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Risk Factors in Early Arteriovenous Fistula Failure

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Abstract

Introduction. Nearly 20-60% of arteriovenous fistula (AVF) failure occurs at early stage. It was our aim to evaluate some risk factors in early AVF failure and postoperative complications of AVFs created for hemodialysis (HD) in two hospitals.

Methods. For this retrospective study data were evaluated from 210 patients who underwent AVF procedures for HD and selected by simple sampling method. All procedures were performed under local anesthesia and general anesthesia. Clinical, biochemical characteristics, AVF site and type, anesthetic techniques and postoperative complications of AVFs were collected from a check list. Both descriptive and statistical analysis methods were applied (P value <0.05).

Results. Overall 218 AVFs were created**.** Early AVF failure or thrombosis was seen in 25 cases (25/218 [11.46%]). Analyzing the risk factors of early failure or thrombosis of AVFs, multivariate logistic regression showed a significant correlation between female sex (OR=3.146, 95% CI 1.662-6.124), age >65 years (OR=3.410, 95% CI 1.541-5.523), diabetes (OR=1.125, 95% CI 0.873-2.576), hypertension (OR=1.411, 95% CI 0.831-3.351) and general anesthesia (OR=1.599, 95% CI 1.184-2.048) with early failure or thrombosis of AVFs**.**

Conclusion. Our rate of AVFs failure is comparable to published reports. Female sex, age >65 years, diabetes, hypertension and general anesthesia have negative effect on AVFs patency.

Keywords: arteriovenous fistulae, early failure

Introduction

Chronic renal failure (CRF) is unalterable decline of kidney work that usually develops to-end stage renal disease (ESRD). In this condition, renal replacement therapy (RRT) or hemodialysis (HD) is necessary for survival. Unfortunately, in recent years due to increasing rates of diabetes, hypertension, ageing population and etc. the incidence of ESRD is rising worldwide [1,2]. Just during the last 2 decades, the annual growth of patients was 6-12% in many developed countries [3].

Patients with ESRD need to receive HD through a durable access to the circulatory system to feed the extracorporeal circuit until RRT [4]. The ideal permanent vascular access should provide suitable supply blood flow rates to deliver the prescribed dialysis dose and minimal complication rates from infection and thrombosis. There are three main types of permanent vascular access used in HD patients: arteriovenous fistula (AVF), synthetic arteriovenous graft (AVG), and central venous catheter (CVC).

AVF is a surgically created communication between artery and vein that results in increased blood flow through an accessible conduit- it is created to meet this minimum flow requirement in patients. Today, it has been well established that autologous arteriovenous fistula (AVF) has higher patency rates and lower access complication rates as well as low risk of infection, hospitalization, and death than other forms of vascular access including grafts or catheters among ESRD patients and is a milestone of hemodialysis.

Similar to other performed procedures, AVFs are susceptible to access failure and associated complications. One of the usual complication is primary failure and presented as an AVF that never develops to support cannulation with 2 hemodialysis needles or unsuccessful within the first 3 months after its beginning cannulation [5]. Unfortunately, approximately 20-60% of AVF failure occurs at early stage [6]. This high failure rate depends on preoperative arterial and venous diameters, postoperative flow through the AVF, anesthetic and surgical techniques, AVF site, etc. [7].

If we could find the modifiable risk factors related to patency loss of AVF, it would be a substantial knowledge for improvement of AVF survival, life and health quality of the hemodialysis patients and decrease relevant costs. This work obviously decreased patients and their families' discomforts and distress and conspicuously

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increased their psychophysical health status. In this study, it was our aim to evaluate some risk factors in early AVF failure (patient clinical and paraclinical characteristics, AVF site and type, anesthetic techniques) and postoperative complications of AVFs created for HD in two hospitals.

Materials and methods

This observational retrospective analysis was performed in 210 patients who underwent upper limb vascular access (AVF procedures) for HD selected by a simple sampling method between March 2013 and April 2016 in two hospitals (Takestan Tamin Ejtemaei Hospital, Takestan, Iran and Velayat University Hospital, Qazvin, Iran). All patients had chronic renal failure and were appropriately referred by nephrologists for vascular access. All subjects accepted the information sheet and signed the consent form.

We categorized the subjects in two groups: a group with early AVF failure and a group with successful AVF creation.

Data collection tool consisted of a check list that contained the following information: demographic data such as gender, age, smoking, cause of renal failure, clinical and biochemical characteristics [waist circumference (WC) Body Mass Index (BMI), systolic and diastolic blood pressure (SBP,DBP), fasting blood sugar (FBS), lipid profile (Chol, LDL-C, Triglyceride, HDL cholesterol)], type of anesthesia (regional, general), type of AVF (Brescia-Cimino, Snuffbox, Brachiocephalic or Brachiobasilic), early complications (thrombosis, infection, psuedoaneurysm, hyperemia, hematoma, revisions due to hemorrhage). Subjects with medical history of myocardial infarction and associated interventional therapy, limb amputation due to peripheral artery occlusive disease, coagulopathy disorders, septicemia, Hb<7.5g%, veins<3 mm diameter, and arteries<2 mm diameter were excluded from the study [8].

Height and weight were assessed barefoot with tender underwear by using a wall-mounted stadiometer and calibrated digital scales, respectively. Height was rounded to the nearest 0.5 cm and weight to the nearest 0.1 kg. BMI was defined as weight in kilograms divided by height in meters squared (kg/m^2). On the basis of BMI, subjects were divided to normal weight (BMI= 18.5-24.9), overweight (BMI>25-29.9), and obese (BMI>30). WC was measured midway between the iliac crest and border of lower rib. Waist girth more than 102 cm for men and 88 cm for women indicated central obesity. Blood pressure was measured by trained and approved staff with a random zero sphygmomanometer, after the participant had been sitting for 5 minutes. The measurement of BP was done in the left mid arm by using a suitable gauge cuff. Systolic (the appearance of the first Korotkoff sound) and diastolic (the Korotkoff sounds were vanished) blood pressure were measured two times and mean of them was representative of BP.

Venous blood samples were obtained before the AVF surgery for measurements of fasting glucose levels as well as a lipid profile by certified staff after an overnight fast. After centrifugation, separated serum was immediately frozen at -20°C. Biochemical analyses were performed by using available calibrated auto-analyzer, Selectra 2, and kits of Pars Azmoon (Pars Azmoon Inc., Iran). Serum fasting blood glucose, total cholesterol, triglyceride and high density lipoprotein cholesterol, HDL-C were assayed using salt fractionation, glucose oxidase, enzymatic method, enzymatic method with glycerol phosphate oxidase and enzymatic method after precipitation with phosphotungstic acid, respectively. Low density lipoprotein cholesterol, LDL-C was calculated by using Friedwald,s formula (triglyceride≤400 mg/dl) [9].

The inclusion criteria were as follows: abdominal obesity (WC≥102 cm in men and ≥88 cm in women) or BMI>30, [2] elevated triglyceride level (≥150mg/dL); [3] low HDL cholesterol level (<40mg/dL for men and <50mg/dL for women); [4] elevated blood pressure (systolic≥130 mm Hg or diastolic≥85 mm Hg); and [5] elevated fasting plasma glucose concentration (>100 mg/dL) [10,11].

In the beginning of the study, careful examination of the arteries and superficial veins of the upper extremity (arterial pulse strength, presence of a recent access, formation of a prominent elastic structure upon application of pressure, and vein diameters) was performed in all study patients. For those patients who had more than one suitable site, the most distal one was generally selected in order to preserve the proximal site.

Thrombosis formation within the first month was supposed to be "early". Fistulae that were created two or more times were considered to be "repetition". All of the patients were followed up for the period starting from the creation of the AVF to the first HD.

Surgical and anesthetic techniques

Since our intention was to preserve the opportunity to move the AVF more proximally, the non-dominant upper extremity was primarily chosen for AVF. All surgical interventions were performed under local anesthesia, but if the local anesthesia was deemed inadequate, the patient was given general anesthesia. When creating the fistula, some factors including history of thrombophlebitis, prominence of superficial veins, segmental stenosis in the proximal vessel, atherosclerosis of the radial artery, and blood flow were considered.

Ethical approval

All subjects accepted the information sheet and signed the consent form. The patient-related information was

kept confidential. The study was approved by the Ethics committee of the Takestan Tamin Ejtemaei before its initiation, and the protocols used conformed to the ethical guidelines of the 1975 Helsinki Declaration.

Statistical analysis

The statistical evaluation was performed by the statistical SPSS Software (Statistical Package for Social Sciences, version 11.0, SPSS Inc., Chicago, Ill, USA). Descriptive statistics such as mean and standard deviation were applied. One-way ANOVA, Student's t-test, chi-square, or Fisher's exact test were used, where appropriate, for comparing clinical data between groups. P value less than 0.05 was considered significant.

Results

Although 210 patients participated in this study, overall 218 AVFs were performed (AVFs were created two times in 8 patients due to early failure). Of these patients 109(51.91%) were male and 101(48.09%) were female. The mean age was 50±3.5 years (range 29-72 years). Twenty-five (11.9%) subjects had smoking habit. Basic clinical and biochemical characteristics of participants are summarized in Table 1.

Table1. Basic clinical and biochemical characteristics of 210 participants

Variables	Mean± SD
Gender Male Female	N= 109 (51.9%) N= 101 (48.1%)
Age (Yrs)	50±3.5
WC (cm)	76±31
BMI (Kg/m2)	22.9±8.6
SBP (mmHg)	105±40
DBP (mmHg)	65± 25.5
TG (mg/dl)	135±100
Chol (mg/dl)	110±70
HDL (mg/dl)	25±14
LDL (mg/dl)	120±20
FBS(mg/dl)	178±42

WC: Waist Circumstances SBP: Systolic Blood Pressure, Diastolic Blood Pressure, FBS: Fasting Blood Serum, TG: Triglyceride, LDL: Low Density Lipoprotein, Chol: Cholesterol, BMI: Body Mass Index

Diabetes and hypertension were two major causes of ESRD in our patients; they are shown in Figure1.
Of the 218 AVFs, complete brachial plexus block was achieved in 141 (64.67%) cases. Thirty-eight (17.43%) cases were converted to general anesthesia and 39(17.88%) had AVF under general anesthesia from the start. Also, of all the AVFs, 145 (66.51%) cases were Brescia-Cimino AVF, 54(24.77%) cases were snuffbox AVF, and 19(8.71%) were antecubital brachiocephalic or brachiobasilic AVF (Table 2 summarizes types of AVF created based on the technique of anesthesia).

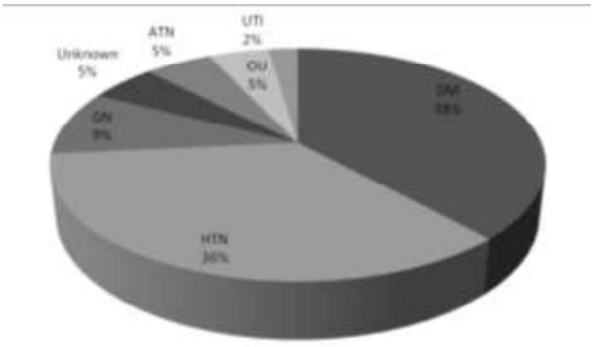

Fig. 1. Causes of ESRD in study patients
ATN=acute tubular necrosis; DM=diabetes mellitus; GN= glomerulonephritis; HTN=hypertension; OU=obstructive uropathy, UTI=urinary tract infections.

Table 2. Types of AVF created based on anesthesia type

Parameters	General anesthesia (n=77)	Regional anesthesia (n=141)
Brescia-Cimino	50	95
Snuffbox	21	33
Brachiocephalic	4	9
Brachiobasilic	1	5

The majority of patients (188/210 [89.52%]) in this study were undergoing their first AVF formation, whereas 22 patients (10.48%) had at least one previous fistula. Surgical intervention was performed on the left upper extremity in 139 (66.19%) patients and on the right upper extremity in 71 (33.81%) patients. Overall early AVF failure or thrombosis was seen in 25 cases (25/218 [11.46%]). Of these patients 16 cases was seen in Brescia-Cimino AVF group (16/145 [11.03%]), 7 cases in snuffbox AVF group (7/54 [12.96%]) and 2 cases were seen in antecubital brachiocephalic or brachiobasilic AVF group (2/19 [10.52%]). These results showed no significant difference between types of AVF on early failure or thrombosis (p=0.08) (Table 3).

Table 3. Effect of type of AVF on early failure or thrombosis

Type of AVF	No. of early failure or thrombosis of AVFs	Percentage
Brescia-Cimino (no=145)	16	11.03%
Snuffbox (no=54)	7	12.96%
Brachiocephalic or Brachiobasilic (no=19)	2	10.52%

p value between the three types of AVF=0.08; One-way ANOVA test

All cases with early AVF failure were subjected to repeated surgical intervention (AVFs were created two times in 8 patients). Also, thrombectomy was utilized successfully in 17 patients who presented with thrombosis. Therefore, early patency was found in 88% (185/210) of the AVFs created.

For analyzing the risk factors of early failure or thrombosis of AVFs, the multivariate logistic regression showed no significant correlation between male sex, smoking, body mass index >30 kg/m^2, hyperlipidemia, regional anesthesia and type of AVFs with early failure or thrombosis of AVFs. However, this analysis indicated that female sex (OR=3.146, 95% CI 1.662-6.124), age >65 year (OR=3.410, 95% CI 1.541-5.523), diabetes (OR=1.125, 95% CI 0.873-2.576), hypertension (OR=1.411, 95% CI 0.831-3.351) and general anesthesia (OR=1.599, 95% CI 1.184-2.048) were associated with early failure or thrombosis of AVFs (Table 4).

Overall complications were observed in 32/218 [14.67%] AVFs. Of these cases, 17 had early thrombosis and 15 cases had complications in the surgical area. Three patients had hyperemia at the incision site, 4 had infection at the incision site, 5 had hematoma at the incision site and 3 patients had revisions due to hemorrhage (Table 5). Regression of hyperemia and infection was achieved by standard antibiotic therapy, and re-exploration was performed for hematoma. There were no major complications from general or regional anesthesia in the present study. The patients commenced dialysis program approximately 4.6±2.4 weeks after AVFs were created.

Table 4. Multivariate logistic regression analysis for overall early failure or thrombosis of AVFs

Factors	Odd Ratio (95% Confidence Interval)	p-value
Male sex	2.430 (0.984-4.988)	0.078
Female sex	3.146 (1.662-6.124)	0.005*
Age > 65 years	3.410 (1.541-5.523)	0.012*
Smoking	1.635 (0.686-3.600)	0.118
Body mass index >30 kg/m^2	1.321 (0.574-2.792)	0.087
Diabetes	1.125 (0.873-2.576)	0.011*
Hypertension	1.411 (0.831-3.351)	0.014*
Hyperlipidemia	2.026 (1.110-2.836)	0.443
Regional anesthesia	2.754 (1.029-3.151)	0.104
General anesthesia	1.599 (1.184-2.048)	0.044*
Brescia-Cimino AVFs	2.445 (0.877-3.956)	0.062
Snuffbox AVFs	1.211 (0.548-1.011)	0.451
Brachiocephalic AVFs or Brachiobasilic AVFs	1.470 (0.954-1.689)	0.069

Table 5. Effect of type of AVF on complications

Parameters	Early thrombosis	Hyperemia	Infection	Hematoma	Revisions due to hemorrhage	Total number of complications
Brescia-Cimino (no=145)	12 (6.89%)	0	2 (1.37%)	4 (2.75%)	2 (1.37%)	20 (13.79%)
snuffbox (no=54)	3 (5.55%)	2 (3.70%)	2 (3.70%)	1 (1.85%)	1 (1.85%)	9 (16.66)
Brachiocephalic or Brachiobasilic (no=19)	2(10.52%)	1 (5.26%)	0	0	0	3 (15.78)
Total complication	17	3	4	5	3	32

p value between the three types of AVF= 0.06; One-way ANOVA test

Discussion

The early failure rates in previous literature reports are very diverse. Early failure rates in the range of 12%-29% have been observed in previous studies (12-17). Early failure is due to: severe dehydration, use of ill-suited veins, obstruction of the outlet, a vein kink near the anastomosis, a poor anastomosis, and compression of a hematoma [18,19].

In this study we evaluated 218 AVFs created in all patients. Early patency was found in 88% (185/210) of the AVFs created. So, early AVF failure or thrombosis was seen in 25 cases (25/218 [11.46%]). Of these 25 AVFs created, early thrombosis was seen in 17 cases (17/218[7.79%]).

In a similar study that evaluated 169 AVFs created in patients, early patency was found to be 73.6% and early failure was seen in 26.4% [20]. Also, Ekicei *et al.* [21] reported a 12% early thrombosis rate. This rate is higher than our results. We believe our lower early thrombosis rate is attributed to the use of topical papaverine and use of mechanical dilatation with a probe for spasm of both the veins and the arteries. Therefore, a proportion of early failure can be attributed to technical inadequacy, which can be avoided.

For analyzing the risk factors of early failure or thrombosis of AVFs, the multivariate logistic regression analysis indicated that female sex (OR=3.146, 95% CI 1.662-6.124), age >65 years (OR=3.410, 95% CI 1.541-5.523), diabetes (OR=1.125, 95% CI 0.873-2.576), hypertension (OR=1.411, 95% CI 0.831-3.351) and general anesthesia (OR=1.599, 95% CI 1.184-2.048) were associated with early failure or thrombosis of AVFs. Compared to our results, those of Miller *et al.* [22] showed a lower success

rate in women than in men. Gibbons [23] also reported lower patency rates in women. Previous data represented the fact about the hormonal responses that could in a direct manner help causing the access failure [24].
The influence of gender related to this concept has not been confirmed in some previous studies [21,25]. Also, in the group of patients with different known comorbidities, uremia, hypertension, dyslipidemia, diabetes mellitus etc., susceptibility to accelerated atherosclerosis and presence of a chronic low-grade inflammation, the creation and maintenance of vascular access has become more challenging concept [26,27].
Most often, neointimal hyperplasia and thrombus formation lead to narrowing juxta artery-vein anastomosing area and therefore early arteriovenous fistula failure [28].
The proliferation of smooth muscle cell of media layer in the venous intima is defined as neointimal hyperplasia and real underlying etiology of this process is controversial [29].
Several mediators including basic fibroblast and platelet-derived growth factors mediated proliferation of smooth muscle cell layer [30].
Although some literature reported that diabetes mellitus was one of the factors affecting the primary patency of AVF [31,32], Wolowczyk *et al.* [33] and Ekicei *et al.* [21] found that diabetes had no effect on AVF patency rates. We know that diabetes mellitus leads to impaired immunologic defense, especially cell mediated immunity [34]. Moreover, uremia may create immunosuppressive condition. So, this combination may lead to increased risk for bacteremia and AVF complication in HD patients. AVF patency also depends on the availability of a suitable vein and likewise on the ability of the artery to dilate, the dispensability of the arterial wall being an additional factor [35]. During the primary fistula creation, more vascular dystrophic calcifications of media layer were detected in diabetics and hypertensive patients in this study. More than half of all patients suffered from diabetes and arterial hypertension which were distinguished as independent risk factors associated with a decreased patency rate.
Advancing age in HD subjects cause malnutrition. This condition is a common problem in older dialyzed populations, causing immune defect and facilitating infection and AVF complications.
On the other hand, some other causes including peripheral arterial disease with thickened or even calcified arteries might have impaired fistula maturation [36].
In this study more patients underwent regional anesthesia instead of general anesthesia for vascular procedures. One of such procedures is vascular access for HD patients who usually have high prevalence of coronary artery disease, diabetes mellitus, and hypertension in addition to the ESRD. Similar to previous studies [37,38], we found early failure rate in general anesthesia higher than in regional technique. We believe these results are due to stress of induction and hypotension associated with general anesthesia technique [39].
In the early period following AVF formation, there may be a need for hospitalization or surgical revision due to local complications, including thrombosis, hyperemia, infection, hematoma or hemorrhage [40,41]. The most common complication, early and late, is thrombosis of the fistula [33]. In the present study, 32 complications including early thrombosis, hyperemia, infection, hematoma, and hemorrhage at the incision site, were occasionally observed. Early thrombosis found in 17 cases was a common complication in our study.
Our study was performed at two hospitals as an observational retrospective analysis, and study subjects may have not represented all risk factors in early AVF failure in hemodialysis patients. These limitations should be considered when interpreting the results of our study.

Conclusion

Our rate of AVFs failure is comparable to published reports. Female sex, age >65 years, diabetes, hypertension and general anesthesia have negative effect on AVFs patency.

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Conflict of interest statement. None declared.

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