The association of demographic, clinical, and thrombophilic factors with the failure of arteriovenous fistula among hemodialysis patients

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ABSTRACT

الأهداف: تقييم اتحاد العوامل السكانية، والسريرية، والتخثرية، مع فشل الصارفة الشريانية الوريدية (AVF) بين المرضى الخاضعين للتنقية الدموية المزمنة.

الطريقة: شملت الدراسة 62 مريضاً (33 ذكر، 29 أنثى) يخضعون لبرنامج تنقية الدم المزمنة في مارس 2005م، لدى مركز التنقية بكلية الطب بجامعة دايكل – تركيا. تم تقسيم المرضى لمجموعتين وفقاً إلى ما يحتاجون إليه (المجموعة الثانية)، أو إلى مالا يحتاجون إليه (المجموعة الأولى)، في تركيب أكثر من صارفة واحدة.

النتائج: كانت العوامل الآتية هي الأكثر شيوعاً في المجموعة الثانية: جنس الأنثى، مدد تنقية دم أطول، نوبات إنخفاض في الضغط أثناء التنقية، إرتفاع في مستوى الفسفور ومركب فسفور الكالسيوم (CaP)، ومعدل هرمون طبيعي للغدة جار الدرقية (iPTH)، كما لوحظ أيضاً حدوث حالات أكثر من تضخم البطين القلبي الأيمن (AVF).

خاتمة: انفكاك الصارفة الشريانية الوريدية (AVF)، والحاجة المتكررة لزيادة تركيب الصارفة الشريانية الوريدية (AVF)، مع فترة التنقية الدموية. نعتقد أن جنس الأنثى والعوارض المتكررة لارتفاع ضغط الدم داخل التنقية، وارتفاع مستوى مصل الفسفور و(iPTH) وارتفاع منتج (CaP) تعد عوامل خطر ذات صلة بفشل الصارفة الشريانية الوريدية (AVF) بين مرضى التنقية الدموية.

Objective: To evaluate the association of demographic, clinical, and thrombophilic factors with the failure of arteriovenous fistula (AVF) among patients undergoing chronic hemodialysis.

Methods: Sixty-two (33 males, 29 females) patients undergoing chronic hemodialysis were included in the study in March 2005 at the Hemodialysis Center of the Medicine Faculty at Dicle University, Diyarbakir, Turkey. The patients were divided into 2 groups according to whether they needed (group II) or do not need (group I) more than one fistula placed.

Results: Female gender, longer vintage of hemodialysis, frequent intradialytic hypotensive episodes, elevated levels of phosporous, calcium-phosporous product (CaP), and intact parathormone (iPTH), and left ventricle hypertrophy were more likely in group 2.

Conclusion: Arteriovenous fistula loss, and recurrent requirement of AVF constitution increase with hemodialysis vintage. We believe that female gender, frequent intradialytic hypotensive episodes, elevated serum levels of phosporous, iPTH, and high CaP products are risk factors related to the failure of AVF among hemodialysis patients.

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Arteriovenous fistula (AVF) is the best choice of vascular access for patients undergoing chronic hemodialysis (HD).[1] The AVF is a unique vascular access with the longest life, and the highest effectivity, as well as the lowest incidence of infection, and thrombosis potential.[1,2] However, among chronic HD patients, hospitalization, morbidity, and even mortality rates caused by vascular access complications are not rare. These complications depend on the etiology of end stage renal failure, patient's age, gender, age at HD, anatomic malformations in vasculary structure, patient dependent factors such as hemostasis (thrombophilic features), canulation technics of AVF, intradialytic hypotensive episodes, and stenosis, thrombosis, pseudoaneurism, and infections of AVF.[3,4] In this study, we aimed to

evaluate the effect of demographic, and clinical features, and thrombophilic factors on the failure of AVF among patients undergoing chronic HD.

Methods. Sixty-two (33 males, 29 females) patients undergoing chronic HD who accepted and gave informed consent were included in the study in March 2005 at the Hemodialysis Center of the Medicine Faculty at Dicle University, Diyarbakir, Turkey. This study was cross sectional. Patients who had arterio-venous graft, and temporary or permanent central venous catheters were excluded. The patients were divided into 2 groups according to the number of arterio-venous access, group 1, patients who had single native fistula (n=32), and group 2, patients who had more than one fistula (n=30). The demographic features (age, gender), clinical features [vintage of dialysis, urea reduction ratio (URR), standard urea kinetic model (Kt/V), mean arterial pressure (MAP), number of intradialytic hypotensive episodes, and left venctricle hypertrophy (LVH)] were obtained from patients' records. Mean arterial pressure was calculated by [diastolic blood pressure+systolic blood pressure-diastolic blood pressure/3] formula using postdialytic arterial blood pressures taken by manual sphygmomanometer. An arterial blood pressure value lower than 90/60 (systolic/diastolic) mm Hg at any time of HD session was accepted as a hypotensive episode. Blood samples for laboratory examination were taken after a 12-hour fasting period before dialysis, and administration of heparin. Serum levels of calcium (CA), phosphorus (P), C-reactive protein (CRP), homocystein, and intact parathormone (iPTH) were studied. Calcium-phosporous product was calculated. Biochemical parameters (Ca, P) were measured using routine biochemical procedures on Aeroset/C8000 autoanalyzer (Abbott Diagnostics, Illinois, USA). C-reactive protein levels were measured by electrochemiluminescence method on Roche Elecsys 2010 immunoassay analyzer. Homocystein was measured using competitive immunoassay on IMMULITE 2000. Intact parathormone (iPTH) was detected with 2-site chemiluminescent enzyme-labeled immunometric method on IMMULITE 2000. Protein C, protein S, von Willebrand's factor (vWF), antithrombin (AT) III, and fibrinogen were evaluated as thrombophilic factors. Protein C, protein S, and ATIII were measured using the automated latex ligand immunoassay method in citrated plasma on IL Coagulation Systems (Instrumentation Laboratory, Lexington, USA). Automated latex enhanced immunoassay was used to establish vWF silver, and Clauss method for detecting fibrinogen in citrated plasma on IL Coagulation Systems. Complete blood counts (CBC) were measured on Cell-dyn 3700 (Abbott Diagnostics, Illinois, USA). Left ventricle hypertrophy was assessed using transthorasic M-Mode echocardiography on Hewlett-Packard Sonos 4500® Echocardiography Systems (California, USA).

Statistical analysis was carried out using SPSS 11.0 program by the methods of student's t test, chi-square and Pearson's correlation. A $p<0.05$ was accepted as significant. Data are shown as mean±SD.

Results. In group 1 (n=32, 21 males and 11 females), the mean age was 41.1±13.7 years, and the mean vintage of HD was 24.4±21.2 months. In group 2 (n=30, 12 males and 18 females), the mean age was 42.0±15.3 years, and the mean age vintage of HD was 36.2±26.7 months. These differences in gender (p=0.043), and dialysis vintage were statistically significant (p=0.030) There was no significant difference between groups in URR, Kt/V, serum levels of Ca, homocystein, and CRP. Serum levels of P (p=0.004), Ca-P product (p=0.017), and iPTH differed significantly (p=0.006) (**Table 1**). In group 2, 56.6% (n=17) of patients had second, 30% (n=9) had third, 6.6% (n=2) had fourth, and 6.6% (n=2) had fifth AVF. Although there was no difference in MAP between groups (p=0.890), LVH was significantly higher among female patients (p=0.028), and LVH was significantly more frequent in group 2 than in group 1 (p=0.002). Nineteen of 27 patients who had LVH

Table 1 - Demographic, and clinical features of group 1 and group 2.

Parameters	Group 1 (n=32)	Group 2 (n=30)	*p*-value
Gender: male/female	21/11	12/18	0.043
Age: years	41.1±13.7	42.0±15.3	0.820
Time on dialysis: months	24.4±21.2	36.2±26.7	0.030
URR: (%)	71.4±5.74	72.2±4.81	0.574
Kt/V	1.27±0.07	1.3±0.08	0.211
Calcium: mg/dl	8.8±0.8	8.8±0.8	0.987
Phosphorus: mg/dl	5.0±0.9	5.6±0.7	0.004
CaP: mg^2/dl^2	44.1 ± 8.3	49.4±8.7	0.017
iPTH: pg/ml	274.5 ± 96.7	385.7±195.7	0.006
Homocysteine: µmol/L	20.0 ± 7.3	21.9±10.4	0.413
CRP: mg/L	9.6±96	7.6±7.2	0.370
MAP: mmHg	100.4 ± 14.7	100.9±11.1	0.890
Hypotensive episode: -/+	26/6	12/18	0.001
LVH: -/+	24/8	11/19	0.002

URR - urea reduction rate, Kt/V - standard urea kinetic model, Ca - calcium, CaP - calcium phosporous product, iPTH - intact parathormone, CRP - c-reactive protein, MAP - mean arterial pressure, LVH - left ventricle hypertrophy.

Table 2 - Comparison of hematological, and thrombophilic parameters of group 1 and group 2.

Parameters	Group 1 (n=32)	Group 2 (n=30)	*p*-value
WBC: K/UL	6.8±1.6	6.5±1.8	0.554
Hemoglobin: gr/L	10.7±1.0	10.2±1.2	0.145
Platelets: K/uL)	268.4±96.2	241.6±88.3	0.259
PTT: seconds	12.9±0.8	12.9±1.2	0.785
INR: INR	1.11±0.80	1.10±0.12	0.704
aPTT: seconds	28.6±4.9	32.4±12.4	0.115
Fibrinogen: mg/dl	423.1±146.7	361.6±88.1	0.052
vWF: (%)	155.6±33.4	155.7±50.1	0.990
ATIII: (%)	92.2±13.8	89.2±12.4	0.371
Protein C: (%)	88.2±25.3	79.2±25.3	0.166
Protein S: (%)	89.8±23.5	85.5±22.4	0.470

WBC - white blood cell, aPTT - activated partial tromboplastin time, INR - international normalization ratio, PTT - prothrombine time, vWF - von Willebrand factor, ATIII - antithrombin 3

(p=0.002), and 18 out of 24 patients who had recurrent hypotensive episodes during HD session (p=0.001) required recurrent surgical operations due to the loss of AVF. There was no statistically significant difference in comparison of thrombophylic factors between groups (p>0.05), and in CBC values. Complete blood count, and thrombophylic factors of patients, and significant values were shown in **Table 2**.

Discussion. It is worth noting that an efficient HD is impossible without a vascular access that supplies adequate, and reliable blood flow through the hemodialyser. None of the options of vascular access can provide the success and durability supplied by AVF.[1-4] The mean life of a standard AVF is accepted as 5 years.[1] As the survival of HD patients becomes longer, risk factors leading to AVF loss increase markedly. The cause of deteriorating vascular structure includes, diabetes, atherosclerosis, advanced patient's age, dialysis vintage, anatomic malformations, thrombophilic features, poor canulation techniques, frequent infections of AVF, intradialytic hypotensive episodes, and vascular steal syndrome. These factors can negatively affect the life expectancy, and efficiency of AVF. Loss of AVF, due to these causes, is often unavoidable.[4,5] Consequently, it would be necessary to place a new access.[4-7]

In our study, while the duration of dialysis was 36.2±26.7 months among patients with more than one AVF, it was 24.4±21.2 months among patients with only one fistula (p=0.030). Atherosclerotic changes associated with ageing can make constituting adequate AVF difficult.[8] In our study, a statistically significant difference in age was not found between the group with multiple AVF (group 2), and the group with single AVF (group 1). We believe, that this is probably due to the limited number of patients with advanced age (>65 years). From the total number of patients, 7 (11.3%) patients were over 65 years. In females, AVF insufficiency is more frequent than males.[9,10] Although the reason for this condition is not clear, we think it is caused by higher susceptibility of females to complications related to AVF. Our findings are consistent with these investigations.

Intradialytic hypotension is a frequent problem among HD patients. In most studies, it is reported that frequent hypotensive episodes may cause AVF loss.[11-13] In this study, we found that the number of intradialytic hypotensive episodes (p=0.001), and LVH (p=0.002) were significantly more prevalent among patients with more than one fistula. Hyperphosphatemia is an important problem in HD patients. High P, and elevated serum levels of iPTH play a role in triggering of secondary hyperparathyroidism, and related mineral metabolism complications such as vascular calcifications,[14,15] In addition, these factors contribute to thrombogenesis, one of the leading causes of vascular access failure.[16] In our study, statistically significant differences were found between groups 1, and 2 with regard to serum levels of P, iPTH, and CaxP. These results, on secondary hyperparathyroidism, are consistent with Morena et al's[15] data.

Data on the relationship of thrombophilic factors, and AVF survival and efficiency are controversial. It is suggested that thrombophilic factors may lead to insufficiency of vascular access by increasing tendency to thrombosis.[17-24] While many studies suggest that, factors such as protein C, protein S, vWF, and ATIII might increase the development of thrombosis among HD patients,[19-21] other investigations disagree.[22,23] In this study, no significant difference was observed between the groups in homocysteine, which is known to be harmful on endothelium,[23] and thrombophilic factors (protein C, protein S, vWF, ATIII, and fibrinogen).

In conclusion, AVF loss and recurrent requirement for AVF constitution increases with increasing duration of HD. We think that, female gender, frequent intradialytic hypotensive episodes, elevated serum levels of P, iPTH, and high Ca-P product may be risk factors related to the failure of arteriovenous fistula. Further studies are needed in this study.

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