10 (13.7)	63 (86.3)	
Age in years				0.626
<65	194	24 (12.4)	170 (87.6)	
≥65	75	7 (9.3)	68 (90.7)	
Previous catheter				0.05
Yes	249	26 (10.4)	223 (89.5)	
No	20	5 (25.0)	15 (75.0)	
Anatomical site				0.863
RCAVF	10	1 (10.0)	9 (90.0)	
BCAVF	195	21 (10.7)	174 (89.3)	
BBAVF	64	9 (14.0)	55 (86.0)	
Side of AVF				0.861
Left	220	25 (11.4)	195 (88.6)	
Right	49	6 (12.2)	43 (87.8)	
Hypertension				0.378
Yes	242	26 (10.7)	216 (89.3)	
No	27	5 (18.5)	22 (81.5)	
Diabetes mellitus				0.954
Yes	181	21 (11.7)	159 (88.3)	
No	88	10 (11.2)	79 (88.8)	
Dyslipidaemia				0.907
Yes	98	11 (11.2)	87 (88.8)	
No	171	20 (11.7)	151 (88.3)	
CAD				0.576
Yes	63	9 (14.3)	54 (85.7)	
No	206	22 (10.7)	184 (89.3)	
CHF				0.685
Yes	46	4 (8.7)	42 (91.3)	
No	223	27 (12.1)	196 (87.9)	
CVA				0.864
Yes	28	4 (14.3)	24 (85.7)	
No	241	27 (11.2)	214 (88.8)	

AVF = arteriovenous fistula; RR = relative risk; BMI = body mass index; RVAVF = radio-cephalic AVF; BCAVF = brachio-cephalic AVF; BBAVF = brachio-basilic AVF; CAD = coronary artery disease; CHF = congestive heart failure; CVA = cerebellar vascular accident.

Table 3: Risk and 95% confidence interval following univariate and multivariate (logistic regression) analyses

Characteristic	Univariate	Multivariate
	RR (95% CI)	RR (95% CI)
Gender	2.277 (1.065–4.869)	1.860 (0.782–4.425)
Hypertension	0.530 (0.158–1.518)	0.606 (0.153–2.409)
BMI	1.544 (0.650–3.668)	1.526 (0.604–3.854)

RR = relative risk; CI = confidence interval; BMI = body mass index

lower mean age of the current study's cohort, as well as the exclusion of older patients who died before using AVF from the statistical analysis.

The current study found a significant difference in the proportion of males and females who had early AVF maturation failure. Female patients had a higher rate of early AVF maturation failure compared to male patients. This finding is consistent with a cohort study done in the USA, in which fistula adequacy for dialysis was lower in females compared to males (31% versus 51%). In fact, increasing blood flow through the arteriovenous connection and adequate dilation of the blood vessel are essential for AVF maturation.[10] This significant difference in failure proportion between males and females can be explained by the smaller vessels of female patients compared to males, which decreases the chances of a new fistula maturing to an adequate size in them. Another possible explanation is the differences in vascular reactivity and platelet aggregation after vascular injury between the sexes. In addition, there are differences in the ability of veins to dilate when exposed to high pressure (such as after AVF creation) between the sexes.[11]

The current study found no significant difference in the proportion of early AVF maturation failure between obese, overweight and normal BMI patients. This finding is inconsistent with that of a cohort study done in the USA, which found that obese patients had a higher failure rate compared to non-obese patients, with a relative risk of 3.05. This is because obese patients have higher levels of C-reactive protein, which induces blood vessel intimal hyperplasia, resulting in stenosis and thrombosis. Obese patients also have a hypercoagulable state, which increases the likelihood of thrombus formation and, subsequently, reduces the chance of an AVF to mature and be usable. A second potential explanation is that obesity makes it difficult for the surgeon to identify suitable vessels for fistula creation. Additionally, obese patients could have very deep arteriovenous connections that cannot be successfully cannulated with the dialysis needle. Consequently, the fistula must undergo transposition to be sufficiently superficial to offer anatomic landmarks and allow for safe cannulation.[12,13] The differences in findings between the current study and previous ones can perhaps be explained by the small sample size of this study and the relatively lower mean BMI of this study's cohort.

The current study indicated that there is no relation between hypertension and failure of AVF maturation. This result is similar to that of studies conducted by Kim *et al.* in the USA.[14,15]

DM was considered a significant predictor of AVF maturation failure in a study conducted in San Francisco, USA. This is because DM causes metabolic changes that can cause endothelial changes and growth factor deregulation, with increased matrix deposition, all of which may lead to stenosis and thrombosis and thus failure of AVF maturation.[16] The current study has shown that DM is not a significant risk factor for AVF maturation failure, a finding that is in line with that of a study conducted by the University of Arizona Health Sciences Center in Tucson, USA.[15]

DLP was found to be a non-significant factor affecting AVF maturation. This result conflicts with that of a study from Canada, which indicated that DLP was a significant risk factor for AVF maturation failure, explaining that DLP aids the formation of calcified plaques, which lead to subintimal hyperplasia and decreased vessel diameter, causing AVF maturation failure.[4] The differences between these studies' results may be due to the different sample sizes and the fact that the prevalence of DLP in the group with and without failure was almost the same.

CAD is one of the main causes of atherothrombosis, which can cause thrombosis of the connected vessels in an AVF and thus cause failure of AVF maturation.[17] A prospective study of 422 patients showed that CAD is a significant factor affecting the failure of AVF maturation. This result conflicts with that of the current study, which indicated that CAD does not significantly affect AVF maturation. The conflict between the two results can be explained by the differences in sample size between the two studies as well as the difference in the type of study itself.[18]

CVA was found to be a non-significant factor in the current study; this result coincides with that of a study in Canada.[18] The agreement between the results strongly indicates that there is no relationship between CVA and failure of AVF maturation.

The current study's results have shown that CHF is not a significant factor affecting AVF maturation. This result is supported by three other studies conducted in Portugal, Canada and USA.[18–20]

There is a discrepancy between studies about the relationship between previous CVC insertion and the failure of AVF maturation. A study in the USA found previous CVC to significantly affect AVF maturation, explaining that previous CVC forms stenosis, which

affects vascular access outcomes.[15] The current study's finding that previous CVC is not a significant risk factor aligns with the results of a study done in Tucson (USA) from 2003–2007 among 298 patients.[20]

Lauvao *et al*. reported that there is no relationship between the type/site of AVF (RCAVF, BCAVF or BBAVF) and its maturation, which aligns with the current study's results.[16] However, this finding can be attributed to the dependence of AVF maturation on the diameter of the vessels used and on how healthy they are.

It is recommended that AVFs be created on the non-dominant arm or the arm that is not frequently used. This is to allow patients to have a free dominant hand with which they could easily complete their desired activities while receiving dialysis. However, if the non-dominant arm is not suitable for AVF creation, the dominant arm will be used.[16] This study showed no significant difference in failure proportion between AVFs created on the right and left arm of the patients. This finding is consistent with that of a single-centre cohort study done in the United Kingdom, which found no significant difference in failure proportion between fistulas in dominant and non-dominant arms.[21]

One of limitations of the current study is its retrospective nature, which may have affected the results due to the absence of some data in the patients' record. Second, it was a single-centre study, and although SQUH is a large referral centre, it does not adequately represent other centres in Oman. Finally, the current study's cohort was small and the duration of follow-up was short.

Conclusion

The proportion of early AVF maturation failure was 11.5% in the current study's cohort, which is lower than the range reported in the international literature. Female patients were at higher risk of AVF maturation failure than the male patients. Preoperative ultrasound-guided vein mapping is helpful for evaluating and choosing the appropriate vessel for AVF creation and for postoperative follow up to check the AVF's maturity or detect early complications. This group of patients should be closely monitored as endovascular or surgical intervention can be offered to improve the primary patency of a fistula.

AUTHORS' CONTRIBUTION

DR conceptualised and designed the study. ES and KW contributed to the methodology design. SHa, SHu and HM collected the data under the supervision of DR. All authors drafted the manuscript and approved the final version.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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