Research paper

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A prospective study of factors associated with successful maturation of arteriovenous fistulas for hemodialysis

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Keywords

flow-mediated dilation; arteriovenous fistula; mapping vessel dilation

Abstract

Aim: Our objective was to determine the factors associated with the successful maturation of arteriovenous fistulas during hemodialysis. **Material and methods:** This prospective study included patients treated with hemodialysis and predialysis patients. Clinical, biochemical, sociodemographic, vascular ultrasound mapping, flow-mediated dilatation, and surgical factors were analyzed. Success in the maturation process was defined by ultrasonographic criteria at six weeks. **Results:** Thirty-seven patients were included. With a mean ± standard deviation age of 40 ± 14 years, 73% were male, 65% had type-2 diabetes mellitus, and 95% had hypertension. Arteriovenous fistulas were brachycephalic in 18 patients (49%), brachymedian in nine patients (24%), brachycommunicating posterior in five patients (14%), brachibasal in three patients (8%), radiocephalic in two patients (8%), and radiocephalic in two patients (5%). Fourteen percent of patients had unsuccessful maturation. The vein diameter was 4.3 ± 1.0 mm (maturation group) vs 3.2 ± 0.9 mm (non-maturation group), $p = 0.04$. The artery diameter was similar: 4.5 ± 0.6 vs 4.5 ± 0.4, $p = 0.88$. Logistic regression analysis revealed that the diameter of the vein for which the surgery was performed was the factor associated with successful maturation in our population, odds ratio = 4.77 (1.14–19.97), p-value = 0.032. **Conclusions**: It is highly important to plan vascular access in patients to perform vascular mapping and measure veins and arteries in patients. Vein measurement is a significant factor in successful maturation of the arteriovenous fistulas.

Introduction

The guidelines recommend performing arteriovenous fistula surgery preferably as the first vascular access[1]. However, the failure rate of the maturation process of arteriovenous fistulas has reached 38.9% according to published studies[2–4]. An arteriovenous fistula is created by an anastomosis between the artery and vein, and successful maturation requires an increase in diameter and blood flow, and an adequate depth because enough pressure is needed[5].

The factors associated with the failure of arteriovenous fistula maturation have been discussed across the world[6]. Many study results are different, and some are replicated; however, there is no consensus[7]. Planning includes early referral, selection of an ideal site for the arteriovenous fistula, adequate evaluation of comorbidities and timely follow-up, and artery and vein evaluation through physical examination, Doppler ultrasound, and angiography[8]. There is strong evidence of the need for preoperative ultrasound arterial and venous mapping for access planning and autologous arteriovenous fistulas as the first choice[9]. It is important to determine the size of the veins and arteries and compliance; age, sex and comorbidities; and the functioning of the vascular endothelium. Some research has shown that this factor is important for the maturation of arteriovenous fistulas[6,10,11]. Studies have found that several of these factors are implicated in the maturation of arteriovenous fistulas[12,13]. The aim of this study was to evaluate the factors associated with the successful maturation of arteriovenous fistulas.

Methods

Patients

This study included 37 patients with end-stage chronic kidney disease who were treated with hemodialysis or predialysis, and were aged between 18 and 64 years. The patients who met the inclusion criteria were identified and recruited for the study. None of the patients had type 1 diabetes mellitus, secondary hypertension, or systemic lupus erythematosus. All the patients signed an informed consent form. The Research and Ethics Committee of the Hospital General de México approved the study protocol (DI/18/105/-B/03/066).

Associated factors

For each selected patient, a medical history was obtained; demographic and clinical data, and history of previous vascular access were collected; and preoperative blood samples were taken. The patients who were on hemodialysis had indications for a nonrestricted diet and the use of erythropoietin. All patients were hospitalized one day before surgery, and blood samples were obtained to determine laboratory parameters such as serum hemoglobin (g/dL), albumin (g/dL), cholesterol (mg/dL), and triglycerides (mg/dL). Intraoperative parameters, such as surgical time, arteriotomy size, bleeding, blood pressure, heart rate, and other hemodynamic parameters, as well as surgeon experience, were evaluated.

Vascular Mapping

Prior to surgery, the veins and arteries were evaluated by measuring the diameter, depth, and blood vessel flow, as well as the compliance of the vein and other parameters. Each patient was examined by a single evaluator with training in vascular ultrasound, and a Mindray brand ultrasound with a vascular multi-frequency linear transducer (between 7.5 and 12.5 mHz) was used (Mindray, MX7, Shenzhen, China). This portable device was preferred in all patients (instead of a stationary ultrasound) to warrant bedside assessment in hospitalized patients. All the procedures were carried out by a nephrology interventionist with training provided through an interventional nephrology fellowship certificated by the Latin American Society of Nephrology and Hypertension. The results were discussed with an angiologist and interventional nephrologist to reach an agreement about the fistula configuration.

The patient was in a supine position, with the limb supported on a hard and smooth surface. Pre-surgical mapping was performed on both upper limbs. It began with the arterial assessment of the distal part of the arm, exploring the radial and ulnar arteries in the forearm and, subsequently, the brachial artery, reaching the axillary artery in M mode, assessing depth and diameter. The color Doppler effect was also assessed, placing the transducer at 46 to 60 degrees to observe vascular flows, velocities, and resistances, continuing with the evaluation of the veins from the distal part, evaluating the cephalic vein of the forearm, the median vein, the cephalic of the arm and the basilica in M mode and color Doppler. The first examination was performed without a compressor, and another examination was conducted with a compressor to determine the depth, compression, and vein pathway.

Flow-mediated dilation

Flow-mediated dilation measures the increase in brachial artery diameter in response to an increase in blood flow and the release of nitric oxide in the endothelium[14]. The patients were placed in supine decubitus, and the brachial artery was mediated at rest on three different occasions. An average was obtained; later, a handle was placed to compress the forearm with a pressure up to 200 mmHg for 5 minutes. Later, the diameter of the brachial artery was reevaluated, obtaining a percentage of the difference between the baseline and the posterior measurement.

Evaluation of the success of arteriovenous fistula maturation

Sutures were removed after 10 days, and the arteriovenous fistula was subsequently evaluated ultrasonographically to determine successful maturation over the course of six weeks. Maturation success was determined by compliance with the rules of six, which consists of an adequate flow volume of approximately 600 ml/min, and the drainage vein of a minimum diameter of 0.6 cm at a skin depth of 0.6 cm[15,16].

Statistical analysis

The proportions of female and male patients were presented as absolute values and percentages, and were compared among the groups (maturation or no maturation) by Fisher's exact test. All the quantitative variables had a normal distribution and were presented as the means ± standard deviations. Clinical and dialysis prescription variables were compared between the maturation or no maturation groups by Student's t tests for independent groups. Clinical, ultrasonographic, and biochemical variables of all the patients were compared between the maturation or no maturation groups by paired Student's t tests. Variables with significant differences between the maturation and without maturation groups were selected to further assess the association of each variable with successful maturation using binary logistic regression analysis for each variable. The statistical analysis was performed with SPSS version 21.0 (Statistical software, IBM, Chicago IL, USA).

Results

The characteristics of all participants are shown in Tab. 1. There was a nonsignificant trend toward older age among the patients without maturation compared to those with maturation. All the other characteristics were similar between the groups. All the patients had residual diuresis, had been taking antihypertensive drugs, used erythropoietin, and had a similar number of sessions (Tab. 1). Body mass index (BMI), hypertension, diabetes mellitus, and biochemical parameters evaluated between the patients at maturation or without maturation are summarized in Tab. 1. Glucose, urea, creatinine, and hemoglobin were evaluated in all patients.

The presurgical characteristics of the vessels and of the surgeries are shown in Tab. 2. There were no significant differences in the flow-mediated dilatation test, surgical time, bleeding or resistance index. However, a significant difference was observed in the diameter of

Tab. 1. Patient characteristics. The results are shown as the mean ± standard deviation or absolute value (percentage)

Variable	All (N = 37)	Successful maturation Yes (N = 32)	Successful maturation No (N = 5)	p-value
Age (years)	49 ± 14	48 ± 14	56 ± 7	0.080
Sex Male Female	 27 (73%) 10 (27%)	 27 (78%) 7 (22%)	 2 (40%) 3 (60%)	0.110
BMI (kg/m²)	23.6 ± 3.5	23.4 ± 3.4	24.9 ± 4.0	0.460
Educational level Until elementary school Above high school	 29 (78%) 8 (22%)	 25 (78%) 7 (22%)	 4 (80%) 1 (20%)	1.000
Marital status Married Other	 14(38%) 23(62%)	 12(38%) 20(63%)	 2(40%) 3(60%)	1.000
Smoking	24 (65%)	22 (69%)	2 (40%)	0.320
Diabetes mellitus	24 (65%)	21 (66%)	3 (60%)	1.000
Etiology Diabetes Others	 23 (62%) 14 (38%)	 20(63%) 12(38%)	 3(60%) 2(40%)	1.000
Hypertension	35 (95%)	30 (94%)	5 (100%)	1.000
Number of antihypertensives	2 (1–2)	2 (1–2)	2 (2–3)	0.323
Beta-blockers	2 (5%)	2 (6%)	0 (0%)	0.750
ACEIs	1 (3%)	1(3%)	0 (0%)	1.000
Angiotensin receptor antagonist	13(35%)	12(38%)	1(20%)	0.640
Time in HD (months)	10 (7–18)	10 (8–17)	11 (7–36)	0.721
HD sessions	2 (2–2)	2 (2–2)	2 (2–2)	0.757
Residual uresis (ml)	459 ± 451	454 ± 437	490 ± 592	0.900
Hemoglobin (mg/dL)	9.4 ± 1.3	9.3 ± 1.3	10.1 ± 1	0.160
Creatinine (mg/dL)	9.9 ± 3.4	10 ± 3.3	9.7 ± 4.6	0.880
Urea (mg/dL)	129 ± 50	126 ± 49	149 ± 60	0.450
Glucose (mg/dL)	100 ± 33	100 ± 34	102 ± 27	0.870
Number of venous catheters	2 (1–2)	2 (1–2)	1 (1–3)	0.924

ACEIs – angiotensin-converting-enzyme inhibitors; BMI – body mass index; HD – hemodialysis

Tab. 2. Presurgical characteristics of the vessels and the surgery used to create arteriovenous fistulas. The results are shown as the mean ± standard deviation, median (25th percentile – 75th percentile) or absolute value and percentage

Variable	All (N = 37)	Successful maturation Yes (N = 32)	Successful maturation No (N = 5)	p-value
AVF arm Left Right	 32 (86%) 5 (14%)	 27 (84%) 5 (16%)	 5 (100%) 0 (0%)	1.000
AVF vein diameter (mm)	4.2 ± 10.4	4.3 ± 1	3.2 ± 0.9	0.04
Artery diameter (mm)	4.6 ± 0.6	4.5 ± 0.6	4.5 (0.41)	0.88
Artery area (mm²)	23.5 ± 9.6	24.4 ± 9.9	17.7 ± 4.3	0.15
Resistance index	0.9 ± 0.1	0.91 ± 0.12	0.97 ± 0.04	0.27
Flow-mediated dilation (%)	13.7 ± 6.2	13.8 ± 6.4	13.7 ± 5.9	0.97
Surgical time (minutes)	89 ± 23	88 ± 23	98 ± 23	0.67
Bleeding (ml)	10 (8–20)	10 (8–19)	10 (8–20)	0.75
Atherotomy (mm)	6 (5–7)	6 (6–7)	8 (5–8)	0.38
Artery wall (mm)	0.7 (0.69–0.8)	0.7 (0.69–0.85)	0.7 (0.7–0.76)	0.75
Artery dilation (mm)	0.6 ± 0.2	0.6 ± 0.25	0.62 ± 0.25	0.90

AVF – arterio venous fistula

Tab. 3. Postsurgical characteristics of the vessels used to establish arteriovenous fistulas. The results are shown as the mean ± standard deviation, median (25th percentile – 75th percentile) or absolute value and percentage

Variable	All (N = 37)	Successful maturation		p-value
		Yes (N = 32)	No (N = 5)	
Thrill	35 (95%)	32 (100%)	3 (60%)	0.01
Vein diameter (6 week) (mm)	6.3 ± 1.06	6.6 ± 0.82	4.7 ± 1.17	0.02
Blood flow (ml/min)	1178.8 ± 764	1321 ± 722	271 ± 170	0.00
Depth (mm)	1.9 ± 0.8	2 ± 0.8	1.6 ± 0.6	0.00
Anastomosis (mm)	4.3 (4–4.8)	4.4 (4–4.8)	4.4 (4–4.8)	0.18

the vein on which the surgery was performed. The vein diameter was 4.3 ± 1.0 mm (maturation group) vs 3.2 ± 0.9 mm (non-maturation group), $p = 0.04$. The artery diameter was similar: 4.5 ± 0.6 vs 4.5 ± 0.4, $p = 0.88$. Logistic regression analysis revealed that the diameter of the vein for which the surgery was performed was associated with successful maturation in our population, odds ratio = 4.77 (1.14–19.97), p-value = 0.032. Of the 37 patients with arteriovenous fistulas, 18 had brachycephalic fistulas (49%), nine had brachymedian fistulas (24%), five had brachycommunicating posterior fistulas (14%), three had brachibasil fistulas (8%), two had radiocephalic fistulas (8%), and two had radiocephalic fistulas (5%). In all the patients, autologous arteriovenous fistulas were performed without the use of native or synthetic grafts. This approach was preferred due to less complicated procedures and lower costs. Table 3 shows the changes in the postsurgical features of the mature fistulas.

Discussion

In this study, we investigated the characteristics of the study population that could predict successful maturation of arteriovenous fistulas. Many patients have more than one risk factor for multiple comorbidities. Dialysis patients are among the most common patients[17]. Comorbidities may be problematic with respect to the maturation of arteriovenous fistulas. Diabetes mellitus has been linked to fistula maturation failure; it has been proposed that the number of comorbidities associated with diabetes influences fistula failure, and this seems to be true in our study[18]. In this study, we found no difference between the fistula maturing and nonmaturing groups regarding the presence of comorbidities[19]. Some other factors under discussion have included the female sex and older age. Many studies have shown that advanced age is a risk factor for decreasing life expectancy[20]. Our population was young, with an average age of 49 years. However, the presence of comorbidities appears to have a stronger effect on survival than age itself[21]. Advanced age is often associated with comorbidities, but as an isolated variable it should not affect decisions regarding the creation of vascular access[22]. However, in fistulas where the flow has been established in older patients, it can be seen that the survival rate of older patients in comparison with the groups of young patients shows no difference, while the success rates of fistulas in some other studies reveal that it does not interfere with the age. In investigations where an age of more than 65 years caused primary fistula failure, vascular mapping was not performed[23]. In the study carried out by our team, we did not observe a significant difference in age between the failure or success groups either, but vascular mapping was performed for all the patients.

Most related research has shown differences between men and women. In one study, affected women had a greater risk of failure of arteriovenous fistula maturation compared to men[24]. However, some other changes include women having a higher overall maturation rate than men, but the patency being shorter for women than for men at three and 12 months[25]. Race was another important risk factor for failure at maturation. Hispanic individuals are half as likely to develop chronic kidney disease, however, this phenomenon is not a very clear risk factor for failure of arteriovenous fistula maturation[26]. According to the 2016 Unites States Renal Data System (USRDS) data[25], the highest failure rate for successful arteriovenous fistula was in non-Hispanic patients at 29.2%, whereas the highest failure rate was observed in black patients. Success at 12 months was greater in Hispanics than in individuals of other races. This study was carried out in a low-income Mexican population; therefore, evaluating the success rate in this population is important for other groups with the same characteristics. Patients with kidney disease have certain limitations, and there is a greater risk of type 2 diabetes mellitus and other comorbidities, in addition to differences in the depth of the vessels, in patients with kidney disease. However, these patients have higher survival[27,28]. In the USRDS Dialysis Morbidity and Mortality Wave II study[29], an association was found between BMI ≥35 kg/m^2 and failure of arteriovenous fistula, and secondary dysfunction was also documented[30]. Other surgical techniques are suggested to increase the success of fistulas in obese patients[31,32]. In our study, we cannot argue for or against this point since the patients in our population had a BMI less than 25 kg/m^2, both those with and without adequate maturation.

The flow needs to be increased in the artery that supplies the arteriovenous fistula to irrigate correctly[33]. Flow-mediated dilation measures the ability of the arteries to dilate, and patients with higher flow-mediated dilation are expected to be more likely to have successful fistula completion. After release of the brachial cuff, blood flow increases in response to local vasodilators, nitric oxide is released from the endothelium, and there is subsequent dilation of healthy arteries[7,34]. Flow-mediated dilation is considered a marker of endothelial function because it measures the endothelium-dependent arterial response[35,36].

These tests are likely to be unfavorable for arteriovenous fistula failure[37]. We evaluated flow-mediated dilatation to observe its relationship with arteriovenous fistula flow or diameter at six weeks; however, this study could not determine such a relationship.

Vascular evaluation was performed in our study. It involved studying the vessels in patients in preparation for vascular access. Vascular mapping is considered the standard of practice for vascular evaluation prior to the creation of an arteriovenous fistula[38]. The number of failures is lower in the groups where vascular mapping is used, which is more beneficial as a routine[39]. Each patient was evaluated three times before the skin incision was made for surgery: first in the outpatient department when referred, then one day prior to the arteriovenous fistula, and finally in the operating room prior to the start of the procedure. These careful reviews are performed and greatly improve upon any errors that may arise; similarly, the best anatomy is chosen in each patient, and vascular mapping is of utmost importance for successful surgery. Physical examination of the veins without accompanying vascular mapping has been adequate in only one-third of cases in some studies[40]. With the initial evaluation and subsequent use of vascular mapping, the surgical plan for arteriovenous fistulas can be modified in up to one-third of cases[41]. In other studies, physical examination, ultrasound and venography were performed. In 9% of the patients, the surgical plan based on the physical examination was modified by the ultrasound results by 22.6% according to the results of venography. In our study, all patients underwent physical and ultrasound examinations, and only 13% of the patients failed this way[42].

The anatomy of the vessels is very important for creating vascular access and for successful surgery, with a minimum threshold of 2 mm established for arterial diameter[43]. Several authors have suggested using a different arterial diameter than this value, with good results[44,45]. The size of the artery is important, as is its quality; with the increasing age of the dialysis population and the growing prevalence of diabetes and hypertension as comorbidities, arterial occlusive disease is becoming more common. Patients with diabetes mellitus exhibit calcifications that can complicate the technical aspects of anastomosis creation and can hinder the maturation process by preventing compensatory artery hypertrophy[46]. Another problem is related to the veins, which are frequently an issue in renal patients due to abnormalities that may occur and iatrogenic multiple punctures. The diameter and depth of the vein and the dilation capacity of the vein should also be evaluated[47]. As with the artery, there is no established standard for the size of the vein, although the most commonly approved size is 2.5 mm[48]. In our study, the diameters of the veins were demonstrated to be an important predictive factor. In an observational study of 122 patients, only the diameter of the vessels and the compliance of the veins had a significant predictive value, reaching a maturation success rate of up to 89%[48].

In our study, we observed a larger vein size than in the aforementioned studies, and the vein dimension was almost double of that suggested in the guidelines. This is why we believe that when evaluating a patient, vascular mapping and the correct measurement of glasses will result in the correct choice of surgery for each patient. In Mexico, prolonged waiting times and saturation of interconsulting services often mean that a patient must be subjected to the insertion of a catheter, which leads to increased mortality, morbidity, and costs and supersaturation during hospitalization and emergency department admission. The creation of an interventional nephrology service would decrease waiting times, as the same nephrologist would identify and treat the problem, reducing the need to place a catheter and therefore, decreasing the risk of infection related to it, limiting hospitalizations, and increasing the opportunity for research and innovation in this area[42].

After evaluating the demographic factors, we found no differences in sex, age, or comorbidities. Of the total of 37 patients with fistulas, most had a brachiocephalic fistula, which had the best anatomical characteristics, vein compliance, and best approach. We found no difference from the flow-mediated dilation test in our study. We observed an important and significant difference in the diameter of the vein used to make the fistula. We think that, in our study population, the diameter of the vessels, as well as vascular mapping, were of utmost importance and represented the factor with the most significant impact. It is important that nephrologists have an opportunity to plan vascular access early, that they evaluate patients for substitution treatments, that they have the knowledge and ability to decide on the vessel to be approached with the support of the vascular surgeon, and that this approach is not a unilateral decision. Collaboration with angiologists is necessary to improve the quality of care for these patients.

Limitations

One limitation of our study was the number of patients enrolled. Another limitation was the age of the study patients.

Conclusions

It is highly important to plan vascular access in patients to perform vascular mapping and measure veins and arteries. Vein measurement is a key factor in the successful maturation of arteriovenous fistulas.

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Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Author contributions

Original concept of study: NESF, RVO. Writing of manuscript: NESF, RVO. Analysis and interpretation of data: JRB, GQG, RVO. Final acceptation of manuscript: RVO. Collection, recording and/or compilation of data: JRB, MPN, CLG.

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