

Risk Factors Predicting the Successful Function and Use of Autogenous Arteriovenous Fistulae for Hemodialysis

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Abstract

Background For patients with end-stage renal failure hemodialysis with an autogenous arteriovenous fistula (AVF) has proven to be the ideal vascular access.

Objective The aim of this study is to discover potential predictors of a well-functioning hemodialysis fistula.

Methods From December 2009 to March 2011, 80 patients undergoing first time AVF creation were enrolled in our retrospective study. We analyzed pre- and postoperative vessel diameters and flow characteristics gained by duplex ultrasonography (DUS) and intraoperative ultrasound transit-time flow measurements regarding intraoperative blood flow and pulsatility index (PI). Follow-up was defined until the end of the first month with regular hemodialysis, 10 weeks after AVF creation. We performed statistical analyses by employing Spearman correlation, *t* test, analysis of variance, χ^2 test, and receiver operating characteristics (ROC).

Results At the end of the follow-up, 62 patients (78%) featured functioning AVFs and 18 patients (22%) featured nonfunctioning AVFs. Factors influencing AVF function were radial artery diameter ($\chi^2 = 5.23$, $p = 0.02$), intraoperative flow ($\chi^2 = 7.09$, $p = 0.01$), intraoperative PI ($\chi^2 = 6.5$, $p = 0.01$), and postoperative flow ($\chi^2 = 16.29$, $p = 0.01$). According to the ROC analyses, we could develop cut-off values for predicting an ideal AVF function: radial artery diameter more than 2.3 mm, cephalic vein diameter more than 2.7 mm, intraoperative mean flow more than 113 mL/min, PI less than 1.4, and postoperative mean flow more than 160 mL/min.

Conclusion Intraoperative ultrasound transit-time flow measurements gained at surgery and postoperative follow-up with DUS can help identify AVFs that are unlikely to function and therefore need early intervention.

Keywords

- ▶ vascular science
- ▶ shunts
- ▶ peripheral vascular disease
- ▶ peripheral arteries

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Introduction

Autogenous arteriovenous fistula (AVF) is the primary and best choice for vascular access in a chronic hemodialysis patient.^{1,2} When an AVF successfully matures after the surgical creation, it may work for years with a low risk of complications. The most common problem with AVFs is the lack of maturation, leading to inability to access the fistula or thrombosis. Nonmaturation depends not solely on the quality and size of the vessels, but also on the ability of vessel adaptation induced by the augmented blood flow volumes. Recently, several duplex-derived criteria have been developed. These show a favorable effect on AVFs by using well-sized radial arteries and cephalic veins.^{3,4} Therefore, preoperative assessment of the arm blood vessel characteristics with definition of suitable vessels emerges to an indispensable tool.

We propose that routine completion of duplex ultrasound (DUS) imaging during AVF creation can provide accurate hemodynamic characterization of early access work, predict access patency, and allow detection of nonfunctioning conduits for remedial intervention. This work should enlighten if positive correlations between the preoperative duplex-gained vessel data and intraoperative AVF blood flow and pulsatility index (PI) exists. The analyses should allow to develop cut-off values.

Data of this study were collected retrospectively. Follow-up finished after 4 months with regular hemodialysis three times a week. We interpreted the AVF as functioning for data analysis.

Methods

Patient Characteristics

From December 2009 to March 2011, we performed AVF construction in 80 patients with end-stage renal failure (53 men, 27 women; mean age 69 years) at our institution. The patients gave their informed consent before surgery. This study was approved by the Ethics Committee of the

Robert Bosch Hospital, Stuttgart, Germany. Inclusion criteria were new hemodialysis patients receiving first time AVF and willing to complete the follow-up. The demographic data of the patients are presented in ►Table 1.

All patients were regularly seen by the nephrologists and the decision to start dialysis treatment was made on the severity of worsening of renal function. At enrolment, patients were diagnosed with stage V of chronic kidney disease (CKD) according to the working list of the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative.⁵

The common causes of CKD among the patients included in this study were diabetes mellitus, hypertension, and glomerulonephritis. The enrolled patients featured accompanying diseases such as diabetes mellitus (65%), hypertension (70%), and coronary heart disease (20%).

Patient Cohorts

The patients enrolled into this study were categorized into two groups. Depending on the clinical end point, AVF function during follow-up period was arranged either in the functioning or nonfunctioning group as depicted in ►Tables 1 to 4.

Preoperative Angiological Evaluation

The construction of an AVF between the radial artery and the cephalic vein was planned for all patients. Routinely, all patients underwent preoperative clinical and noninvasive angiological testing that included arterial and central venous Doppler waveforms, radial artery diameter measurements (luminal diameter), and superficial vein mapping (with and without a tourniquet) by the attending vascular surgeon. The radial artery was palpated at the wrist before examination with DUS to mark the direction and exact position of the vessel. Further, a normal Allen test on the chosen side was compulsory.

DUS was performed by the vascular surgeon with a Siemens ACUSON Antares ultrasound system equipped with a VF13–5 transducer probe (Siemens AG, Erlangen, Germany) based on a standardized protocol. A two-dimensional linear

Table 1 Summary of the demographic data of patients in the functioning or nonfunctioning AVF group

Variable	Total patients (n = 80)	Group functioning AVF (n = 62)	Group nonfunctioning AVF (n = 18)	p value
Age, y, mean ± SEM	69 ± 1	68 ± 2	73 ± 2	0.09
Gender				
Male	50	42	8	0.06
Female	26	16	10	
Body mass index, kg/m ² , mean ± SEM	27 ± 1	28 ± 1	27 ± 1	0.61
Comorbidities, n (%)				
Diabetes mellitus	52 (65)	41 (66)	11 (61)	0.75
Hypertensive disease	56 (70)	44 (71)	12 (67)	0.76
Coronary artery disease	16 (20)	13 (21)	3 (17)	0.71

Abbreviations: AVF, arteriovenous fistula; SEM, standard error of mean; y, years.

Note: The significances between both groups were calculated employing *t* test with Welch Correction. Considering the demographic data and comorbidities of the patients, only the variable age is significantly different, with older patients in the nonfunctioning group.

Table 2 Pre- and intraoperative vessel parameters

Variable	Total patients (n = 80)	Group functioning AVF (n = 62)	Group nonfunctioning AVF (n = 18)	χ^2	p value
Preoperative diameter radial artery, mm, mean \pm SEM	2.4 \pm 0.1	2.5 \pm 0.1	2.19 \pm 0.1	5.23	0.01
Preoperative diameter cephalic vein, mm, mean \pm SEM	3.1 \pm 0.1	3.2 \pm 0.1	2.8 \pm 0.8	3.7	0.07
Intraoperative AVF flow, mL/min, mean \pm SEM	180 \pm 15	201 \pm 18	111 \pm 17	7.09	0.01
Intraoperative AVF PI, mean \pm SEM	0.9 \pm 0.1	0.77 \pm 0.1	1.21 \pm 0.2	6.5	0.04
Postoperative AVF flow, mL/min, mean \pm SEM	327 \pm 26	401 \pm 27	87 \pm 24	16.29	0.01

Abbreviations: AVF, arteriovenous fistula; PI, pulsating index; SEM, standard error of mean.

Note: Depicted diameters refer to intraluminal values. All variables featured significant influences on the AVF function with the cephalic vein diameter, exceptionally. Data are expressed as mean \pm SEM.

Table 3 Calculation of Spearman correlation coefficient (ρ) between two variables

Variable	By variable	Spearman correlation coefficient (ρ)	p value
Intraoperative AVF flow	Preoperative radial artery diameter	0.37	0.01
Intraoperative AVF PI	Preoperative radial artery diameter	- 0.20	0.07
Postoperative AVF flow	Preoperative radial artery diameter	0.25	0.03
Intraoperative AVF flow	Preoperative cephalic vein diameter	0.36	0.01
Intraoperative AVF PI	Preoperative cephalic vein diameter	- 0.16	0.17
Preoperative AVF flow	Preoperative cephalic vein diameter	0.24	0.04
Preoperative AVF flow	Intraoperative AVF PI	- 0.04	0.01
Intraoperative AVF flow	Intraoperative AVF PI	- 0.04	0.01

Abbreviations: AVF, arteriovenous fistula; PI, pulsating index.

Note: The highest correlations were found between intraoperative AVF flow and preoperative radial artery diameter, intraoperative AVF flow and preoperative cephalic vein diameter, intraoperative AVF flow and intraoperative PI, and postoperative AVF flow and intraoperative PI.

Table 4 Analyses of the ROC analyses

Variable	Cut-off values	Specificity	Sensitivity	Area under the curve	95% confidence interval	p value
Preoperative diameter radial artery	2.3 mm	0.61	0.74	0.71	0.57-0.84	0.01
Preoperative diameter cephalic vein	2.7 mm	0.56	0.77	0.67	0.52-0.83	0.08
Intraoperative AVF flow	113 mL/min	0.67	0.76	0.76	0.62-0.89	0.03
Intraoperative AVF PI	1.4	0.39	0.97	0.68	0.53-0.83	0.02
Postoperative AVF flow	160 mL/min	0.94	0.91	0.96	0.88-1.03	0.01

Abbreviations: AVF, arteriovenous fistula; PI, pulsating index; ROC, receiver operating characteristics.

Note: The highest values (e.g., high sensitivity) were revealed by intraoperative AVF flow, intraoperative AVF PI, and postoperative AVF flow. The diameter of the radial artery (2.3 mm) and cephalic vein (2.7 mm), intraoperative flow (113 mL/min), intraoperative PI (1.4), and postoperative flow (160 mL/min) were fundamentally predictive requirements for an optimal AVF function.

electronic probe at 7.0 MHz, pulse wave Doppler at 5.0 MHz, and color Doppler at 5.0 MHz were used. The angle of the emitted Doppler ultrasound wave from the probe was adjusted to 60 degrees to achieve the Doppler signal of the strongest intensity. The internal diameter of the vessel was measured using M-mode technique. Transverse examinations were made over the artery and the cross-sectional area of the artery was calculated. Time-averaged velocity (TAV) was calculated directly from a Doppler spectral waveform by the duplex scanner system. The volume flow was obtained from TAV and the cross-sectional surface area. Measurements were performed before AVF creation, and 2 days and 6 weeks after AVF creation.

Operative Procedure

All patients were scheduled for a primary AVF creation between the radial artery and cephalic vein. All the patients gave their informed consent before surgery. At our institution, two vascular surgeons (E.U. and S.S.-G.) performed the arteriovenous access surgery as an anastomosis between the cephalic vein and radial artery—a so-called Brescia-Cimino shunt.⁶ The chosen anesthetic procedures were local anesthesia (20%, $n = 16$), regional axillary block (60%, $n = 48$), or general anesthesia (20%, $n = 16$); the last one for excessively anxious patients.

The radial artery and cephalic vein were exposed through a longitudinal or transverse incision of 4 to 5 cm proximal of the radial styloid process. After sufficient dissection, the cephalic vein was isolated, divided, and hydrodiluted with heparinized saline. During the hydrodilatation, the continuity of the cephalic vein and any recognizable resistance changes were followed closely. For the standard arteriotomy, the radial artery was incised 10 mm. The end-to-side, vein-to-artery anastomosis was performed with a running 8/0 Seralon polyamide suture (Serag-Wiessner KG, Naila, Germany).

Intraoperative Flow Quantification

AVF flow was measured 5 minutes after anastomosis completion. The systolic blood pressure was preserved between 100 and 120 mm Hg. The handheld 3- or 4-mm ultrasound transit-time flowprobe connected to a MediStim VeriQ System (MediStim ASA, Oslo, Norway) was placed to encircle the cephalic vein, approximately 5 to 10 mm behind the anastomosis. The following features were obtained during the measurements: (1) the mean flow as milliliters per minute and (2) the PI. PI was calculated by a device according to the relation $PI = (PSV - MDV)/MV$ (PSV, peak systolic velocity; MDV, minimum diastolic velocity; and MV, mean velocity).

Anticoagulation

Following exploration of the arteries and veins and before placing the clamp, 5,000 IE heparin was routinely administered intravenously to each patient during AVF creation. During the postoperative course, patients without a risk factor for thrombosis were just anticoagulated with a single dose of heparin, 5,000 IE/d subcutaneously. Otherwise, like in the case of three patients with atrial fibrillation subcutaneous heparin 5,000 IE was administered twice a day, and later as

outdoor patients they were set on phenprocoumon with international normalized ratio values in the therapeutic range of 2 to 3.⁷

Maturation and Postoperative Follow-Up

DUS of the AVF was performed before discharge from the hospital on the second postoperative day with a Siemens ACUSON Antares™ ultrasound system equipped with a VF13–5 transducer probe based on a standardized protocol by the vascular surgeon. The percent stenosis diameter was calculated as the relationship between the minimal luminal diameter at the stenosis site and the diameter of a nearby normal segment. A lumen reduction of 50% or greater was considered major stenosis. The flow rate of the fistula in milliliters per minute was estimated according to the following formula and considered normal when greater than 160 mL/min:

$$V = \pi r^2 \times V_{\text{average}} \times 60$$

where V indicates flow in milliliters per minute; r , ray of the segment; V_{average} , average of the speeds obtained in centimeters per second by DUS; and 60, correction factor.

Clinical criteria were used for detection of nonfunctioning AVFs. The inability to cannulate the AVF or to obtain sufficient dialysis blood flow of at least 250 mL/min within 6 weeks with three sessions per week after fistula creation was indicator of a poorly functioning AVF, regardless of whether it is patent. Follow-up was defined until the end of the first month with regular hemodialysis, in other means 10 weeks after AVF creation. All patients with nonmaturing AVFs underwent duplex evaluation. These patients were screened from the brachial artery down to the radial artery via anastomosis and upward to the upper arm following the cephalic vein to detect stenosis or thrombosis.

Statistical Analysis

Patient characteristics and duplex parameters of functioning and nonfunctioning AVFs were compared with unpaired t test with Welch correction and one-way analysis of variance with Bonferroni multiple comparison test as post hoc test. Further statistical analyses were performed with matched pairs including Spearman correlation coefficient, receiver operating characteristics (ROC), and χ^2 test using the JMP program (version 9, SAS Institute, Cary, North Carolina, United States). A p value of less than 0.05 was considered to indicate a statistically significant difference. Numerical data are expressed as mean \pm standard deviation (SD).

Results

In the functioning group, 62 patients (78%) presented with AVFs with a normal maturation. In the nonfunctioning group, 18 patients (22%) featured 13 nonmaturations and 5 early thrombotic occlusions, respectively. These patients were treated by remedial thrombectomy ($n = 5$) and new access creation ($n = 7$) between the radial artery and the cephalic vein in an upper segment unless they rejected these procedures. Six of those patients were enrolled into the peritoneal

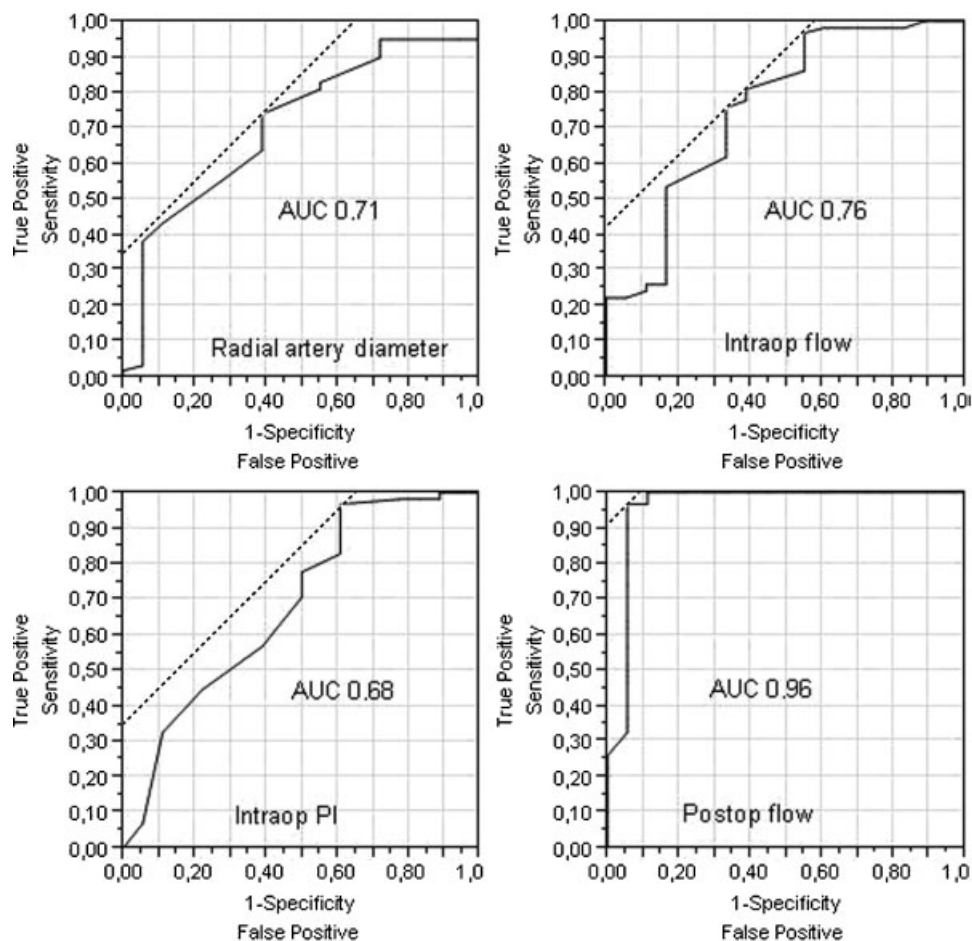


Fig. 1 The ROC. Depicted are the ROC curves for parameters with the highest sensitivity, for example, to predict a nonfunctioning autogenous arteriovenous fistula. AUC, area under the curve; ROC, receiver operating characteristics.

dialysis program because they rejected the repeated surgical access creation and wished more flexibility in determining the location of dialysis at home, at work, or on vacation. In these patients, a short-term alternative dialysis was performed by a tunneled central venous catheter till the beginning of the peritoneal dialysis.

The results of the duplex findings of the AVFs are exposed in ►Tables 1 and 2. The comparison of intraoperative flow and postoperative flow were significantly higher in the functioning group compared with the nonfunctioning group.

There were four variables with significant influence on the AVF function. There was a significant difference about the radial artery diameter ($\chi^2 = 5.23$, $p = 0.02$), intraoperative AVF flow ($\chi^2 = 7.09$, $p = 0.01$), intraoperative PI ($\chi^2 = 6.5$, $p = 0.01$), and postoperative AVF flow ($\chi^2 = 16.29$, $p = 0.01$). The cephalic vein diameter ($\chi^2 = 3.41$, $p = 0.08$) was not significant.

To determine a threshold value for the five variables, ROC analyses were performed. These analyses concerned the maximal combination of sensitivity and specificity—the essence of the ROC calculation. The area under the ROC curves demonstrated, at best, a moderate prediction. According to our data, fundamentally predictive requirements for an ideal AVF function were following cut-off values for the diameter of the radial artery (2.3 mm) and cephalic vein (2.7 mm),

intraoperative AVF flow (113 mL/min), intraoperative PI (1.4), and postoperative AVF flow (160 mL/min). The complete results of the ROC analyses are displayed in ►Table 2 and ►Fig. 1.

Discussion

Remedial or secondary procedures performed on nonfunctioning AVFs may favorably extend patency, but postoperative identification of a compromised conduit has relied on physical examination or unsuccessful first dialysis cannulation. Further imaging techniques evolved for assessing AVF maturation or failure in the postoperative course. But more uniformly applied methods to identify nonfunctioning AVFs and produce a greater overall benefit in patency are lacking.

This study was undertaken to improve the fraction of accesses achieving functional maturation using routine transit-time flow measurement immediately after access construction in the operation theater and early duplex evaluation before discharge. The aim is to identify nonfunctioning AVFs and to select them for remedial intervention to optimize access flow rate and potential access longevity. In this study, we hypothesized that flow characteristics found after access construction and especially with low flow would be at highest risk for nonmaturation and/or thrombosis. Noticing the

limited published hemodynamic data for access grafts and fistulae, clearly defined velocity thresholds for potential stenosis and dysfunctional conduits are rare. It is worth to mention, that a low value of mean flow detected by transit-time flow measurement is not alone an indicator of an imperfect anastomosis, like known from coronary artery bypass grafting.⁸ The PI and the waveform characteristics are also important, although the measurement of PI was not employed so frequently in studies dealing with AVFs such as in few of them.^{9,10} The presence of systolic spike and a high PI value is diagnostic. In the present series also, all the AVFs with a PI more than 1.4 had a higher probability for failure. We classified nonfunctioning AVFs as those with low mean flow measured after access construction with accompanying high PI values and low mean flow in the early duplex scanning before discharge.

Our study differs from previous works in one important respect. Previous studies have used hemodynamic parameters such as mean flow to predict AVF function.^{11–13} In contrast to that, we hypothesized that a combined assessment of intraoperative mean flow with PI and early postoperative mean flow could improve the predictive power of AVF maturation, respectively. The influence of the remaining variables such as age, gender, cardiovascular risk factors, and vessel diameter were also investigated as some of them have been characterized as predictors for AVF function in previous studies.^{14–16}

In this study of patients undergoing AVF creation, predictors for fistula function and failure emerged as being radial artery diameter, intraoperative mean blood flow, PI, and postoperative mean flow. These variables featured significant correlations between each other. The results are in accordance to data from previous studies.^{11,17,18}

One of our objectives was to confirm our hypothesis noninvasively. With transit-time flow measurement, flow volume is directly assessed without any need for additional calculation related to cross-sectional area, so the results are immediately available, easily interpretable, and accurate.^{3,4,19,20} Transit-time ultrasound is diameter-independent and less affected by flow profile than is conventional DUS. Conventional DUS measures point velocity and assumes laminar flow, which is not present in AVFs.^{3,19} In 1998, Johnson et al³ used intraoperative transit-time ultrasound for blood flow measurement in a large number of patients with AVFs and polytetrafluoroethylene grafts. They correlated the blood flow with the final result. Using 320 mL/min as a cut-off value, they found a relationship between flow rates and outcome. A high flow (320 mL/min) in the AVF predicted a lesser need for reintervention and a superior final survival, independent of demographic variables such as the age, race, sex, and the presence of diabetes. However, they showed that, when the AVF flow was 170 mL/min, the predicted failure within 90 days approached 56%. In 2000, Won et al¹⁹ employed the same transit-time ultrasound for intraoperative blood flow measurements of AVFs and concluded that fistulas with flow less than 160 mL/min had a higher failure rate and no correlation between early patency and parameters of diabetes, old age, gender, flow rate of radial artery, and the

size of cephalic vein. Just in accordance to referred data,^{3,19} our study also points out that the intraoperative mean blood flow is predictive for early failure or the need of reintervention. Nevertheless, the intraoperative PI and postoperative mean flow had even higher sensitivities to predict AVF dysfunction. These data allowed us also to express cut-off values to predict AVF function. Thus, intraoperative mean flow less than 113 mL/min, PI more than 1.4, and postoperative mean flow less than 160 mL/min were predictors for AVF dysfunction. In addition, a radial artery diameter of less than 2.3 mm was a predictor for AVF dysfunction, but with a lower sensitivity. Interestingly, our cut-off value for the intraoperative mean flow as a predictor for an ideal AVF function was low.^{21,22}

Intraoperative blood flow measurement using transit-time flow measurement has become routine in AVF surgery in our institution. We consider that high blood flow values during AVF creation decide about the success of operation and imply best short-term patency rates. Thus, when low flow is met during operation, a proximal anastomosis between the radial artery and cephalic vein becomes necessary.

In conclusion, radial artery diameter, intraoperative mean flow, PI, and postoperative mean flow are important predictors of the AVF function. By using the ultrasound transit-time flowmeter, flow information can be gained with ease, accuracy, and reliability. This minimally invasive method could contribute to improve the surgical results further.

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Disclosures

No conflict of interest exists for any of the authors.

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