Access Flow Monitoring of Patients with Native Vessel Arteriovenous Fistulae and Previous Angioplasty

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Abstract. Screening strategies based on measurement of access blood flow (Qa) allow detection and angioplasty of subclinical stenosis in native vessel arteriovenous (AV) fistulae. However, little is known about the efficacy of Qa measurements for detecting recurrent stenoses in fistulae and that of angioplasty for correcting them. A total of 303 patients were studied over 30 mo; 69 (23%) of these had stenoses, of whom 53 underwent angioplasty. Of those undergoing angioplasty, 30 patients had 46 episodes of recurrent positive studies and underwent repeat fistulography. In 31 of these episodes (19 patients), stenosis was again identified and treated successfully with angioplasty. Overall positive predictive values for stenosis were similar in first and subsequent episodes of stenosis (71% versus 67%), and angioplasty was associated with sustained increases in Qa for both first and subsequent episodes. Assisted patency in fistulae that required repeat angioplasty was 87% (median follow-up 10 mo after the second angioplasty). In conclusion, Qa is effective for detecting first and subsequent lesions in patients with AV fistulae, and angioplasty of first or subsequent lesions is associated with sustained increments in Qa. Continued screening after correction of first stenoses appears reasonable, because of both the frequency of recurrent stenosis and the success of repeat intervention.

Ultrasound dilution measurement of access blood flow (Qa) has been shown to accurately identify first episodes of subclinical stenosis in native vessel fistulae (1). Most such stenoses, once identified, are amenable to percutaneous angioplasty, which is associated with short-term improvements in Qa and dialysis delivery. Although access screening programs have been shown to prolong the use-life of polytetrafluoroethylene (PTFE) grafts (2) and cohorts of mixed access type (3), little data exists on the effect of such programs on native arteriovenous dialysis fistulae (4–6).

The diagnostic performance of Qa in native vessel fistulae that have previously undergone angioplasty for stenosis is unknown. The positive predictive value of screening might differ substantially in this population compared with unscreened fistulae, both because of the prevalence of stenosis and because of mechanical effects of angioplasty on the native vessel conduit. Finally, the effectiveness of angioplasty for correcting recurrent stenoses in fistulae is unclear. These data will become increasingly relevant as access screening programs are implemented in more dialysis centers and the prevalence of fistulae with previously angioplastied stenosis increases.

There were two objectives for the current study. The first was to determine the positive predictive value of ultrasound dilution techniques (UDT) for the detection of subclinical stenoses in fistulae that have previously undergone angioplasty. The second was to document the efficacy of angioplasty at correcting stenoses in fistulae that have previously undergone angioplasty. In both cases, results from those with recurrent positive screening studies were compared with those with first positive studies. We hypothesized that a strategy of continuing to screen fistulae with UDT after angioplasty would be useful for detecting and treating recurrent stenoses.

Materials and Methods

Study Design

This was a prospective observational study. We began routinely screening patients with functioning native vessel fistulae in October 1999 as per published guidelines using UDT. No other access screening was performed. All incident and prevalent chronic hemodialysis patients at our institution with a functioning native vessel AV fistula since screening began were eligible for inclusion. Results of access screening in fistulae that underwent angiography because of clinically suspected access dysfunction were excluded, as the focus of this analysis was on cases of subclinical stenosis. Patients were followed from the time of their first screening study until access failure. Patients who died, were transplanted, or transferred out of the hemodialysis unit had follow-up censored at the time of their event.
**Dialysis Technique**

Patients were dialyzed according to their usual prescription during the study. No patients received anti-platelet or anticoagulant agents specifically to maintain access patency. Blood pump speeds were set as high as venous pressures would allow, and fistulae were cannulated with 15-gauge needles whenever possible.

**Procedure for Access Screening**

Screening studies were performed bimonthly with a Transonic HD01 Monitor (Transonic Systems Inc, Ithaca, NY), using indicator dilution technology, where the ultrasound velocity through blood is the indicator and dilution is provided by the bolus of normal saline. The validation of this device has been described elsewhere (7,8).

Each patient had Qa measured twice in succession during the same dialysis treatment, and the mean value was recorded. Access recirculation (AR) was measured once using UDT and repeated if the first value was non-zero. Studies were not performed during the last hour of hemodialysis or during periods of clinically significant hypotension (at the discretion of the dialysis unit nurses).

The value of Qa indicating that angiography was required (the "threshold value") was set at $\pm 500 \text{ ml/min}$ as per Canadian guidelines (9). A fall of Qa in excess of 20% from baseline (\(\Delta Qa \geq 20\%\)) or the presence of AR $\geq 5\%$ were also indications to perform angiography. Previous work has shown that the inability to measure Qa (displayed on the Transonic device as an “unusual curve”) has a high positive predictive value for stenosis in fistulae that are appropriately cannulated and appear suitable for study (1). This finding was therefore also considered a positive result in this analysis. For diagnostic purposes, the baseline Qa in patients with previous angioplasty was considered to be the first post-PTA Qa value.

Results of screening were reviewed by a team of dedicated nursing staff. The attending nephrologist was not routinely notified of the results of screening studies; angiography was ordered by the team when the specified criteria were met. Angioplasty was arranged routinely by the team for most stenoses that were identified; difficult cases were discussed at a multidisciplinary conference with vascular radiologists and surgeons.

**Angiography**

Patients with positive screening studies underwent biplanar fistulography. Diagnostic fistulography was performed with a Siemens Polystar digital subtraction angiography unit (Siemens, Ehranghen, Germany). The fistula was accessed with a standard 19-gauge butterfly needle within several centimeters of the arteriovenous anastomosis, facilitated by inflation of a BP cuff above the elbow. In cases of difficult access, a coaxial micropuncture set (Cook, Bloomington, IN) was used. The BP cuff was inflated to 220 mmHg to enable reflux across the arteriovenous anastomosis during contrast injection. The BP cuff was deflated, and overlapping venograms were continued proximally to the level of the right atrium.

Hemodynamically significant stenoses ($\geq 50\%$) in the arm were evaluated in tangential projections; central stenoses were evaluated in anteroposterior and craniocaudal projections. Fistula stenosis was defined by a greater than 50% reduction in vessel diameter, as reported by the attending radiologist.

**Angioplasty**

Patients with documented stenosis underwent angioplasty unless the attending radiologist felt that the lesion was technically unsuitable for a percutaneous procedure. Stenoses were treated using standard angioplasty technique using noncompliant balloons, and a transvenous approach was employed in most cases. For lesions occurring at or within 3 to 4 cm of the anastomosis, a retrograde puncture of the fistula was performed with placement of a short 6 French vascular sheath. For more proximal lesions, an antegrade fistula puncture was used. Heparin was administered at the discretion of the treating radiologist, and doses ranged between 0 and 5000 units. All patients in whom angioplasty required traversal of the anastomosis with a guidewire and catheter were given heparin.

**Success of Angioplasty: Functional Markers**

In accordance with the Society of Interventional Radiology consensus document defining reporting standards (10), anatomic success of angioplasty was defined as less than 30% residual diameter stenosis at the site(s) of treatment; clinical success was defined as resumption of at least one session of normal dialysis. The functional success of angioplasty was determined by post-procedure Qa. Pre- and post-procedure values for Qa were defined by the routine measurements immediately preceding and following the intervention. Qa was routinely measured bimonthly; therefore, the interval between measurement of these parameters and performance of angioplasty was 2 or more.

We have used the term “first positive study” to refer to a positive ultrasound dilution study in fistulae with no previous history of angioplasty. If stenosis was identified and angioplastied and screening studies were subsequently found to be positive, the term “recurrent positive study” has been used.

**Statistical Analyses**

Paired two-sided $t$ tests were performed on pre- and post-procedure values for Qa, which were first log-transformed to normalize their distributions. Kaplan-Meier plots were used to illustrate unadjusted patency rates. Results are expressed as mean $\pm$ SD or as percentages. The unit of analysis was the arteriovenous fistula being used for dialysis at the time of each patient’s first screening study, unless otherwise stated. All analyses are intention-to-treat unless otherwise specified. Statistical analysis was performed using SAS 8.2 (Cary, NC).

**Results**

**Patient Characteristics**

There were 312 patients who had functioning native vessel fistulae and who were eligible for inclusion. Fistulae in 9 (2.9%) of 312 of these patients had single venous segments of less than 3 cm in length and were thus unsuitable for UDT study. The remaining 303 patients underwent screening with ultrasound dilution techniques over a 30-mo period (median follow-up, 15 mo).

**Positive Screening Studies**

Nearly one third of all patients (98 of 303; 32%) had at least one positive UDT study. The majority (67 of 98; 68%) had Qa $\leq 500 \text{ ml/min}$ (mean $318 \pm 101 \text{ ml/min}$), and a substantial minority (34 of 98; 35%) had $\Delta Qa \geq 20\%$ from baseline (mean fall $43 \pm 20\%$). Only 13 of 98 patients had AR $> 5\%$, and 11 of 98 had an unusual Qa curve (unmeasurable Qa). Some patients met more than one criterion for a positive study.

There were 46 instances of recurrent positive studies in 30 patients who had previously undergone angioplasty for lesions detected by screening. The median time to a recurrent positive
test was 77 d after the first angioplasty (range, 45 to 450 d). The anatomic distribution of first and subsequent stenoses were similar (Table 1). Median time between positive screening studies and angiography was 18 d; median time to angioplasty after diagnostic angiography was 23 d.

Positive Predictive Value of Access Screening for Stenosis

First positive studies were associated with stenosis in 69 (70%) of 98 cases. The positive predictive value (PPV) for stenosis for each criterion is shown in Table 2. Many individuals with Qa $\leq$ 500 ml/min also had a fall in Qa of $\geq$ 20%. However, the converse was not true, and 17 patients with Qa $>$ 500 ml/min had $\Delta$Qa of $\geq$20%, of whom stenosis was found in 59% (10 of 17).

The performance of UDT was similar in first and recurrent positive studies. For statistical testing, we formed two mutually exclusive groups of patients: those with only one positive test, and those with recurrences (limiting analyses to the first recurrence only). In this analysis, the PPV for stenosis were not significantly different: 65% (95% CI, 50% to 78%) and 60% (95% CI, 36% to 80%; $P = 0.72$), respectively, for Qa $<$ 500, 62% (95% CI, 43% to 78%) and 60% (95% CI, 36% to 80%; $P = 0.92$), respectively, for $\Delta$Qa $>$ 20%, and 70% (95% CI, 40% to 89%) and 0% (95% CI, 0 to 66%; $P = 0.15$), respectively, for unmeasurable Qa.

Table 2 shows diagnostic performance for all first positive tests compared with all recurrent positive tests, which (although some patients appear in both categories) reflects the likelihood that stenosis will be found in fistulae with recurrent positive UDT if screening is continued after first angioplasty. Significant AR was not useful in addition to measuring Qa (in patients with or without previous PTA) in either comparison, because all patients with AR $\geq$ 5% and stenosis also had Qa $<$ 500 ml/min and thus would have undergone angiography anyway.

For both first and recurrent positive studies, the overall performance of UDT was similar in brachial and radial fistulae and in incident and prevalent fistulae. Stenosis was found in 7% of fistulae studied within 2 mo of the first dialysis treatment.

Outcome of PTA for First Positive Studies

Of the 69 patients with stenosis, two died and four completely thrombosed their fistulae before angioplasty could be performed (median time to thrombosis after fistulography, 21 d; mean Qa, 265 $\pm$ 51 ml/min). In ten of the remainder, the anatomy on fistulography was judged unsuitable for angioplasty, and access failure rates were high in this group. Time to access failure for all individuals who underwent first PTA and for those who could not undergo PTA is shown in Figure 1.

Functional Outcome of PTA for Subsequent Stenoses

Overall, there were 31 episodes of repeat stenosis in 19 patients (range, 1 to 5 episodes). In five episodes (four patients), the anatomy was deemed unsuitable for PTA by the attending radiologist. The remaining 26 lesions in 15 patients underwent angioplasty, and angiographic improvement was

Table 2. Positive predictive value of ultrasound dilution parameters for stenosis in native vessel fistulae with first and recurrent positive screening studies

<table>
<thead>
<tr>
<th></th>
<th>PPV for Stenosis: First Positive Test</th>
<th>PPV for Stenosis: Recurrent Positive Test</th>
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<tbody>
<tr>
<td>Qa $\leq$ 500 ml/min</td>
<td>76% (51/67)</td>
<td>73% (30/41)</td>
</tr>
<tr>
<td>Fall $\geq$ 20%</td>
<td>68% (23/34)</td>
<td>71% (22/31)</td>
</tr>
<tr>
<td>AR $\geq$ 5%</td>
<td>69% (9/13)</td>
<td>100% (4/4)</td>
</tr>
<tr>
<td>Unmeasurable Qa</td>
<td>73% (8/11)</td>
<td>0% (0/3)</td>
</tr>
<tr>
<td>Overall</td>
<td>70% (69/98)</td>
<td>67% (31/46)</td>
</tr>
</tbody>
</table>

*Overall PPV refers to the proportion of fistulae in which stenosis was found after a positive screening study by any criterion. Unmeasurable Qa is displayed on the Transonic device as “unusual curve.” There were 46 instances of recurrent positive studies in 30 patients with previous angioplasty.

Figure 1. Patency rates in fistulae with positive screening studies stratified by performance/non-performance of angioplasty. The figure shows cumulative patency rates for patients with positive screening studies who underwent angioplasty (solid line), and patients with positive screening studies in whom angioplasty was technically infeasible (dashed line). Time: 0 represents the date of the first angioplasty or the date of the positive screening study if no angioplasty was performed.
noted after all 26 procedures. Of the 15 individuals that underwent repeat PTA, 13 (87%) remain patent at a median follow-up of 313 d after the first repeat PTA. The Kaplan-Meier plot of time to access failure or next PTA in all patients with stenosis (intention-to-treat) is shown in Figure 2. After median follow-up of 10 mo after the first angioplasty, the proportion of all patients who had undergone a first angioplasty and whose Qa remained higher than the pre-procedure value was 83%.

**Overall Patency**

The overall patency rate during the 900-d study period was 90.4% (282 of 312) after median follow-up of 436 d. One-year and two-year patency rates were 93% and 85%, respectively. These rates included all fistulae in the dialysis program but excluded failures occurring in those that had been in use for less than 2 mo as per NKF-DOQI guidelines (11). Only four patients had negative UDT studies within 2 mo of access failure.

**Discussion**

We found that ultrasound dilution techniques were similarly effective for detecting first and recurrent episodes of subclinical stenosis in patients with native accesses. Stenosis detected in this way was usually amenable to angioplasty, which resulted in sustained post-procedure increments in Qa. Angioplasty for subclinical lesions was also associated with a low rate of serious complications and excellent long-term patency rates.

There are several reasons why the performance of access screening might differ in patients with and without previous angioplasty. First, limiting analyses to those patients who have had lesions corrected might influence the positive predictive value of screening studies by altering the pre-test likelihood of stenosis. Second, unlike PTFE grafts, stenosis might affect flow patterns through native vessel conduits (2,12,13), which might interfere with the transmission of a saline bolus that is necessary to perform UDT (7). Finally, the ideal frequency of screening might differ in individuals with previous stenosis, either because of more rapid progression of stenosis or recoil of the native vessels after angioplasty (14). Despite these theoretical considerations, the Qa < 500 ml/min and fall of 20% from baseline parameters both performed well and detected more first and recurrent lesions together than either used alone.

The substantial (7%) incidence of stenosis in fistulae studied within 2 mo of the first dialysis treatment suggests that screening should begin soon after patients commence dialysis. Many of those undergoing angioplasty have had recurrent lesions detected by screening (36%), and several have had multiple recurrences; we therefore believe that screening should continue indefinitely after correction of a first stenosis. It is unclear whether the frequency of recurrent lesions could be reduced by changes in angioplasty technique, and this requires further investigation.

The cumulative patency rate in all fistulae with subclinical stenosis was 79%, and assisted patency in such fistulae that were technically suitable for angioplasty was 87% after median follow-up of 16 mo. These compare well with the NKF-DOQI target for cumulative patency of 70% at 1 yr (11). Access screening may be responsible for the low overall rate of fistula loss in the current study (0.08 episodes per patient-year), which is similar to the short-term results obtained in another report (15). However, we cannot confirm that screening as practiced in our unit prolongs access survival, which would require a randomized trial. The alternatives to our strategy consist of screening with other techniques or avoiding the use of screening altogether. In our opinion, both these alternatives are unsatisfactory in native vessel fistulae.

Unlike PTFE grafts, AV fistulae are not well suited for screening with static or dynamic pressure monitoring (2). Although screening for AR can detect stenosis, its performance is inferior to that of Qa in AV fistulae (16). Avoiding the use of any screening strategy and performing angioplasty only for thrombosis or clinically evident stenosis is associated with significantly lower patency rates (50 to 70% at 12 mo) (17,18). In addition, angioplasty of subclinical stenosis is associated with improved dialysis delivery (1); therefore, this expectant strategy might result in morbidity due to under-dialysis.

Our study has several limitations to consider, the most important of which is that it is uncontrolled. In addition, we did not perform angiography in individuals without positive screening studies, so we are unable to calculate the sensitivity and specificity of Qa measurements for stenosis. Finally, the limited number of patients with recurrent positive studies means that we had low statistical power to compare the PPV for stenosis in this subgroup with those who had only one positive UDT examination.

Despite these limitations, this study describes outcomes after 30 mo of access screening in a large series of patients with native vessel fistulae. These data suggest that continued access
screening is beneficial in patients with subclinical stenosis who have previously undergone PTA, because of both the frequency of recurrent stenosis and the durable success of repeat intervention.

References