The importance of age in terms of fistula patency in chronic hemodialysis patients: 7-year follow-up

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INTRODUCTION

The number of patients undergoing hemodialysis is gradually increasing due to prolonged life span, imbalances in socio-economic conditions, increases in drug consumption, and infectious diseases. It is important to ensure that arteriovenous fistulas remain open without any complications due to reasons such as high comorbid conditions and the need for long-term durability in dialysis patients. Creating an autogenous arteriovenous fistula in patients with chronic renal failure facilitates hemodialysis and increases the patient’s quality of life. An ideal vascular access method to be created for hemodialysis applications is long-lasting and should have low complication rates, adequate should allow blood flow to pass. Many patients who need dialysis cannot be kidney transplant candidates and die in the waiting phase of the transplant [1-3]. These patients need to be hospitalized many times a year, which increases the average number of hospital days per year. After the first AVF creation process of Brescia et al. in 1966 [4], hemodialysis procedures became easier and complications decreased and patients’ lifespan increased. Even if AVF creation is performed in different localizations and using different products over the years, this fistula application is still used as the first option [3,4]. Any intervention and application to the vascular struc-
tures used in fistula formation will disrupt the fistula vascular structure and will cause problems in both fistula function and problems in patient psychology and stability over time. Due to the repeated interventions for hemodialysis patients, limitations appear over time in the vascular access site. Over the years, existing vascular structures have become completely devastated and unusable to perform dialysis in patients. The crucial factor for hemodialysis patients is to ensure the patency of AVFs as long-term as possible without complications. In arteriovenous fistulas opened for hemodialysis, in addition to hemodynamic changes, complications such as bleeding, thrombosis, extremity ischemia, local infection, edema, venous hypertension, and venous aneurysm are frequently encountered. Complications lead to increased morbidity and prolonged hospital stay and negatively affect patients’ quality of life and duration. Several factors are related to or not related to the patient, affecting the patency or occlusion of AVFs. In this study, we tried to determine whether post-middle age affects primary fistula patency.

METHODS

From May 2013 through Oct 2020, 442 patients underwent arteriovenous access for hemodialysis in Atatürk University Cardiovascular Surgery Clinic. Of the patients operated for AVF, 256 (57.9%) were male and 186 (42.1%) were female. Their mean age was 63.8 years (range 31 to 77 years). The patients were divided into 2 groups. Patients under 40 years of age were considered as Group I (n=201) and patients over 40 years of age were considered as Group II (n=241). We collected the following parameters at the time of creating the AVF: demographics (age and gender), comorbidities (hypertension, diabetes, peripheral arterial disease, hypercholesterolemia, obesity, smoking, etc.). All preoperative data are shown in Table 1. The patients were prospectively followed for 6.5 ± 1.3 years (mean 5.1 years). Patients were followed up for kidney transplantation or death. The effects of age for primary patency rates were investigated. Primary patency was the interval from the time of access placement until any intervention designed to maintain or re-establish patency, until access thrombosis, or until the time of measurement of patency.

Exclusion criteria

Congestive heart failure, pregnancy, chemotherapy for malignant disease, hereditary thrombotic disposition, vasculitis, upper extremity trauma, orthopedic surgeries and phlebitis, arm-related venous thrombosis and arterial embolism, ejection fraction below 30%, and vessel diameter below 2 mm (Doppler USG) were not included in the study.

Surgical procedure

The arm to be opened with the AVF was kept away from interventional procedures and trauma. For the quality of vascular structures, vascular structures, and diameters were evaluated with duplex ultrasonography and venography in addition to physical examination. Those with vessel diameters greater than 2 mm were preferred to perform AVF. A single dose of anti-biotherapy was applied to all patients in the study before the procedure. All patients were operated on by the same surgical team. The non-dominant upper limb (usually the left arm) was preferably used. It was not preferred due to the risk of lower extremity infection and limitation of movement. In general, AVFs were used for hemodialysis using the patient’s own autogenic vessels and performed from distal to proximal. After the arterial and venous vessels were prepared, 0.5 ml heparin was administered to the patients. Anastomoses were done using 7/0 polypropylene (either end-to-side or side-to-side procedure). The wound was then closed in one layer and the hand was held up. The presence of trill on the venous structure after the operation was evaluated as a successful result. The patients were discharged on the first postoperative day. Anticoagulant treatment of low molecular weight heparin was administered to the patients. Anastomoses were done using 7/0 polypropylene (either end-to-side or side-to-side procedure). The wound was then closed in one layer and the hand was held up. The presence of trill on the venous structure after the operation was evaluated as a successful result. The patients were discharged on the first postoperative day. Anticoagulant treatment of low molecular weight heparin was administered to all patients within 10 days. Later, acetylsalicylic acid treatment was started according to the patient’s suitability. Local anesthesia or axillary block was preferred for surgical intervention.

Assessment of fistula maturation

The patients were followed primarily for fistula patency in the postoperative period. Patients who had no problem with fistula opening were discharged and wound care recommendations were made. Hand and finger exercises were said to be done in terms of AVF development. For a functional AVF, sufficient vascular space and at least 300-400 ml/min blood circulation are required. That’s why these patients were evaluated by Doppler USG after the first week and their AVF flow was measured. Patients who were found to have sufficient flow were recommended to wait for about 1 month in terms of fistula development and adequate hemodialysis.
Ethics statement

Ethical permission was given by the Erzurum Regional Training and Research Hospital ethics committee and informed written consent was obtained from all participants and/or parents or guardians. The Hospital Ethical Committee Permission was obtained before the commencement of the study. Furthermore, all procedures were carried out by the Declaration of Helsinki.

Statistical analysis

Student t-test was used to compare age between groups, and the chi-square test was used for gender comparison. Kaplan Meier survival analysis and log-rank test were used to assess the obstruction status of the fistula for 7 years. Age-related data were presented with the mean ± standard deviation of the arithmetic mean. Categorical variables were expressed as counts and percentages. Statistically, 0.05 levels were accepted as significant.

RESULTS

The pre-operative data analysis made between both groups is presented in Table 1. There were no differences between the two groups in preoperative patients’ characteristics, and there was no statistical significance. There was no statistically significant difference between the groups in terms of gender. There were no differences between the two groups in terms of the number of patients with hypertension, diabetes mellitus between groups. There was also no difference between the groups in terms of etiological factors (Table 1). In the literature, many types of surgery have been used

| Parameters                                      | Group I (n=201) | Group II (n=241) | P values |
|------------------------------------------------|---------------|-----------------|---------|
| Gender (M/F)                                   | 116/85        | 140/101         | 0.150   |
| Body mass index (kg/m²)                        | 23.1 ± 6.64   | 23.4 ± 8.67     | 0.899   |
| Hemoglobin (g/dL)                              | 10.6 ± 1.09   | 10.4 ± 1.13     | 0.377   |
| Hypertension                                   | 181           | 202             | 0.429   |
| Albumin (g/dL)                                 | 3.1 ± 0.97    | 3.0 ± 0.98      | 0.702   |
| White blood cell, (10³/mm³)                    | 8.8 ± 4.18    | 9.1 ± 4.77      | 0.371   |
| C-reactive protein, (mg/dL)                    | 3.9 ± 6.09    | 4.1 ± 6.71      | 0.533   |
| eGFR (mL/min/1.73 m²)                          | 12.8 ± 16.22  | 13.1 ± 17.55    | 0.527   |
| Previous percutaneous catheter                 | 82            | 103             | 0.124   |
| Previous tunneled cuffed catheter              | 65            | 98              | 0.198   |
| Smoker habits                                  | 172           | 211             | 0.522   |
| Diabetes Mellitus                              | 165           | 203             | 0.634   |
| Hypercholesterolemia (LDL > 130 mg/dL)         | 115           | 154             | 0.411   |
| Obesity (Body-mass index > 30 kg/m²)           | 36            | 49              | 0.112   |
| Chronic obstructive pulmonary disease (COPD)    | 41            | 66              | 0.501   |
| Cardiovascular disease                         | 21            | 33              | 0.788   |
| Inotrope and vasopressor use                   | 4             | 6               | 0.303   |
| Cerebro-vascular disease                       | 8             | 11              | 0.522   |
| Peripheral vascular disease                    | 16            | 21              | 0.117   |
| Etiology of hemodialysis                       |               |                 |         |
| Glomerulonephritis (48.6 %)                    | 96            | 119             | 0.122   |
| Chronic pyelonephritis (22.7 %)                | 45            | 55              | 0.453   |
| Polycystic kidney disease (17.3)               | 36            | 40              | 0.422   |
| Diabetes mellitus (5.8 %)                      | 11            | 15              | 0.675   |
| Hypertension (3.2 %)                           | 8             | 6               | 0.899   |
| Amyloidosis (1.3 %)                             | 3             | 3               | 0.590   |
| Other (1.1 %)                                   | 2             | 3               | 0.233   |
| Evaluation of preoperative venous structure    |               |                 |         |
| Duplex Ultrasound                              | 195           | 229             | 0.111   |
| Venography                                     | 6             | 12              | 0.405   |
for AVF. The most common types of surgical intervention to create AVFs were snuff-box, Brescia-Cimino, basilic vein transposition, brachiocephalic, upper radio cephalic (Table 2). There was no statistical difference between the groups in terms of AVFs types. Besides, the information about operations is also summarized in Table 2.

In addition to the structural and functional features in patients with AVF, complications occurring in the first week after surgery are shown in Table 3. The most common complication was hematoma due to bleeding. In the first week, 21 patients in group I and 26 patients in group II had no trill in AVF and obstruction developed. As soon as occlusion was detected in these patients, thrombectomy was performed and AVFs were made functional. All patients were successfully included in the hemodialysis program. There was no statistically significant difference between the groups in terms of the features and complications shown in Table 3. A hematoma evacuation procedure was performed in patients with hematomas. The bleeding stopped with minimal pressure in patients with bleeding. In some patients, the incision of the patient was reopened for bleeding. Bleeding sites were found and bleeding was stopped (ligation or cauterization).

The overall primary patency rates were 90.2%, 85.6%, 75.4%, 63.4%, 57.1%, 48.2% and 41.2% after 1, 2, 3, 4, 5, 6 and 7 years, respectively in Group I. In patients over 40 years of age (Group II), these rates were 83.3%, 71.2%, 61.9%, 57.7%, 43.7%, 34.8%, and 28.5% after 1, 2, 3, 4, 5, 6 and 7 years, respectively (Figure 1). There was a significant difference between under the age of 40 and over 40 years old about primary fistula patency (p<0.001). In patients under 40 years of age, the rate of primary patency rates in 7 years was found to be higher than in those aged over 40 years. Besides, mean fistula occlusion was 41.4 months in patients under 40 years of age; this rate was 28.7 months in patients over 40 years of age. This period was statistically significant (p < 0.001).

DISCUSSION

Establishment, use, and follow-up of AVFs, which are one of the hemodialysis methods in patients with chronic kidney failure, affect the quality of life of patients and are an important criterion for survival. A

| Variables                             | Group I (n=201) | Group II (n=241) | P values |
|---------------------------------------|----------------|-----------------|---------|
| Operation time (min.)                 | 48±9           | 51±10           | 0.211   |
| Mean arterial diameters (mm)           | 3.7±1.5        | 3.5±1.4         | 0.505   |
| Mean arterial diameters (mm)           | 3.1±0.9        | 3.0±0.8         | 0.477   |
| Local anesthesia (lidocaine)          | 187            | 227             | 0.133   |
| Axillary blockade (bupivacaine)       | 14             | 14              | 0.655   |
| Used extremity                        |                |                 |         |
| Right arm                             | 33             | 54              | 0.688   |
| Left arm                              | 168            | 187             | 0.308   |
| Add sedation administration for anesthesia | 11             | 16              | 0.522   |
| Incision closure technique            |                |                 |         |
| Primary suture                        | 99             | 124             | 0.452   |
| Matrix Suture                         | 55             | 72              | 0.128   |
| Continuous Subcutaneous Aesthetic Suture | 27             | 23              | 0.359   |
| Staples                               | 20             | 22              | 0.741   |
| Fistula sites                         |                |                 |         |
| Antecubital                           | 47             | 75              | 0.189   |
| Wrist                                 | 139            | 146             | 0.233   |
| Fistula types                         |                |                 |         |
| Snuff-box                             | 53             | 44              | 0.566   |
| Brescia-Cimino                        | 86             | 102             | 0.432   |
| Basilic vein transposition            | 19             | 31              | 0.981   |
| Brachiocephalic                       | 28             | 44              | 0.521   |
| Upper radio cephalic                  | 15             | 20              | 0.433   |
A functional AVF that can remain open without thrombosis positively affects the patient’s future life. For this reason, patients with AVF are closely followed by nephrology and vascular surgery teams in many clinics. For the creation of AVFs and long-term patency rates with successful results, surgeons should be performed with special care and followed by the same surgeons. In our patient groups, senior surgeons took part in the development of AVF, and the patients were followed closely [5,6].

The use of the left or right arm is still the first preferred method to create AVFs. It is important to start the procedure from the most distal part of the upper extremities (snuff-box fistula) to maintain a solid vascular structure in the subsequent fistula formation processes. Although the vessel diameters in this region are small, the use of this distal site in case of occlusion and fistula function deterioration provides space for the subsequent creation of a new fistula. If the distal cuts are unsuitable or have been used before, the middle and upper sections of the arm should be used to create the AVF. In general, the AVFs generated for hemodialysis should be performed from the autogenous vascular structures of the patient and the distal to the proximal (snuff-box, Brescia-Cimino, upper radio cephalic, brachiocephalic) [7,8]. Although there was no consensus on the difference in patency rates of distal AVFs concerning proximal AVFs, in our patients, we attempted to use the distal site as the first choice for AVFs, considering that there might be fistula distortions after months and years. Many studies have shown different rates of patency of upper extremity AVFs. Despite these differences, there was no statistically significant difference in patency rates for upper extremity AVF types in some studies [9,10]. Based on the hypothesis that AVF patency rates for the upper and lower arms did not differ in many studies, we included all upper extremity AVFs in our study, without distinction between upper and lower arms [11-13].

The most commonly used technique for creating AVF is the end-to-side technique. Side-to-side or end-to-end techniques have been used in previous years, and over

| Complications and features                  | Group I (n=201) | Group II (n=241) | P values |
|--------------------------------------------|----------------|-----------------|----------|
| Hematoma                                   | 58             | 66              | 0.517    |
| Bleeding                                   | 36             | 41              | 0.720    |
| Revision for bleeding                      | 25             | 34              | 0.289    |
| Infection                                  | 9              | 11              | 0.092    |
| Early occlusion (non-function AVF)         | 21             | 26              | 0.296    |
| Blood flow rate                            |                |                 |          |
| Starting Current (200-300 mL/min.)         | 62             | 69              | 0.709    |
| Mature fistula current (800-1200 mL/min.)  | 99             | 128             | 0.816    |
| Over current (>1200 mL/min)                | 40             | 44              | 0.632    |
| AVFs depth from skin surface               |                |                 |          |
| < 0.5 cm                                   | 102            | 111             | 0.138    |
| 0.5-1 cm                                   | 63             | 77              | 0.278    |
| > 1 cm                                     | 36             | 53              | 0.470    |
| No surgical intervention                   |                |                 |          |
| Distal ischemia                            | 4              | 5               | 0.150    |
| Steal syndrome                             | 7              | 9               | 0.681    |
| Venous hypertension                        | 9              | 11              | 0.719    |
| Median nerve injury                        | 3              | 4               | 0.631    |

Table 3. Postoperative parameters and complications of AVF during postoperative and near follow-up period (first week).
time these techniques have been abandoned. Although all 3 techniques have advantages or disadvantages (distal ischemia, aneurysm, venous hypertension, steal syndrome, or edema), many studies have shown that the end-to-side technique causes fewer complications\cite{14,13-15}. We also preferred the end-to-side technique in all our patients and we observed that there were no differences between the groups in terms of adverse events caused by these techniques.

There was no significant difference between the groups in terms of characteristics, surgical procedures, and complications in the preoperative, operative, and postoperative periods. The differences in the age of the patients were not significant in terms of procedural features and complications. While these results we found were compatible with some studies, they also showed differences according to some studies\cite{16,17}. Especially gender, presence of DM, smoking, and hypertension have been shown to negatively affect AVF patency in many studies\cite{18-21}. However, in some studies conducted with different centers, it was observed that these factors did not affect the fistula patency\cite{13,22}. In this study, in which the effect of the difference in the age of the patients on AVF patency was investigated; Fistula opening rates were found to be lower in patients older than 40 years compared to those under 40. While this result was compatible with some studies\cite{16}, it showed a difference with some studies\cite{17,23}.

This study has some limitations. First of all, it is not possible to determine exactly which group had more mortality over the years and mortality times due to the lack of data in the records. Secondly, the effect of co-morbidities (such as hypertension, diabetes) and complications that developed over the years on fistula patency was not investigated in this study. Finally, due to the low socio-economic factors in our country and our region, retrospective data collection, follow-up of patients, and hemodialysis procedures performed in different centers were not evaluated in this study. Therefore, it would be beneficial to carry out further studies by re-evaluating many missing parameters in the future.

**CONCLUSION**

For hemodialysis, arteriovenous fistulas are vital for patients with chronic kidney failure. Repetitive entry-exit procedures applied to vascular structures during the hemodialysis procedure may cause vascular tissue damage and narrowing and occlusion over time. Many factors (demographic, hemodynamic, biological parameters, and comorbidity conditions) are effective in maintaining the patency of fistulas. Previous studies have stated that one of these factors is the age of the patient. In this study, we investigated the effect of middle and old age on AVF patency, and as a result, we determined that younger age (under 40 years) was effective in keeping AVFs open for longer.

**DECLARATIONS**

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