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Clinical Research

Clinical Value of Intraoperative Flow Measurements of Brachiocephalic Arteriovenous Fistulas for Hemodialysis

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Background: The aim of this study was to analyze the clinical outcomes of autogenous brachiocephalic arteriovenous fistulas and to investigate the factors associated with 1-year patency after initiation of hemodialysis.
Methods: We retrospectively reviewed the medical records of 41 patients who underwent surgery to create an autogenous brachiocephalic arteriovenous fistula between January 2015 and December 2017, received hemodialysis at the same hospital for longer than 1 year, and were monitored for their vascular access status. Intraoperative flow was measured using transit-time ultrasonography.
Results: The 1-year primary and secondary patency rates were 61% (n=25) and 87.8% (n=36), respectively. The functional group (subjects who required no intervention to maintain patency within the first year after hemodialysis initiation) displayed a significantly higher median intraoperative flow rate (450 mL/min) than the non-functional group (subjects who required intervention at least once regardless of 1-year patency) (275 mL/min) (p=0.038). Based on a receiver operating characteristic curve analysis, all patients were additionally subdivided into a high-flow group (>240 mL/min) and a low-flow group (≤240 mL/min). The high-flow group included a significantly greater number of functional brachiocephalic arteriovenous fistulas than the low-flow group (74.2% vs. 20%, respectively; p=0.007).
Conclusion: Transit-time flow, as measured with intraoperative transit-time ultrasonography, was associated with patency without the need for intervention at 1 year after initiation of hemodialysis.

Keywords: Renal dialysis, Surgical arteriovenous shunt, Chronic kidney failure

Introduction

End-stage renal disease (ESRD) is a major public health problem, and preserving vascular access for maintenance hemodialysis is a lifelong challenge for ESRD patients. Autogenous arteriovenous fistulas (AVFs) are the preferred method of vascular access for hemodialysis maintenance in ESRD patients due to their relatively long patency, low rate of infectious or thrombotic complications, and durability despite repeated needling [1,2]. However, maturation failure is one of the most serious limitations to patency. According to a previous report, 17% of autogenous accesses failed within the first 3 months [3]. The aim of the present study was to analyze the clinical outcomes of autogenous brachiocephalic AVFs in order to investigate the factors associated with patency without the need for intervention.

Methods

Between January 2015 and December 2017, 3 surgeons operated on 81 patients to create autogenous antecubital brachiocephalic AVFs for hemodialysis access. Among these patients, 41 continued hemodialysis at the same hospital for at least 1 year. Patients were followed up with regarding their vascular access status. We retrospectively reviewed the medical records of these 41 patients.

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Preoperative assessment

First, an appropriate site for AVF creation was selected. If the diameter of the forearm veins was less than 2 mm under compression, and if the veins were stiff on palpation or showed signs of thrombophlebitis following recent intravenous injection or blood sampling, no forearm AVF was created and a brachiocephalic AVF was chosen instead. Physical examinations and routine laboratory tests were conducted preoperatively. Physical examinations for brachiocephalic AVFs involved measuring the diameter of the antecubital and upper arm cephalic veins while compressing the proximal upper arm with a stretchable rubber phlebotomy tourniquet, palpation of the upper arm cephalic vein under compression to examine elasticity, and Allen's test. If the upper arm cephalic vein had a gross tourniquet-derived diameter larger than 3 mm and was elastic upon palpation without any fibrotic segment, we performed brachiocephalic AVF. Venography was performed selectively in patients with a history of hemodialysis catheter insertion into the ipsilateral subclavian or internal jugular vein. Informed consent was obtained before surgery.

Operative techniques

Brachiocephalic AVF creation was performed under local anesthesia or brachial plexus block. The final decision regarding creation of the AVF site was made based on the vascular conditions identified during surgery. Before anastomosis, the diameter of the upper arm cephalic vein was measured intraoperatively by inserting a 3-mm metal-tipped vascular dilator without resistance. The vein was gently dilated using saline injection without excessive pressure in order to prevent intimal damage. End-to-side anastomosis was performed with a polypropylene 7-0 (Ethicon Inc., Somerville, NJ, USA) continuous running suture. Intraoperative transit-time flow (TTF) was measured with a handheld 3-mm TTF probe (HT313; Transonic Systems Inc., Ithaca, NY, USA) by encircling the cephalic vein approximately 5–10 mm proximal to the anastomosis site at 5 minutes post-anastomosis. Measurements were repeated until the flow stabilized. The wound was closed layer by layer after bleeding was controlled.

Surveillance of arteriovenous fistula

At a renal replacement therapy unit AVF surveillance was conducted to monitor for pain during hemodialysis, prolonged bleeding after hemodialysis, and abnormal physical examination findings. Patients were also monitored for findings such as high venous pressure or suboptimal blood flow in order to identify imminent AVF failure. The criteria for intervention included a high-pitched or systolic bruit on auscultation, inability to attain an optimal dialysis flow rate of 250 mL/min, an increase in dialysis venous pressure above 150 mm Hg, or a rise of 30 to 50 mm Hg above the baseline value. Any symptoms related to AVF such as pain, limb swelling, or hand ischemia were also considered to indicate AVF failure. Primary patency was defined as the duration between AVF surgery and the first intervention to restore or maintain patency, including percutaneous angioplasty, surgical revision, or thrombectomy. Secondary patency was defined as the duration between AVF surgery and permanent AVF failure.

Statistical analysis

We divided the patients into a functional and a non-functional group in order to analyze the clinical outcomes. The functional group was defined by a patent AVF at 1 year after initiation of hemodialysis without the need for intervention. The non-functional group was defined by an AVF requiring intervention regardless of patency. Based on the receiver operating characteristic (ROC) curve analysis conducted to obtain the cutoff value of intraoperative TTF, the included patients were also divided into a high-flow and a low-flow group. Between-group comparisons were made using the Fisher exact test for categorical variables and the t-test (or the Wilcoxon rank-sum test for variables that did not show a normal distribution) for continuous variables. All statistical analyses were performed using IBM SPSS ver. 24.0 (IBM Corp., Armonk, NY, USA) and R ver. 3.4.4 (R Project for Statistical Computing, Vienna, Austria; (https://www.r-project.org/). Within R, the pROC [4] and Epi [5] packages were used for a ROC curve analysis. All p-values of less than 0.05 were considered to indicate statistical significance.

This study was approved by the Institutional Review Board of Jeju National University Hospital (IRB approval no., JEJUNUH 2019-08-008).

Results

The study included 24 (58.5%) men and 17 women with a mean age of 64.5 years (range, 39–88 years). The underlying diseases of ESRD were diabetes (n=27, 65.9%), hypertension (n=15), glomerulonephritis (n=1), and polycystic kidney disease (n=1). No definite cause was reported in 1

Table 1. Clinical demographics of functional and non-functional AVFs at 1 year after initiation of maintenance hemodialysis

Characteristic	Non-functional AVF (n=16)	Functional AVF (n=25)	Total (N=41)	p-value
Sex, male	11 (68.8)	13 (52.0)	24 (58.5)	0.344
Age (yr)	65.1±12.5	64.0±13.9	64.5±13.2	0.801
Hypertension	5 (31.2)	10 (40.0)	15 (36.6)	0.742
Diabetes	12 (75.0)	15 (60.0)	27 (65.9)	0.501
Other disease-causing end-stage renal disease	2[a)] (12.5)	1[b)] (4.0)	3 (7.3)	0.550
Intraoperative transit-time flow (mL/min)	275.0 (173.0–475.0)	450.0 (320.0–580.0)	400.0 (275.0–550.0)	0.038[c)]

Values are presented as number (%), mean±standard deviation, or median (range).
AVF, arteriovenous fistula.
[a)]Glomerulonephritis and unknown kidney disease. [b)]Polycystic kidney disease. [c)]The Wilcoxon rank-sum test was performed on these data.

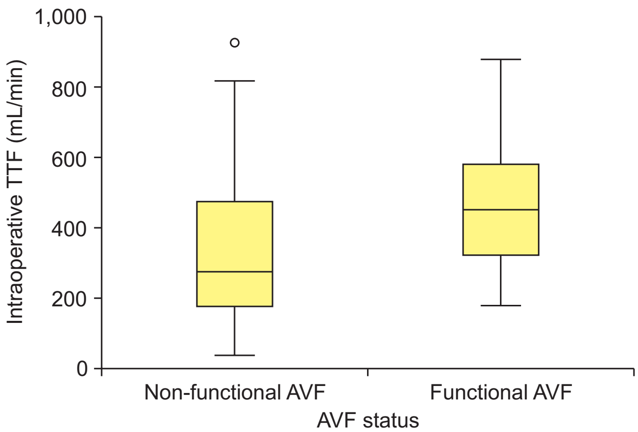

Fig. 1. A box plot of intraoperative TTF by AVF status regarding 1-year patency (functional or non-functional). AVF, arteriovenous fistula; TTF, transit-time flow.

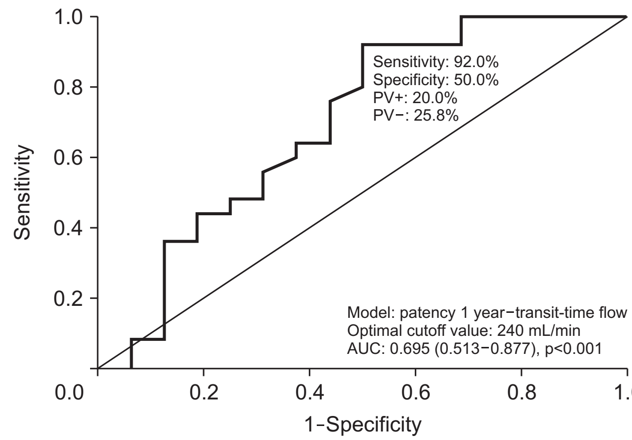

Fig. 2. Receiver operating characteristic curve. PV+, positive predictive value; PV-, negative predictive value; AUC, area under the curve.

case. We defined hemodialysis initiation as 3 consecutive successful hemodialysis treatments with brachiocephalic AVF without any symptoms or signs of AVF malfunction. Under this definition, the average duration from AVF creation to the initiation of hemodialysis was 94.2 days. The 1-year primary and secondary patency rates were 61% (n=25) and 87.8% (n=36), respectively.

The characteristics of the functional and non-functional groups are presented in Table 1. No statistically significant differences were found with regard to age, sex, or underlying diseases between the 2 groups. The median values of intraoperative TTF (mL/min) were 275.0, 450.0, and 400.0 in the non-functional AVF group, the functional group, and the total study population, respectively, with a statistically significant difference between the functional and non-functional groups (p=0.038). A box plot was used to illustrate the interquartile range, the range containing the central 95% of observations, and the maximum and minimum values (Fig. 1).

The non-functional group included 8 patients with AVFs that were patent at 1 year after single percutaneous angioplasty, 3 patients with AVFs that were patent at 1 year with percutaneous angioplasty or thrombolysis performed more than twice, 3 patients for whom attempts to initiate hemodialysis failed in spite of intervention, and 2 patients with AVFs that showed early failure within 3 months after hemodialysis initiation. Based on the radiological findings, the factors requiring intervention were maturation failure (n=6), juxta-anastomotic stenosis (n=4), non-anastomotic multifocal venous stenosis (n=4), thrombophlebitis (n=1), and central venous stenosis (n=1). Of the 5 cases that lacked patency at 1 year after initiation, 3 involved maturation failure, 1 involved multifocal venous stenosis, and 1 involved thrombophlebitis. All of the cases of juxta-anastomotic stenosis recovered patency after a single intervention.

The ROC curve of the intraoperative TTF revealed an optimal cut-off of 240 mL/min with a relatively high sensitivity (92.0%) and a moderate specificity (50.0%) (Fig. 2). The area under the ROC curve was 0.695, indicating that this test was relatively poor at discriminating between those with and those without functional AVF. When the

Table 2. Clinical characteristics based on intraoperative TTF

Characteristic	Low-flow TTF (≤240 mL/min) (n=10)	High-flow TTF (>240 mL/min) (n=31)	Total (N=41)	p-value
Sex, male	7 (70.0)	17 (54.8)	24 (58.5)	0.480
Age (yr)	64.7±12.9	64.4±13.5	64.5±13.2	0.949
Hypertension	4 (40.0)	11 (35.5)	15 (36.6)	1.000
Diabetes	8 (80.0)	19 (61.3)	27 (65.9)	0.447
Other disease-causing end-stage renal disease	0	3[a] (9.7)	3 (7.3)	0.564
Functional arteriovenous fistula	2 (20.0)	23 (74.2)	25 (61.0)	0.007

Values are presented as number (%) or mean±standard deviation.
TTF, transit-time flow.
[a]Glomerulonephritis, unknown kidney disease, and polycystic kidney disease.

patients were divided into high-flow (TTF >240 mL/min) and low-flow (TTF ≤240 mL/min) groups based on the results of ROC analysis, the high-flow group displayed a significantly larger proportion of functional AVFs than the low-flow group (74.2% and 20%, respectively; p=0.007) (Table 2). The high-flow group included 8 cases of non-functional AVFs, 4 of which were due to maturation failure, 3 of which were attributed to juxta-anastomotic and non-anastomotic venous stenosis, and 1 of which resulted from thrombophlebitis. Patency was not restored in 2 of these cases, one of which involved maturation failure and the other thrombophlebitis.

Discussion

Brachiocephalic AVFs represent a traditional option for upper-arm autogenous vascular access that has been reported to have a higher patency rate than forearm autogenous arteriovenous access [6]. Bae et al. [7] also reported that brachiocephalic AVF was associated with a shorter time to first needling and fewer interventions before maturation than radiocephalic AVF. However, brachiocephalic AVFs have their own limitations, such as an association with cephalic arch stenosis, which has a reported incidence of as high as 77% in patients with brachiocephalic AVF [8]. Because the cephalic arch may be the sole outflow of brachiocephalic AVF, these AVFs can lead to subsequent thrombotic or stenotic failure that requires surgical interventions, such as central transposition [9]. The present study showed that cases of venous stenosis, including juxta-anastomotic and non-anastomotic multifocal venous stenoses, required intervention. However, the exact cause could not be identified because of limited clinical information regarding factors such as vein diameter or preoperative radiological evaluation of the vein. The factors related to the maturation and patency of brachiocephalic AVFs should be further investigated.

In a systematic review of 34 studies, the primary patency rate for autogenous AVFs was found to be 72% at 6 months and 51% at 18 months, whereas the secondary patency rate was 86% at 6 months and 77% at 18 months [3]. Our results revealed 1-year primary and secondary patency rates of 61% and 87.8%, respectively, which are similar to those found in the aforementioned review. However, Lin et al. [10] found that comprehensive care that included patient education and access flow surveillance followed by early intervention improved the 1-year secondary patency rate to 94% in the high-flow group (intraoperative TTF >200 mL/min) and 80% in the low-flow group for radiocephalic AVFs. At our institution, nephrologists and nurses in the renal replacement therapy unit are the health professionals primarily in charge of AVF care. A multi-disciplinary approach is needed to improve AVF outcomes in the future.

Parameters related to the patency of various types of autogenous AVFs, including older age, distal location, or small venous diameter, were negative prognostic factors for AVF maturation. Ahn et al. [11] reported that previous ipsilateral central venous catheterization was an independent risk factor for maturation failure, and increased body mass index or obesity-related decrease in intraoperative flow was associated with decreased AVF patency [12]. Intraoperative TTF was a predictor of patency, especially for radiocephalic AVFs. In 1998, Johnson et al. [13] reported for the first time that intraoperative TTF was correlated with the AVF outcome and that radiocephalic AVF flow less than 170 mL/min predicted failure in up to 56% of AVFs within 90 days. Another report by Won et al. [14] found that a radiocephalic AVF flow less than 160 mL/min was associated with a high early failure rate, and intraoperative low flow was determined to be an independent risk factor. A report by Berman et al. [15] was the first study to establish the minimal flow rates needed for maturation and subsequent patency of brachiocephalic AVF. According to the report of Berman et al. [15], a cutoff of 308 mL/min was needed for maturation and patency of brachiocephalic AVFs, while the present study found that a discriminating value of 240 mL/min was required for functional AVFs. These differences in cutoff values may be attributed to differences in patient-related parameters, such as arterial diameter, venous diameter, and body weight. However, the aforementioned 2 reports suggest that intraoperative flow measurements are correlated with the patency and maturation of brachiocephalic AVFs.

We used intraoperative transit-time ultrasonography, which allows for the measurement of TTF, instead of Doppler ultrasonography. Transit-time ultrasonography is a readily applicable method for the measurement of intraoperative flow because no calculation of cross-sectional area or technical expertise is required [16]. Furthermore, this imaging technique is independent of diameter and is less affected by flow profile than conventional duplex ultrasonography [14,15]. Conversely, Farrington et al. [17] used color and spectral Doppler ultrasonography conducted by experienced sonographers for a postoperative evaluation within 6 weeks after AVF creation. They predicted AVF patency after maturation based only on postoperative AVF diameter. Given this information, the modality used and the time of AVF flow measurement are still topics of debate.

The interpretation and utilization of intraoperative TTF for further intervention is still unclear. According to a cutoff value based on ROC analysis, the functional group included 2 patients (8% of the functional group) with intraoperative TTF that placed them in the low-flow group. Thus, creation of an AVF based on the intraoperative TTF alone could entail needless procedures. One of the reports suggested that intraoperative venography should be conducted and the technical features that may contribute to low flow (such as anastomotic strictures) should be determined when the intraoperative TTF is lower than their own threshold value [10]. In the absence of surgical correction of errors on venography, close surveillance has been recommended to facilitate assisted maturation and patency. New creation of an AVF in the same operative field based only on intraoperative TTF requires caution despite the diminishing clinical effectiveness of repeated percutaneous intervention of AVF because preserving vascular access is important for the lifelong health of ESRD patients [18]. Furthermore, the intima-media thickness, inflammation, and myointimal hyperplasia in patients with pre-existing arterial diseases evaluated using Doppler ultrasonography have been found to affect AVF maturation [12]. A comprehensive study is needed to clarify the effective use of intraoperative TTF and to interpret various options for preoperative and intraoperative measurements.

In conclusion, intraoperative transit-time ultrasonographic flow measurements of autogenous brachiocephalic AVFs were associated with the maintenance of AVF patency without intervention at 1 year after the initiation of hemodialysis.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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