



Evaluation of Risk Factors for Arteriovenous Fistula Failure in Patients Undergoing Hemodialysis

ORIGINAL
INVESTIGATION

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ABSTRACT

Objective: The aim of the present study is to evaluate the relationship between demographic characteristics, hematological and biochemical parameters, and elements of the coagulation system that may predispose a person to thrombosis or to anatomical and functional parameters in Doppler ultrasonography scanning and the maturation and adequacy of arteriovenous fistulas.

Materials and Methods: Overall, 36 patients who underwent a native arteriovenous fistula operation were included. Biochemical parameters, hematological parameters, the coagulation system, and a Doppler ultrasonography evaluation were performed before an arteriovenous fistula operation on day 1 after the fistula operation and at the time point when the arteriovenous fistula became dysfunctional.

Results: A thrombus occurred between 1 and 73 days (mean: 28.4±26.1) in 10 patients. It was found that the female gender ($p<0.001$), presence of thrill ($p=0.014$), quality of vein ($p<0.001$), peak systolic velocity and end-diastolic velocity of the radial artery at the snuffbox region on day 1 after the operation ($p=0.035$ and $p=0.049$, respectively), and the cephalic vein diameter in the Brescia–Cimino region ($p=0.011$) were associated with thrombosis formation. No relation was found among blood pressure, fistula region, quality of artery, spasm of artery and vein, hematologic and biochemical parameters, coagulation parameters, active protein C resistance, anti-cardiolipin antibody, D-dimer, C-reactive protein, or erythrocyte sedimentation rate and thrombosis formation ($p>0.05$).

Conclusion: Thrombosis occurs at a relatively early period in approximately a quarter of arteriovenous fistulas. Female gender, quality of vein, and the absence of thrill in the post-operative period are important factors in thrombosis formation.

Keywords: Arteriovenous fistula failure, thrombosis, Doppler ultrasonography

INTRODUCTION

A good access for hemodialysis requires the matching of some requirements such as being ready for use as soon as possible, providing sufficient blood flow with a dialysis machine, easy and safe cannulation, enabling repeated cannulation, and long-term sufficiency (1). Native arteriovenous (AV) fistulas, which are the most commonly used access line, enable sufficient and repeated hemodialysis applications and improves the rate of survival and quality of life in patients with end-stage renal disease (ESRD) when performed timely in an appropriate anatomic location using a fine technique (2, 3). The most-preferred sites for AV fistulas are the wrist (radial-cephalic) as the first choice and the elbow (brachial-cephalic) as the second choice. The most suitable anastomosis technique is side-to-end, in which the end of the vein and distal segment of the artery are used (3-5).

Several factors, including age, diseases that cause renal failure, degree of renal failure and probability of curing, blood pressure and hydration, existence of complications and co-morbid disease, status of arm vessels, urgency of initiating dialysis, and life expectancy, play roles in the selection of the vascular access method and access site (6, 7). Factors that affect the maturation of a fistula include the type of surgical technique, high blood pressure, hand and finger exercises, and the selective obstruction of major venous branches. The utilization of larger veins, high blood pressure, the brachial artery instead of radial artery, utilization of a side-to-end anastomosis method, and anti-coagulant and/or anti-platelet therapy positively affects fistula maturation, while advanced age, obesity, female gender, diabetes, myocardial infarction, coronary bypass, stroke, history of thromboembolic events, systemic coagulability, arterial and venous spasms, and low mean arterial pressure have a negative effect (8-13). The selection of the fistula site and assessment of fistula maturation, adequacy, and function can be easily and rapidly achieved at the bedside without any complication by Doppler ultrasonography (US) (8).

In patients with ESRD, factors that have the potential to influence the maturation and adequacy of AV fistula interventions, such as demographic characteristics, hematological and biochemical parameters, elements of the coagulant system that may predispose a person to thrombosis, and anatomic and functional features of vessels used as

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determined by Doppler US, were assessed in those patients where an AV fistula was preferred as the access line for hemodialysis in the present study.

MATERIALS and METHODS

Patient selection and flow chart

The present study was performed on 36 patients overall [11 females (30.6%) and 25 males (69.4%)] between the ages of 20 and 76 years (mean age 51.1 ± 15.4 years) who had been admitted and underwent native AV fistula operation by the same surgeon to receive hemodialysis for ESRD. The patients were informed about the study, and their written consents were obtained. The study was approved by the İnönü University Ethic Committee. The duration of chronic renal failure (CRF) and ESRD diagnosis varied from 3 to 49 months (mean: 7.2 ± 12.5 months) and 3 to 25 months (mean: 4.6 ± 5.7 months), respectively, whereas hemodialysis duration varied in days (mean: 8.0 ± 6.6 days).

It was found that there was hypertension in 22 (61.1%) patients, dyslipidemia in 8 (22.2%), coronary artery disease in 8 (22.2%), and a history of smoking and alcohol use in 10 (27.8%) and 2 (5.6%) patients, respectively. On obtaining the medical history of patients, the use of anti-hypertensive drugs, ACE inhibitors, calcium channel blockers, erythropoietin, calcium carbonate or calcium acetate, active vitamin D, statin, acetylsalicylic acid, or aluminum were detected in 17 (47.2%), 7 (19.4%), 10 (27.8%), 9 (25%), 9 (25%), 3 (8.3%), 6 (16.7%), 2 (5.6%), 1 (2.8%) patients, respectively.

In total, 29 (80.6%) patients were receiving hemodialysis by catheter, with the duration of catheterization varying between 1 and 28 days (mean: 6.5 ± 6.7 days). The catheterization sites were the right jugular vein in 28 patients, left jugular vein in 1, right subclavian in 4, and right femoral in 3. Age, gender, etiologic cause of renal failure, known duration of disease, duration of hemodialysis, and drugs previously used were recorded for all patients. While it was found that the etiologic causes were diabetes in 9, chronic glomerulonephritis in 7, polycystic renal disease in 3, obstructive nephropathy in 3, and amyloidosis in 2 patients, no etiologic cause could be documented in 12 patients.

The patients were monitored for fistula maturation, complications, and function during AV fistula maturation time and then at least for 4 months. Patients with poor general status, infection, peripheral artery disease, and extremity amputation due to unknown reasons, inconvenient by the Allen test, vessel calcification in the upper limb on radiography, or previous AV fistula operation were excluded.

The appropriate anatomic localization for the AV fistula was confirmed by Doppler US evaluation before the operation in patients with a proper Allen test and without vessel calcification in the upper limb radiograph. Structural properties, diameter, flow volume, flow velocity, and resistive index (RI) of the vessels were assessed by Doppler US. In patients, complete blood count, biochemical parameters, coagulation tests, auto-immune antibodies, electrocardiography, and P-A chest radiography were assessed before the operation. The upper limb, which was considered as suitable for AV fistula operation, was preserved in terms of intravenous interventions over 1 week before AV fistula operation, and no anti-platelet therapy was warranted.

Arteriovenous fistula was made at the most distal localization as possible in the arm without a hemodialysis catheter. Quality, spasm, and diameter of the artery and vein were assessed and recorded during surgery. A snuffbox-type fistula was performed in 32 patients (88.9%), whereas a Brescia-Cimino type was performed in 4 (11.1%). The presence of thrill was assessed after the operation. No bleeding or any other complication occurred during surgery. Thrill in AV fistula was detected in 23 patients (63.9%) during the operation. Pulse but not thrill was observed in 13 patients (36.1%).

Biochemical and hematological measurements and Doppler US evaluation were re-performed on day 1 after the operation.

Eligibility as the hemodialysis access site and maturation of the AV fistula were confirmed by physical examination, and AV fistula was started to be used for hemodialysis in patients who had maturation.

In the follow-up of the AV fistula, blood flow of the fistula and the presence of thrombus were assessed in terms of failure by Doppler US in patients in whom the blood flow could not be detected by auscultation and palpation. AV fistula failure was detected in 10 patients (27.8%), and simultaneous biochemical and hematological tests, coagulation tests, and auto-immune antibody tests were performed in these patients.

Operation technique

The most appropriate region in the forearm to achieve AV fistula was pre-operatively detected via venous and arterial inspection and palpation. It was attempted to form a fistula at the most distal region as possible. The snuff box region was first choice in appropriate cases, whereas a fistula of the standard Brescia-Cimino wrist region was preferred as the second choice.

All the fistula procedures were performed under local anesthesia with 2% prilocaine through a 2–4 cm skin incision. Antibiotic prophylaxis (0.5 g cefazoline) and 5000 IU intravenous heparin were given to all patients immediately before surgery. Snuff box and Brescia-Cimino fistula were performed with a side-to-end anastomosis technique between the cephalic vein and radial artery by continue stitches using 7/0 or 8/0 polypropylene sutures. In cases in which end-to-side anastomosis was performed, a cephalic vein ligation and intersection was performed following dissection of the artery and vein, and then anastomosis was made up to the radial artery after the artery was dilated with heparinized saline solution by using a 20 gauge catheter.

Low molecular weight heparin (2–0.3 mL Fraxiparine, S.C) was given for 72 h after surgery.

Allen test

All modified Allen tests were performed by the same researcher. After observing waves by a pulse oximetry attached to the index finger, a forceful pressure was applied both on the radial and ulnar artery until fluctuation disappears while the patient's hand was in the supine position. Thereafter, pressure on the radial artery was ended and the time passing until fluctuation re-appears on pulse oximetry and the palmar color returns normal was recorded. The same procedure was also performed for the ulnar artery. Patients with a time longer than 10 s were excluded from the study (14).

Doppler US evaluation

Duplex Doppler US evaluation was performed by the same researcher using the same device (HDI 5000, Philips Medical Systems, Bothell; WA) and CL10-5 probe. Anatomical (diameter) and functional (peak systolic flow rate, end-diastolic velocity, RI, flow volume, mean velocity, fistula output, and fistula volume) parameters were assessed during evaluation.

Bleeding time

Bleeding time tests were performed using the cuff of a sphygmomanometer. The cuff was compressed to the upper limb and then inflated until 40 mmHg and fixed at this level. A horizontal, superficial incision was made at the inner surface of the forearm using a sterile lancet or bistoury, paying attention to the subcutaneous veins. A blood drop was removed every 30 s by a blotter without touching the insult. The time passing until the superficial bleeding stopped was taken as the bleeding time.

Hematological and biochemical parameters

Complete blood counting was performed on samples taken into tubes using a Coulter Lh750 Analyzer incelendi (Backman Coulter, Seri No: AH07077-USA).

Biochemical tests were performed using an Olympus AU2700 and Au Olympus AU600. 3 cc blood samples were taken and centrifuged for 10 min at 3000 g. After the serum was separated, glucose, blood urea nitrogen, creatinine, calcium phosphate, lipids, protein, and albumin levels were measured; also parathormone levels were measured in the same serum by a chemiluminescent immunoassay (Immulite 2000) method.

C-reactive protein (CRP) levels were measured by Dade Behring Marburg GmbH using N High Sensitivity CRP reagent in serum, which was obtained by centrifuging for 10 min at 3000 g. The result was expressed as mg/mL.

2 cc blood samples were centrifuged for 10 min at 3000 g, and the serum obtained was divided into aliquots and stored at -20°C . Then, all the anti-cardiolipin antibodies (IgG and IgM) measurements were collectively performed by enzyme immunoassay (EIA) by LABOTEC after thawing the aliquots at room temperature. An anti-cardiolipin antibody (IgG and IgM) level ≥ 10 IU/mL is considered as positive (+), while levels < 10 IU/mL are considered as negative (-).

For protein C, protein S, and APC (active protein C resistance), 2 cc blood samples were taken into tubes containing sodium citrate, and then centrifuged for 5 min at 3000 g. The serum was frozen at -20°C and then collectively tested.

The prothrombin time (STA-Neoplastine Cl Plus kit), active partial thromboplastine time (STA-C.K Prest kit), fibrinogen (STA-Fibrinogen kit), D-dimer (Liatest D-Dimer kit, Latex Agglutination), protein C (STA-Stacot Protein C kit, chromogenic method), and protein S (STA-Free Protein S kit chromogenic method) tests were performed by using STA-Compact.

Statistical analysis

The collected data were analyzed by using SPSS version 10.0 Statistic Software (SPSS; Cary, NC, USA). The results were expressed as the mean \pm standard deviation. The Mann-Whitney U test, Independent samples t-test, and Friedman test were used for comparisons between groups with or without fistula failure. Factors related to fistula failure were evaluated by using regression analysis. The Pearson test was used for the correlation analysis. $P < 0.05$ was considered as statistically significant.

RESULTS

It was found that the time for maturation of the AV fistula, thrombus formation, and Allen test at the radial artery varied between 10 and 44 days (mean: 18.9 ± 8.7), 1 and 73 days (mean 28.4 ± 26.1), and 2 and 10 s (mean: 4.9 ± 2.3), respectively. Age, time in Allen test and duration of CRF, ESRD, hemodialysis, catheterization, and fistula maturation were found to be similar between cases with AV fistula failure and without ($p > 0.05$) (Table 1).

On the initial assessment, no difference was found in systolic and diastolic blood pressure, glucose, blood urea nitrogen, creatinine, uric acid, calcium, phosphate, parathormone, total protein, albumin, lipid profile, erythrocyte sedimentation rate (ESR), bleeding time, APC resistance, PT, APTT, hemoglobin, hematocrit, fibrinogen, protein C, protein S, ACA IgG and IgM antibodies, and D-dimer levels between groups with functional and dysfunctional fistula, while the CRP value (65.6 ± 42.4 vs 39.1 ± 34.8 mg/dL, $p = 0.021$) was found to be higher in the group with dysfunctional fistula. On basal Doppler US evaluation, the diameters of the radial artery (0.2 ± 0.01 cm vs 0.3 ± 0.1 cm, $p = 0.045$) and the cephalic vein in the Brescia-Cimino region (0.1 ± 0.1 cm vs 0.2 ± 0.05 cm,

Table 1. Comparison of demographic parameters in patients with functional (n=26) and nonfunctional (n=10) AV fistula

| | Nonfunctional AV fistula group Mean \pm standard deviation (minimum-maximum) | Functional AV fistula group Mean \pm standard deviation (minimum-maximum) | p |
|---|--|---|-------|
| Age (years) | 50.0 \pm 15.0 (20-50) | 50.8 \pm 15.7 (22-76) | >0.05 |
| Duration of CRF (months) | 6.9 \pm 15.1 (1-49) | 7.3 \pm 11.7 (1-37) | >0.05 |
| Duration of ESRD (months) | 4.4 \pm 7.9 (1-25) | 2 \pm 4.7 (1-25) | >0.05 |
| Duration of hemodialysis (days) | 9.8 \pm 5.1 (5-21) | 8.4 \pm 8.5 (1-31) | >0.05 |
| Duration of Allen test at the radial artery (s) | 5.3 \pm 2.4 (2-10) | 4.7 \pm 2.3 (2-9) | >0.05 |
| Duration of fistula maturation (days) | 20.0 \pm 11.0 (12-34) | 18.6 \pm 8.4 (10-44) | >0.05 |

AV: arteriovenous; CFR: chronic renal failure; ESRD: end-stage renal disease

Table 2. Comparison of Doppler US findings at baseline in patients with thrombus (n=10) and functional AV fistula (n=26)

| | Thrombus Mean±standard deviation (minimum–maximum) | Functional AV fistula Mean±standard deviation (minimum–maximum) | p |
|---|---|--|----------|
| Peak systolic velocity of the radial artery at the snuffbox (cm/s) | 53.1±16.9 (22.0–73.2) | 63.2±23.4 (28–119) | >0.05 |
| End-diastolic velocity of the radial artery at the snuffbox (cm/s) | 11.2±5.9 (3–19.5) | 11.9±5.1 (4–27) | >0.05 |
| Resistive index of the radial artery at the snuffbox | 0.8±0.1 (0.7–0.9) | 0.8±0.1 (0.6–0.9) | >0.05 |
| Flow volume of the radial artery at the snuffbox (mL/min) | 18.3±13.9 (2.7–46.0) | 31.9±28.1 (3.6–119) | >0.05 |
| Diameter of the radial artery at the snuffbox (cm) | 0.2±0.01 (0.2–0.3) | 0.3±0.1 (0.2–0.4) | 0.045 |
| Mean velocity of the radial artery at the snuff box (cm/s) | 6.2±4.6 (1.5–15.3) | 9.0±6.5 (1–25) | >0.05 |
| Peak systolic velocity of the cephalic vein at the snuffbox (cm/s) | 9.2±4.8 (4.7–19.7) | 7.8±3.7 (0–20) | >0.05 |
| End-diastolic velocity of the cephalic vein at the snuffbox (cm/s) | 4.7±1.9 (3–8.5) | 4.0±1.9 (0–10) | >0.05 |
| Diameter of the cephalic vein at the snuffbox (cm) | 0.2±0.1 (0.1–0.3) | 0.2±0.1 (0–0.3) | >0.05 |
| Peak systolic velocity of the radial artery at the Brescia-cimina region (cm/s) | 53.9±15.6 (22–71) | 60.2±19.2 (23–105) | >0.05 |
| End-diastolic velocity of the radial artery at the Brescia-cimina region (cm/s) | 10.0±4.2 (5–18) | 10.2±3.6 (4–18) | >0.05 |
| Resistive index of the radial artery at the Brescia-cimina region | 0.8±0.1 (0.7–0.9) | 0.8±0.1 (0.7–0.9) | >0.05 |
| Flow volume of the radial artery at the Brescia-cimina region (mL/min) | 16.6±11.2 (3.6–39.6) | 26.8±21.5 (3–88) | >0.05 |
| Diameter of the radial artery the at Brescia-cimina region (cm) | 0.3±0.03 (0.2–0.3) | 0.3±0.1 (0.2–0.4) | >0.05 |
| Mean velocity of the radial artery at the Brescia-cimina region (cm/s) | 4.9±3.1 (1.5–11) | 6.7±4.4 (1–17) | >0.05 |
| Peak systolic velocity of the cephalic vein at the Brescia-cimina region (cm/s) | 8.6±11.6 (0–38) | 10.5±6.0 (2.5–32) | >0.05 |
| End-diastolic velocity of the cephalic vein at the Brescia-cimina region (cm/s) | 4.1±4.6 (0–15) | 5.5±3.8 (2–60) | >0.05 |
| Diameter of the cephalic vein at the Brescia-cimina region (cm) | 0.1±0.1 (0–0.18) | 0.2±0.05 (0.1–0.3) | 0.003 |

AV: arteriovenous; US: ultrasonography

p=0.003) were found to be smaller in cases with thrombus formation, while other ultrasonographical parameters were similar in both groups (Table 2).

On the assessment on day 1 after operation, it was found that ESR (104.1±23.4 vs 81.9±36.2 mm/h, p=0.04) and prothrombin time (24.1±17.3 vs 14.6±2.0 s, p=0.041) were higher in the group with dysfunctional fistula, while the other parameters were similar in both groups. On simultaneous Doppler US evaluation in the group with thrombus formation, it was found that the end-diastolic velocity of the radial artery (21.7±33.6 vs 34.5±29.8 cm/s, p=0.049) and cephalic vein (14.5±20.4 vs 35.2±39.2 cm/s, p=0.019) in the snuff box region and the peak systolic velocity (68.4±29.8 vs 100.9±50.9 cm/s, p=0.025), end-diastolic velocity (22.4±18.7 vs 49.7±30.5 cm/s, p=0.011), flow volume (83.6±84.1 vs 208.4±171.2 mL/min, p=0.019) and mean velocity (16.4±15.1 vs 37.9±24.7 cm/s, p=0.004) of the radial artery in the Brescia-Cimino region were lower, and also the cephalic vein diameter was smaller in the same group (Table 3).

On evaluation of Doppler US in the group with dysfunctional fistula, it was found that the RI of the radial artery in the snuff box region first decreased (p<0.05) and thereafter increased (p<0.05) (0.8±0.1 vs 0.5±0.3 vs 0.7±0.3, respectively), while the peak systolic velocity (9.2±4.8 vs 28.4±24.2 vs 4.4±3.2, respectively) and end-diastolic velocity of the cephalic vein in the snuff box region (4.7±1.9 vs 14.5±10.2 vs 2.4±2.0, respectively) first increased

and thereafter decreased (p<0.05). In addition, an initial marked increase and then a decrease were found in the diameter of the radial artery in the Brescia-Cimino region (4.9±3.1 vs 16.4±12.1 vs 4.3±2.7, respectively) (p<0.05).

When structural features of vessels in the fistula region were considered, it was seen that the fistula output (244.6±284.8 vs 363.1±202.1 mL/min, p=0.045) and velocity (78.1±99.6 vs 116.0±72.7 cm/s, p=0.04) were lower in patients with thrombus formation. No difference was found regarding AV fistula localization, and the diameter of the artery and vein used, and the duration of AV fistula maturation between both groups.

When assessed by regression analysis, it was found that the following factors had no effect on the formation of thrombus: cardiothoracic index on P-A chest radiography, evidence of left ventricle hypertrophy on the ECG, anatomical region, quality of artery, spasm of artery and vein, biochemical parameters, lipid profile, ESR, bleeding time, PT, APTT, arterial hypertension, diabetes mellitus, APC resistance and fibrinogen, protein C, protein S, ACA IgG and ACA IgM, D-dimer, and CRP levels (p>0.05). It was detected that female gender (p<0.001), thrill on post-operative period (p=0.014), using a good quality vein for fistula (p<0.001), peak systolic velocity of the radial artery in the snuff box region on day 1 after operation (p<0.035), and the pre-operative cephalic vein diameter at Brescia-Cimino region (p=0.011) were effective factors on thrombus formation.

Table 3. Comparison of Doppler US findings at day 1 after operation in patients with thrombus (n=10) and functional AV fistula (n=26)

| | Thrombus Mean±standard deviation (minimum–maximum) | Functional AV fistula Mean±standard deviation (minimum–maximum) | p |
|---|---|--|----------|
| Peak systolic velocity of the radial artery at the snuffbox (cm/s) | 53.9±57.1 (0–180.0) | 63.1±37.3 (16–114) | >0.05 |
| End-diastolic velocity of the radial artery at the snuffbox (cm/s) | 21.7±33.6 (0–107.0) | 34.5±29.8 (5–71.9) | 0.049 |
| Resistive index of the radial artery at the snuffbox | 0.5±0.3 (0–0.9) | 0.6±0.3 (0.3–1.8) | >0.05 |
| Flow volume of the radial artery at the snuffbox (mL/min) | 76.6±165.9 (0.0–542.0) | 86.6±88.1 (7.2–388.6) | >0.05 |
| Diameter of the radial artery at the snuffbox (cm) | 0.2±0.1 (0–0.4) | 0.3±0.1 (0.2–0.5) | >0.05 |
| Mean velocity of the radial artery at the snuffbox (cm/s) | 13.7±18.9 (0–60.2) | 19.2±13.8 (2–46) | >0.05 |
| Peak systolic velocity of the cephalic vein at the snuffbox (cm/s) | 28.4±34.2 (0–109) | 57.4±55.4 (6–186) | >0.05 |
| End-diastolic velocity of the cephalic vein at the snuffbox (cm/s) | 14.5±20.4 (0–67) | 35.2±39.2 (4–136) | 0.019 |
| Diameter of the cephalic vein at the snuffbox (cm) | 0.2±0.1 (0–0.4) | 0.3±0.07 (0.1–0.5) | >0.05 |
| Peak systolic velocity of the radial artery at the Brescia-cimina region (cm/s) | 68.4±29.8 (20.1–116) | 100.9±50.9 (34–260) | 0.025 |
| End-diastolic velocity of the radial artery at the Brescia-cimina region (cm/s) | 22.4±18.7 (7–69) | 49.7±30.5 (3–116) | 0.011 |
| Resistive index of the radial artery at the Brescia-cimina region | 0.7±0.2 (0.4–0.9) | 0.5±0.2 (0.3–0.9) | >0.05 |
| Flow volume of the radial artery at the Brescia-cimina region (mL/min) | 83.6±84.1 (4.8–277) | 208.4±171.2 (14.4–730) | 0.019 |
| Diameter of the radial artery at the Brescia-cimina region (cm) | 0.3±0.1 (0.2–0.4) | 0.3±0.1 (0.2–0.4) | >0.05 |
| Mean velocity of the radial artery at the Brescia-cimina region (cm/s) | 16.4±15.1 (2–51.4) | 37.9±24.7 (4–86) | 0.004 |
| Peak systolic velocity of the cephalic vein at the Brescia-cimina region (cm/s) | 16.7±31.0 (0–99.6) | 20.7±21.6 (4–93) | >0.05 |
| End-diastolic velocity of the cephalic vein at the Brescia-cimina region (cm/s) | 9.5±18.2 (0–58.3) | 11.9±13.9 (2–60) | >0.05 |
| Diameter of the cephalic vein at the Brescia-cimina region (cm) | 0.2±0.2 (0–0.6) | 0.2±0.04 (0.1–0.3) | >0.05 |

AV: arteriovenous; US: ultrasonography

DISCUSSION

Arteriovenous fistula is functional in 73–93% of patients after the first AV fistula operation (15-18). The complication rate is 20% (10% wound, 8% ischemia) in patients undergoing AV fistula operation, since 24% of these patients need repeated intervention (3, 19). More thrombosis develops in radial-cephalic fistulas than in brachial-cephalic ones. The stenosis rate in the early phase is found to be higher in fistulas performed at the snuff box level than with fistulas performed at either the wrist or more proximal levels. The rate of thrombosis formation varies between 4% and 18% per year (15-18). The follow-up period was 4 months in our patients, and fistula failure due to thrombosis developed in ten (27.7%) of our patients. Of these patients, the snuff box fistula was used in eight (22.2%) patients and the Brescia-Cimino type in patients (5.5%). In our study, however, we failed to show that the anatomic site of the AV fistula is an effective factor in the development of thrombus.

While 1 month is adequate before achieving safe dialysis in some AV fistulas, 6 months is needed in some others (20). In a study by Rayner et al. (21), they failed to show a relationship between cannulation of fistula at any time 14 days after operation and the risk of failure. In our study, there was no relationship between cannulation time of the fistula after operation and an increase in the risk of AV fistula failure.

Thrombosis of the fistula is an important cause of morbidity in patients receiving hemodialysis, and, in most cases, thrombosis and venous stenosis in AV fistula cause vascular access failure (22-24). Thrombosis developing in the first 30 days after surgical intervention usually suggests a surgical problem (25). Intimal fibromuscular hyperplasia at the venous anastomosis site should be an important factor related to thrombosis. Factors other than problems in surgical technique, such as inappropriate veins and insufficient arterial flow, have also been discussed (9, 26). By pre-operatively selecting artery matching with the following criteria, early fistula failure decreases to 8.3% from 36.0%: artery in non-dominant upper limb, lumen 2 mm or larger and a good response to compression, no evidence of stenosis, an available segment ≥ 3 mm, and absence of obstruction or stenosis in ipsilateral veins (13). The non-dominant upper limb was used in our patients. Vascular structures and fistula functions were inspected and assessed by Doppler US during intervention. Changes in the quality of the artery and vein were detected in six of ten cases in which AVF failure developed. The quality of vein was found to be an effective factor in the emergence of thrombosis, while it was found that the diameter of vessels had no effect on thrombus formation. In the present series, the emergence of thrombosis was found to be one of the most common causes of AV fistula failure, and the duration of thrombosis varied between 1 and 73 days. In our study, the most important reasons for thrombosis formation at a relatively early period after operation could be linked to the surgical technique and the vascular structures used for the fistula operation.

Several factors have been investigated in order to establish the etiology of thrombosis and AV fistula failure. In studies investigating these issues, miscellaneous outcomes could be found regarding the effects of identical factors on thrombosis and AVF due to the selected patient population, follow-up period, surgical technique, experience of the surgical team, and the protocols used in the management and usage of AV fistula (9, 10, 25, 27). Data about potential risk factors for thrombosis and AV fistula failure, such as age, gender, smoking, hypertension, diabetes, hypotension during dialysis, fistula site, dialysis duration, type of dialysis membrane, erythropoietin usage, hypo-albuminemia, hyperlipidemia, PTH elevation, elevation in lipoprotein a, and hyper-homocysteinemia conflict in the literature (12, 19, 22, 26, 28-31). In the majority of studies evaluating the demographic data of patients, advanced age and female gender were found to be negative risk factors for AV fistula maturation and thrombosis (9, 19, 22, 27, 29). In the present study, we found that while the above parameters had no effect on thrombosis formation, female gender was an effective factor in thrombus formation. However, we failed to show that CRP and ESR were important in thrombus formation, although a slight increase was shown in these factors before and after fistula in patients with thrombus formation. These conflicting data are related to potential differences in the study design and length of follow-up.

Arteriovenous fistula failure is seen more frequent in the elderly population due to the common presence of co-morbid diseases, such as uremic or ischemic cardiomyopathy, peripheral vascular diseases, hypertension, and diabetes (13, 27). Endothelial injury with calcified radial artery with small lumen, a thickened wall, and diminished nitric oxide production should be present in hypertensive and diabetic elders, and could thereby cause fistula failure. Several endothelial products, pro-inflammatory mediators, cytokines, and growth factors cause venous intimal hyperplasia and stenosis of the vascular access line (26, 32, 33). No data indicating increased thrombosis formation in diabetic patients were seen in our patient group. Although anti-hypertensive drugs, such as calcium channel blockers, aspirin, and ACE inhibitors, could reduce the risk of AV fistula failure and thrombosis, such drugs were not found to be effective factors in the formation of thrombus in our study. These conflicting data are related to potential differences in study design and the length of follow-up.

There are only a limited number of studies in the literature in which all the thrombotic risk factors have been evaluated in relation to AV fistula failure. There are several thrombophilic risk factors and there is a debatable relationship in each (10, 11, 27). There are reports regarding a decrease in factor VIII activity or a reduced response of the plasminogen activator to venous occlusion, decreased platelet sensitivity to antiaggregant prostacyclins, and a decrease in anti-thrombin III, protein S, fibrinogen, and plasminogen (34-37). In our study, it was found that fibrinogen, protein C and protein S levels, bleeding time, PT, APTT, and D-dimer levels had no effect on thrombosis formation. However, it has to be taken into account that there were only a limited number of patients with thrombosis in our study.

Arterial and venous thrombotic events are defined as serious complications in patients receiving regular dialysis as well as them hav-

ing a positive anti-cardiolipin antibody level (12). Besides, there are reports suggesting no relationship between ACA positivity and thrombosis in relation to a selected patient population (12, 38). In our study, anti-cardiolipin antibody (Ig G and Ig M) levels detected in patients with or without thrombus formation were similar before and after fistula operation; thereby, it was shown that these factors were not effective in thrombus formation. These conflicting data are related to potential differences in the study population (e.g., presence or absence of vasculitis).

In an update in the year 2000 K/DOQI (Kidney Disease Outcomes Quality Initiative) guideline, the annual measurement fistula flow rate was recommended for graft stenosis (39). Color Doppler US is the most important non-invasive, inexpensive, easy, painless, portable, and reproducible evaluation method that can be used in the assessment of both anatomical and functional characteristic of vascular structures before operation and the functional monitoring of fistula after operation. Fistula output is accepted as the best method for vascular access monitoring and one of the most important indicators for access failure according to the Vascular Access Society guideline (40). In our study, in the baseline Doppler evaluation, it was detected that the radial artery diameter in the snuff box region and the cephalic vein diameter at the Brescia-Cimino site were smaller in patients with thrombus formation, and it was shown that the vein quality used for fistula and the baseline cephalic vein diameter at the Brescia-Cimino site were important factors in thrombus formation. In addition, the absence of thrill after operation was found to be one of the most important factors in thrombus formation.

A flow rate of <400 mL/min could be accepted as the best marker for fistula failure (22). In the study by Hoebe et al. (22), the sensitivity and specificity of a flow rate of <500 mL/min was 57% and 92%, respectively. In a study with a 4-year follow-up by Basile et al. (41), annual flow measurement was performed, and a flow of <700 mL/min was cited as a valid marker (89% sensitivity and 69% specificity) of thrombosis risk. In our patients with thrombus, the end-diastolic velocity of the radial artery and cephalic vein in the snuff box region and the peak systolic velocity, end-diastolic velocity, flow volume, and mean velocity of the radial artery in the Brescia-Cimino region were found to be lower in the assessment performed on day 1 after the fistula operation. However, among parameters assessed by Doppler US on day 1 after the fistula operation, only peak systolic velocity and end-diastolic velocity of the radial artery in the snuff box region were found to be important factors in thrombus formation. In patients with thrombus formation, changes were seen in the flow volume and RI of the radial artery and peak systolic velocity, end-diastolic velocity, diameter of the cephalic vein in the snuff box region, and the mean velocity of the radial artery in the Brescia-Cimino region. When output measurements were evaluated in groups, it was found that the output and the velocity of the fistula were lower in the patient group with thrombus.

CONCLUSION

Thrombosis occurs and the AV fistula becomes dysfunctional at a relatively early phase in approximately a quarter of AV fistulas, which enable long-term hemodialysis therapy in patients with CRF.

Although female gender, vein quality, and the absence of thrill after an operation seem to be effective factors in thrombus formation, the definite factors determining thrombus formation remain ambiguous. The surgeon should assess the vascular structures and presence of thrill during the operation. Color Doppler US evaluation is a method that could be effectively and widely used for the assessment of vascular structures before fistula and for monitoring fistula functions after operation.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İnönü University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authors' Contributions: Conceived and designed the experiments or case: FS, HT. Performed the experiments or case: AS, BA. Analyzed the data: HT, FS. Wrote the paper: FS, HT, AS, BA. All authors have read and approved the final manuscript.

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