



## Early Failure of Arteriovenous Fistula (AVF): The Effect of Diabetes and Hypertension in a Cross-Sectional Study

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### Abstract

**Background:** Identification and control of clinical predictors of arteriovenous (AVF) failure can improve the long-term outcome of hemodialysis patients. The effects of these factors on the outcome of AVF are not still clear. So, we aimed this study to compare the effect of hypertension and diabetes on early failure of AVF.

**Methods:** In this retrospective study, we evaluated 400 patients with ESRD referred to our clinic for the creation of the first AVF from July 14, 2001, through August 7, 2018. One month after AVF creation, the patients were referred to the clinic for patency control. Demographic characteristics, previous history of diabetes and hypertension, and laboratory data of all patients were recorded preoperatively. Data were entered to SPSS v.24 and Study data were analyzed with chi-square and independent student t-test. Then, early failure of AVF and its relationship with a history of diabetes and hypertension were assessed.

**Results:** There was no statistically significant relationship between the history of diabetes and early AVF failure risk in ESRD patients (OR, 0.78; 95% CI, 0.25 to 2.43). Furthermore, the history of hypertension was significantly lower in the early failure of AVF group (OR, -2.82; 95% CI, -1.42 to -5.59). Although, this effect faded when using regression analysis (OR, -2.67; 95% CI, -0.97 to -7.36). There was a higher Body mass index in the non-early failure group ( $p = 0.041$ ). There was no significant difference in age ( $p = 0.512$ ), gender ( $p = 0.091$ ), history of smoking ( $p = 0.605$ ), treatment with insulin ( $p = 0.683$ ), oral antidiabetic agents ( $p = 0.734$ ), duration of diabetes ( $p = 0.384$ ), and duration of hypertension ( $p = 0.093$ ).

**Conclusion:** We reported that the history of diabetes was not higher in the early failure group, while there was a lower risk of AVF failure in patients with a previous history of hypertension.

**Keywords:** End-Stage Renal Disease (ESRD), Arteriovenous Failure (AVF), Early Failure, Non-Early Failure, Diabetes, Hypertension, Obesity

**Conflicts of Interest:** None declared

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### Introduction

The arteriovenous fistula (AVF) is an anastomosis created between a native artery and vein (1). It is the preferred dialysis access for most patients with end-stage renal

disease (ESRD) due to long-term benefits, including less morbidity and mortality, fewer rates of infection and complications, and lower costs compared to other types of

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#### ↑What is “already known” in this topic:

Primary failure of arteriovenous failure (AVF) can affect long-term morbidity and mortality in end-stage renal disease (ESRD) patients on hemodialysis. So, identification and control of the clinical predictors of AVF failure can improve vascular access selection and outcomes.

#### →What this article adds:

In this study, we assessed patients with ESRD who were undergone AVF creation, and we found that the history of diabetes was not more prevalent in the failure of the AVF group. Also, patients with a history of hypertension were associated with a lower risk of AVF failure.

vascular accesses. However, these benefits are limited by the risk of AVF failure and maturation failure which occurred in up to 60% of these patients (2).

Studies have a different definition of primary failure but overall, early failure is defined as AVF never maturing to support dialysis or that fails within three months of use and diagnosed as thrombosis and immediate failure of fistula (3-5). The overall risk of early failure was 23% but increased to 37% in the elderly (5).

Identification of clinical predictors of AVF failure and interventions to control these factors can improve the long-term outcome of AVF and hemodialysis in ESRD patients (1). This is because dysfunctional AVF is a major cause of morbidity, overall mortality, and excess costs (6). For this reason, there are several major predictors of AVF failure were identified, but there is no concordance in the literature regard to the effects of these risk factors. Most investigators have reported that factors including age, sex, race, diabetes, obesity, location of the fistula, and experience of the surgeon may impact primary failure rates (5).

While DM and hypertension are the most common causes of ESRD (6) but evaluation of their effects on AVF failure is still not clear. Most investigators have reported that diabetes is not significantly associated with primary AVF failure (7). Whereas other studies showed diabetes is accompanied by increased risks of peripheral arterial disease, especially in chronic kidney disease patients that can lead to an increased rate of AVF failure (1, 8). Also, ESRD patients with diabetes can experience a delay in AVF maturation time (9).

This lack of consensus has occurred in the territory of hypertension and AVF failure too.

Of course, this lack of coordination is due to fewer studies in this regard. However, there is a recent study supported that a lower risk of AVF failure was associated with the presence of a positive history of hypertension, but we need more to assess the effect of hypertension on AVF outcomes and complications.

So, due to the high prevalence of primary failure of AVF that can affect long-term morbidity and mortality in ESRD patients on hemodialysis, this study was designed to assess the risk factors of AVF failure in our center, especially a history of diabetes and hypertension in hemodialysis patients.

## Methods

We performed a retrospective study of AVF placed from July 14, 2001, through August 7, 2018, at Hasheminejad Hospital (tertiary care center in Tehran, Iran). Over seventeen years, 400 patients with ESRD who underwent their first AVF creation by the same surgeon were evaluated. In other words, only the first AVF in each patient during this period was analyzed. Also, these patients were informed about the research, and written consent was obtained.

The information recorded at the time of operation included: gender, age, weight, body mass index (BMI), history of hypertension, diabetes, duration of diabetes, medications for diabetes, history of smoking, AVF planning site.

Also, laboratory parameters, including HbA1c, hemoglobin, platelet, red cell redistribution width, lipid profile,

albumin, inflammatory factors, sodium, and creatinine were assessed before AVF creation.

The goal of this study was the assessment of risk factors for early AVF failure. So, one-month after AVF creation, the patients were referred to our vascular access clinic for patency control and detection of early failure or thrombosed AVF. Early failure was defined as a lack of thrill on the palpation or vascular murmur in the examination of AVF. Otherwise, if the fistula was ready for dialysis, it was categorized as a mature fistula. The surgery and evaluation of the AVF failure were performed by one surgeon. Also, he did not become aware of the previous data of each patient.

Finally, patients were categorized into two groups: early failure and non-early failure of AVF. The non-early failure group included patients with mature or non-mature AVF.

Then the effect of the previous history of diabetes and hypertension and other characteristics on the rate of AVF failure was compared between the two groups. Statistical comparisons of individual groups were based on the Student t-test for continuous variables and the chi-square test for discrete variables. Parametric and nonparametric tests were used according to the distribution pattern of the data of each variable. A univariate analysis was done with variables considered relevant to AVF failure. All variables with a  $p$ -value  $< 0.05$  were included in the logistic regression analysis. The statistical analysis was carried out by Statistical Package for Social Sciences for Windows ver. 24.0 (SPSS Inc., Chicago, IL). Test results were presented as mean  $\pm$  SD or percent with 95% confidence intervals (CIs), and a two-sided  $p < 0.05$  was considered statistically significant.

## Results

A total of 400 patients whose AVF was created for the first time were assessed in this study, with a mean age of  $52.82 \pm 16.94$  years, and 136 (34.0%) were female. Antecubital AVF was created in 144 (36.8%) patients, 247 patients (63.2%) received a wrist AVF and AVF place of nine patients was not mentioned in the data collection. About 40% of the patients (159 patients) in our study had diabetes and a history of hypertension was found in 284 patients (71% of patients). Wrist AVF was performed in 247 patients (61%) and antecubital was opened in 144 patients (36%). In this study, the incidence of primary failure was reported in 30 patients (7%).

There was no significant difference in age ( $p = 0.512$ ), gender (OR, 1.03; 95% CI, 0.43 to 2.72), history of smoking (OR, 1.28; 95% CI, 0.51 to 3.20), treatment with insulin (OR, 1.33; 95% CI, 0.34 to 5.32) or oral antidiabetic agents (OR, 1.06; 95% CI, 0.97 to 1.11) between these two groups (early failure and control). In this study, we found that the early failure group had a lower BMI in comparison to the control group ( $23.10 \pm 5.81$  kg/m<sup>2</sup> vs.  $25.24 \pm 4.69$  kg/m<sup>2</sup>, respectively,  $p = 0.041$ ). Also, weight was significantly lower in the early failure group when compared to the control group ( $61.83 \pm 15.61$  vs.  $69.09 \pm 14.26$  respectively,  $p = 0.013$ ).

Other characteristics, including AVF site and laboratory tests, were not significantly different between the two groups.

A comparison of the clinical characteristics of early failure and control groups is also established in Table 1.

In this study, we showed that the history of diabetes was not significantly different in the early failure group in comparison with non-early failure of AVF (23.31% vs. 41.1%,  $p = 0.153$ ).

Duration of diabetes was  $3.72 \pm 8.43$  years in the early-failure group and was  $5.12 \pm 8.14$  in the control group ( $p = 0.384$ ). Compared to the control group, HbA1c was not significantly different in the early failure group ( $p = 0.781$ ). The odds ratio for early failure due to diabetes was 0.78 (0.25 to 2.43) in logistic regression.

In this study, 46.7% of the patients in the early-failure group and 73.2% of the patients without failure had a history of hypertension. In early analysis, hypertension was significantly less associated with early failure of AVF (OR, -2.82; 95% CI, -1.42 to -5.59). The adjusted Odds Ratio with logistic regression for early failure of AVF due to hypertension was -2.67 (95% CI, -0.97 to -7.36),  $p = 0.061$ . We assessed the effects of duration of hypertension on early

failure of AVF and found there is no significant association ( $p = 0.093$ ) between the two groups (Table 2).

## Discussion

Our results support evidence that there is no significant difference between patients who have diabetes compared with those without diabetes in terms of early failure of AVF and diabetes is not necessarily a prognostic factor regarding outcome (10).

On the contrary, many authors have stated that diabetes is associated with a higher risk of AVF failure. In this regard, Jeong et al. reported higher mortality rates and worse AVF patency rates in diabetic patients vs. non-diabetic ESRD patients undergoing hemodialysis (11). In a previously reported systematic review, there is an increased risk of AVF failure in ESRD patients with diabetes (12). Interestingly, various studies have shown that diabetes has not a direct effect on the failure of access; and the comorbidities associated with diabetes, including peripheral arterial disease, do have a definite effect (13). Of course, this is while

Table 1. Patient characteristics

Characteristic	Early failure of AVF (n=30)	Non-early failure of AVF (n=370)	P value
Age (mean $\pm$ SD)	50.83	52.98	0.512
Female, no. (%)	10 (33.3%)	126 (34.1%)	0.931
BMI <sup>Q</sup> (Kg/m <sup>2</sup> )	23.10 $\pm$ 5.81	25.24 $\pm$ 4.69	0.041
Weight (Kg)	61.83 $\pm$ 15.61	69.09 $\pm$ 14.26	0.013
AVF <sup>Y</sup> site: wrist	19 (63.3%)	228 (63.2%)	0.981
AVF <sup>Y</sup> site: antecubital	11 (36.7%)	133 (36.8%)	0.982
Diabetes, no. (%)	7 (23.31%)	151 (41.1%)	0.153
Duration of DM <sup>a</sup> (years)	3.72 $\pm$ 8.43	5.12 $\pm$ 8.14	0.384
Hypertension, no. (%)	14 (46.7%)	270 (73.2%)	0.002
Duration of HTN <sup>h</sup> (years)	2.14 $\pm$ 5.01	4.38 $\pm$ 6.25	0.093
Smoking, no. (%)	5 (16.7%)	49 (13.2%)	0.605
Treatment with Insulin, no. (%)	3 (37.5%)	37 (30.6%)	0.683
HbA1c <sup>g</sup> (%)	6.06 $\pm$ 1.94	5.96 $\pm$ 1.78	0.781
Metformin, no. (%)	0 (0%)	2 (1.5%)	0.734
Hemoglobin (mean $\pm$ SD)	9.39 $\pm$ 1.65	9.22 $\pm$ 1.94	0.652
Platelet (mean $\pm$ SD)	192.23 $\pm$ 70.95	209.58 $\pm$ 81.66	0.262
Total cholesterol (mean $\pm$ SD)	164.89 $\pm$ 46.83	158.37 $\pm$ 4.02	0.554
LDL <sup>*</sup> cholesterol (mean $\pm$ SD)	98.60 $\pm$ 44.92	92.05 $\pm$ 36.75	0.501
HDL <sup>#</sup> cholesterol (mean $\pm$ SD)	44.25 $\pm$ 12.07	39.78 $\pm$ 12.71	0.173
Triglyceride (mean $\pm$ SD)	123.47 $\pm$ 47.74	142.62 $\pm$ 89.15	0.405
Albumin (mean $\pm$ SD)	3.58 $\pm$ 0.55	3.57 $\pm$ 0.92	0.954
ESR <sup>o</sup> (mean $\pm$ SD)	62.85 $\pm$ 38.02	53.04 $\pm$ 32.35	0.392
CRP <sup>o</sup> (mean $\pm$ SD)	42.55 $\pm$ 30.12	23.99 $\pm$ 32.16	0.121
Sodium (mean $\pm$ SD)	140.07 $\pm$ 5.69	138.60 $\pm$ 5.21	0.142
RDW <sup>e</sup> (mean $\pm$ SD)	15.08 $\pm$ 2.06	14.63 $\pm$ 1.67	0.211
Creatinine (mean $\pm$ SD)	7.99 $\pm$ 2.93	8.95 $\pm$ 4.82	0.283
Ferritin (mean $\pm$ SD)	406.39 $\pm$ 405.73	332.31 $\pm$ 374.34	0.291

<sup>Y</sup> Arteriovenous failure, <sup>Q</sup> Body mass index, <sup>a</sup> Diabetes mellitus, <sup>h</sup> Hypertension, <sup>g</sup> Hemoglobin A1c, <sup>\*</sup> Low density lipoprotein, <sup>#</sup> High density lipoprotein, <sup>o</sup> Erythrocyte sedimentation rate, <sup>e</sup> C-reactive protein, <sup>e</sup> Red cell distribution width. Test results were presented as mean  $\pm$  SD or percent with 95% confidence intervals (CIs), and two-sided  $P < 0.05$  was considered statistically significant. AVF place of 9 patients was not mentioned in the data collection.

Table 1. Logistic regression in early failure of AVF

Variate	Odds Ratio	95% Confidence interval		P-value
		Lower	Upper	
Hypertension	2.67	0.97	7.36	0.061
Female	0.61	0.22	1.69	0.343
Age	1.003	0.97	1.03	0.843
Site of AVF	1.06	0.39	2.86	0.912
Hemoglobin	0.88	0.69	1.11	0.285
Platelet	1.006	0.99	1.03	0.113
DM <sup>h</sup>	0.78	0.25	2.43	0.782
BMI <sup>g</sup>	1.09	0.97	1.23	0.141

<sup>h</sup> Diabetes, <sup>g</sup> Body mass index.

diabetes has been shown to have a direct effect on the outflow from fistula<sup>1</sup> and the presence of diabetes might delay the AVF maturation time (9).

There is a general lack of concordance in the literature concerning the effect of hypertension and blood pressure on AV fistula development and patency. In our study, a history of hypertension was significantly less detected in the early failure of the AVF group in comparison with the control group. However, its effect faded after adjustment for other variables, but there was a trend towards statistical significance.

Some studies showed that hypotension was the cardinal cause of failure of AVF in ESRD patients. Talaiezhadeh et al. concluded that monitoring the blood pressure during hemodialysis and preventing hypotension by salted regimen intake can be useful for the prevention of AVF failure. Consistent with a previous study, a lower risk of AVF failure was associated with the presence of a positive history of hypertension; in other words, positive history of hypertension was not associated with higher AVF failure (3).

To our knowledge, no study in the literature assesses the impact of hypertension on the rates of early fistula failure before the initiation of dialysis through this access. So, it seems to be necessary to design and conduct more studies that evaluate the role of hypertension as same as diabetes on AVF outcomes.

This study indicated that patients with early failure of AVF had a significantly lower BMI in comparison with the control group. In this regard, Kats et al. also reported that obesity is associated only with poorer maturity of AVF at BMI  $\geq 35$  kg/m<sup>2</sup> and not with an increased rate of failure. Other studies showed that obesity could be associated with technical difficulty related to the depth of the vessels used to create the fistula. These issues, in addition to better survival of the ESRD patients with higher BMI, mean that their accesses must last longer than those of other patients. Also, in other studies, obesity is described as a risk factor for failure of vascular access separate to the increased incidence of diabetes in this group due to the increased soft tissue mass leading to venous compression and outflow tract obstruction (1). So, evaluation of hemodynamic factors by vascular mapping becomes particularly important in patients with obesity before AVF creation.

We also found no difference between the two groups in terms of AVF site. Hudson et al. reported that sites of AVF influence inflow properties, with increased patency, are associated with increasing size of the feeding artery (distal to proximal). They identified that distal radio cephalic AVF on the non-dominant side of the patient's hand is the preferred site of AVF due to patient comfort along with the preservation of additional possible vascular access sites for the future (1).

Previous studies identified that the female gender is associated with poorer outcomes of AVF in comparison to males, though the reasons are unclear (1). In our study, the female gender rate was not significantly different between the two groups, and interestingly, the number of men was higher in the failure group. However, it was detected in the non-failure group. Although, about 66% of patients in our study were men.

This study showed age was not significantly different between the failure group and the non-failure group. Other literature was unable to identify significant differences in functional access outcomes for older patients. However, other investigators suggested that advancing age, more than or equal to 65 years, is one of the risk factors listed for AVF failure and this effect can be explained by the point that age is a surrogate marker for increasing the burden of comorbidities (1).

In patients with and without early failure, there was a statistically similar number with smoking, treatment with insulin, or oral antidiabetic agents. Also, in this study, we showed that ESR, CRP, hemoglobin, RDW, platelet, albumin, lipid profile, sodium, creatinine, and ferritin were not significantly different in the two study groups. There is a lack of data on this entity in the literature review, and more studies are required to target these factors at the time of fistula creation, which helps in reducing early AVF failure.

This study has some limitations. There was a small sample size in the early failure group, which could have a role in the data conclusion. But it really occurred in our center and a low percentage of early failure of AVF was reported in this study. Also, We did not perform definite markers of failure and maturation of AVF via ultrasonography. However, clinical markers of AVF failure have been identified and reliably used in the literature same as in this study. So, the definition of early AVF failure does not need to assess with imaging. Finally, some data of our patients was not recorded, although it was not great. On the other hand, the strength of this study includes a relatively high number of patients referred to our tertiary center that can be representative of ESRD patients all over our country. Also, the patients were operated on and examined by one surgeon.

### Conclusion

This study supports the evidence that there is no additional risk of early failure of AVF for patients with diabetes. So, preoperative clinical and hemodynamic evaluation can play an important role in achieving success with AV fistula creation in ESRD patients with diabetes. In this study, we showed that a previous history of hypertension is associated with less early failure of AVF. Also, we detected that higher BMI and weight were not associated with early failure of AVF. So, if confirmed by further prospective studies with larger participants and multicentric studies, the preventive measure should be considered in hypertensive and obese patients when planning AVF.

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### Ethical issues

There is a retrospective and data-based study.

### Conflict of Interests

The authors declare that they have no competing interests.

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