Catheter Patency and Function after Catheter Sheath Disruption: A Pilot Study

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Background and objectives: Hemodialysis catheters are frequently complicated by dysfunction from fibrin sheaths. Previous studies of sheath disruption have methodologic limitations but suggest that the patency after disruption is short.

Design, setting, participants, & measurements: A randomized, controlled, pilot trial was conducted to investigate the impact of angioplasty sheath disruption on catheter patency and function. Forty-seven long-term hemodialysis patients with secondary, refractory catheter dysfunction underwent guidewire exchange to replace their catheters.

Results: Sheaths were present in 33 (70%) of the 47 patients. In 18 patients who were randomly assigned to disruption, the median time to repeat dysfunction was 373 d compared with 97.5 d in patients who did not undergo disruption (P = 0.22), and the median time to repeat catheter exchange was 411 and 198 d, respectively (P = 0.17). Mean blood flow (340 versus 329 ml/min; P < 0.001) and urea reduction ratio (72 versus 66%; P < 0.001) were higher in the disruption group. Fourteen patients had no sheaths, and their median times to repeat dysfunction and repeat exchange were 849 and 879 d, respectively. Patients with no sheaths had higher urea reduction ratio (73 versus 66%; P < 0.001) and a lower percentage of inadequate hemodialysis treatments (9.8 versus 27%; P = 0.01) and treatments that required thrombolytics (1.8 versus 5.0%; P = 0.03) than patients with sheaths that were not disrupted.

Conclusions: Disrupting sheaths by angioplasty balloon results in durable catheter patency and modestly improves blood flow and clearance over the duration of catheter use.


In North America, hemodialysis (HD) catheters provide vascular access for 40 to 70% of incident long-term dialysis patients and 27 to 38% of prevalent patients (1–3). Catheter dysfunction has been defined by Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines as “failure to maintain an extracorporeal blood flow sufficient to perform hemodialysis without significantly lengthening the hemodialysis treatment” (4). The guidelines and many research studies set a minimum blood flow target of 300 ml/min (5–11). Using this target, between 55 and 87% of catheters will experience dysfunction at least once (6,12), and 5 to 13% will require catheter replacement to treat dysfunction that is refractory to other measures such as patient repositioning, saline flushes, lumen reversal, and thrombolytic dwells (9–11,13,14).

One cause of refractory dysfunction is a fibrin sheath, sometimes referred to as a catheter sheath or sleeve. “Fibrin sheath” may be a bit of a misnomer because studies demonstrate that sheaths can be composed of thrombus, endothelial cells, smooth muscle cells, and/or collagen, depending on the duration of catheter placement (15–17). Sheaths cover variable portions of catheters, but if they block the inlet and outlet holes of HD catheters, then they can cause dysfunction (18). Radiologic investigation of catheters with refractory dysfunction have demonstrated sheaths around 48 to 82% of HD catheters (12,19–21).

Catheter sheaths may be disrupted by infusion of thrombolitics, stripping, and disruption during guidewire exchange. A median catheter patency of 40 d has been reported after disruption with J-tipped guidewires, pigtail catheters, or Fogarty embolectomy balloons (22). Angioplasty balloon sheath disruption has been associated with a 3-mo patency of 39% (median patency was not described), which was not significantly different from stripping or exchange without disruption (23). The former study had methodologic limitations because a patient could be enrolled more than once, different disruption techniques were used, and measurement of catheter function after exchange was not performed. The latter study was nonrandomized, enrolled patients more than once, and did not use a uniform blood flow target to enroll patients or define catheter dysfunction. We therefore, performed a pilot study to determine the feasibility of a randomized, controlled trial of sheath disruption, estimate the percentage of patients with sheaths, and estimate the effect size of disruption on catheter patency and function.
Concise Methods

The study was conducted at Sunnybrook Health Sciences Centre (SHSC), University Health Network (UHN), and Humber River Regional Hospital (HRRH) in Toronto, Ontario, Canada. Patients with ESRD were eligible for the study when they used a tunneled, cuffed HD catheter placed in the internal jugular vein for vascular access and experienced secondary, refractory malfunction. Refractory dysfunction was defined as three dialysis treatments that had mean blood flow <300 ml/min within the last 30 d (including the most recent treatment) or one treatment that had mean blood flow <200 ml/min (which could include lumen occlusion) and was unresponsive to patient repositioning, saline flushes, lumen reversal, and treatment with at least one dose of tissue plasminogen activator administered as a 1-h dwell or interdialytic dwell. Mean blood flow was defined as blood processed in milliliters divided by the time of dialysis in minutes. Patients were excluded when they had primary catheter dysfunction, defined as dysfunction within 1 wk of catheter insertion. Patients were also ineligible when they had an allergy to contrast dye (disruption requires additional contrast) or any signs of infection (septic pulmonary embolism after disruption was previously described [24]). All patients who had refractory dysfunction and underwent exchange consented to follow-up. Patients with sheaths were randomly assigned to either catheter exchange over a guidewire or exchange over a guidewire with angioplasty sheath disruption. Sheaths were diagnosed by withdrawing the dysfunctional catheter over a guidewire until the tip was near the entry site into the vein. Contrast was injected through the proximal (arterial) port to determine whether a sheath was present. The radiologist randomly assigned patients with sheaths by opening opaque envelopes in the radiology suite. The randomization schedule was stratified by center and by side of catheter (left-sided catheters are at higher risk for dysfunction [25]) using a block-of-four design. Radiologists were instructed to try to maintain blinding during the procedure by not informing patients of the presence of sheaths or disruption. When the patient was randomly assigned to disruption, a noncompliant 12-mm × 4-cm angioplasty balloon was inserted over a guidewire, inflated by hand, and moved in a back-and-forth motion in the region of the proximal right atrium to the confluence of the brachiocephalic vein. The balloon was then removed over a guidewire, and a new HD catheter was partially inserted to level of the clavicle, at which point contrast was injected to confirm disruption of the sheath. After the procedure, the radiologist completed a case report form describing the procedure and sealed it in an envelope to maintain blinding of the research coordinator who performed the follow-up in the HD unit. At the end of the guidewire exchange, there were three groups of patients: Those who had no sheath (“no sheath”), those who had a sheath but did not have it disrupted (“sheath/no disruption”), and those who had a sheath imaged and had it disrupted (“sheath disrupted”).

Demographics, height, weight, presence of diabetes, duration of dialysis, vascular access history, use of antiplatelets or anticoagulants, hemoglobin level, and serum albumin were collected at baseline for each patient. The research coordinators, site investigators, primary nephrologists, dialysis nurses, and patients were blinded for the catheter use or until study termination. At the first dialysis treatment after the exchange, patients were interviewed by the coordinator about the presence of cough, shortness of breath, chest pain, fever, and local symptoms at the exit site (pain, bleeding, redness, and/or swelling) experienced between the exchange procedure and the dialysis treatment.

Patients were followed prospectively at each HD treatment for a minimum of 6 mo. Dialysis nurses completed a study case report form attached to the “run” sheet, which queried exact start time, end time, total volume of blood processed, need for lumen reversal, and thrombolytic use on case report forms. These case report forms instructed nurses to maximize blood flow up to 400 ml/min. Clearance (urea reduction ratio [URR], true blood flow, and recirculation (Transonic Systems, Ithaca, NY) was measured weekly during the first month and then monthly thereafter. Predialysis urea was taken before dialysis initiation after the catheter dwell solution (heparin or citrate) was removed from the lumens of the catheter. The postdialysis urea was taken from the arterial port of dialysis tubing when the dialysis time had elapsed, the machine was put in bypass, and the blood pump speed was decreased to 50 ml/min (UHN and HRRH) or 200 ml/min (SHSC). At one site (SHSC), nurses required a physician order to administer a thrombolytic dwell, and at the other two sites (UHN and HRRH), nurses could administer a dwell at their discretion.

The pilot study was designed to enroll 48 patients over 2 yr. The expected sample size was calculated from the enrollment rate measured during a 6-mo study, conducted before this study, in 50 HD patients who were using catheters at SHSC (four patients were enrolled in 300 catheter-months of observation). Among the three centers, we estimated that 200 patients using catheters would accumulate 3600 catheter-months during an 18-mo period and would result in 48 enrolled patients. A post hoc power calculation to detect differences in the patency outcomes was performed using a two-sided log-rank test with a 0.05 significance level. Calculations were carried out using PASS 2005 (NCSS, Kaysville, UT). Pair-wise differences in categorical variables and continuous variables between the groups were analyzed using Fisher exact test and t test, respectively. Two measures of catheter patency were used: Time to repeat dysfunction (using the same blood flow criteria as study entry) and time to repeat catheter exchange to treat dysfunction. Kaplan-Meier curves for catheter patency were constructed for the three groups and compared using the log-rank test (26). Observations were censored when catheters were removed for any reason other than dysfunction (e.g., infection, use of fistula, dialysis was discontinued) and at study completion.

The continuous measures of catheter function including blood flow rate (blood processed divided by time on dialysis) and URR were analyzed using fixed-effect, longitudinal linear models. These models estimated group means and provided pair-wise comparisons among the three groups while adjusting for repeated measures within individuals. Group and side of catheter were included as covariates in the models. The categorical measures of mean blood flow <300 ml/min, lumen reversal, URR <65%, and need for thrombolytic dwells were first reported as the proportion of HD treatments complicated by this event for each group, weighted for the number of observations per patient. The probability of these events over the duration of catheter use was then analyzed using fixed-effect general estimating equations that adjusted for repeated measures and side of catheter and provided pair-wise comparisons among the three groups. Because of potential imbalance in the groups in the duration of dialysis (vintage), number of previous catheters, and use of warfarin, the models were re-run post hoc to include these variables. Differences were considered significant when two-sided P values were ≤0.05. Analyses were performed using SAS 8e (SAS Institute, Cary, NC) and supervised by a statistician. The research ethics board of each participating institution approved the protocol, all patients provided informed consent to participate, and methods adhered to the Declaration of Helsinki.

Results

Forty-seven patients were enrolled from August 2001 to April 2005. The actual enrollment rate was approximately half the expected rate, so the study was extended for 2 yr. The median age of the patients was 69 yr, and 66% were female. Thirty-three
(70%) of the 47 patients were found to have a catheter sheath at the time of guidewire exchange. There were three protocol violations whereby consented patients with sheaths underwent disruption but were not randomly assigned leaving 44 patients in the primary analysis (14 no sheath, 12 sheath/no disruption, and 18 sheath/disruption). Review of procedures found that one randomization envelope had been inadvertently opened for a patient with no sheath (assignment no disruption), but the rest of the imbalance seemed to have occurred by chance, because the randomization sequence was followed. Baseline characteristics of the groups are presented in Table 1. Right-sided catheters were present in 66% and 55% in the sheath/no disruption and sheath disruption groups, respectively.

All patients received 14-French, tunneled, cuffed, catheters positioned with their tip in the right atrium or the superior vena cava/right atrial junction, 44 High Flow CardioMed catheters (CardioMed Supplies, Gormley, Ontario, Canada), and three Vaxcel catheters (Boston Scientific Corp., Natick, MA).

Effect of Sheath Disruption
The median procedure time in the sheath disruption group and in the sheath/no disruption group was 25 and 27 min, respectively (P = 0.14). At the next dialysis treatment, patients who received disruption reported shortness of breath (n = 1) and bleeding (n = 3), redness (n = 2), and swelling (n = 2) at the exit site. The immediate symptoms reported by the patients with no sheaths versus disruption and time to repeat catheter exchange was 18 and 9%, respectively. Differences in catheter function are presented in Table 2. The sheath disruption group had a higher mean blood flow of 340 versus 329 ml/min (P < 0.001) and a higher clearance (72 versus 66%; P < 0.001) compared with the sheath/no disruption group. There were only trends for a lower frequency of HD treatments with URR <65% (16 versus 27%; P = 0.19) and need for thrombolytic use (2.1 versus 5.0%; P = 0.12) after disruption.

Patients with Dysfunction but No Sheaths
The median procedure time in the no sheath group was 20 min. Immediate symptoms reported by the patients with no sheaths at the next dialysis treatment were pain (n = 2), bleeding (n = 2), redness (n = 2), and swelling (n = 1) at the exit site. In one case, the catheter was removed for severe bleeding from exit site the day after the procedure. The median time to repeat dysfunction was 849 d. The median time to repeat catheter exchange was 879 d compared with 198 d in the sheath/no disruption group (P = 0.04; Figure 1). Patients with no sheaths compared with the sheath/no disruption group had a higher URR (73 versus 66%; P < 0.001), a lower percentage of HD treatments with URR <65% (9.8 versus 27%; P = 0.01), and less frequent thrombolytic use (1.8 versus 5.0% of HD treatments; P = 0.03).

The sheath disruption group and the no sheath group had similar catheter function and frequency of dysfunctional events except for their mean blood flow of 340 and 360 ml/min (P < 0.001), respectively. The entire analysis was repeated including

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the three patients with protocol violations, but it did not sub-
stantively change the results.

**Other Factors that Influenced Catheter Function**

True blood flow measured by ultrasound dilution was 23 to 25 ml/min less than blood pump measurements, and recirculation ranged from 8.6 to 12%, but neither differed among the groups. Left-sided and right-sided catheters provided a mean URR of 66 and 74% ($P < 0.001$), respectively. Left-sided catheters were at greater risk for providing URR $< 65\%$ ($P = 0.003$) but not any other dysfunction-related events. Lumen reversal indepen-
dently increased recirculation from 0 to 18% ($P < 0.001$) and decreased URR by 3.6% ($P < 0.001$). The number of previous catheters (odds ratio [OR] 0.73; 95% confidence interval [CI] 0.59 to 0.9) and vintage (OR 1.0004/d; 95% CI 1.0 to 1.0008) was associated with lumen reversal. Previous number of catheters was also associated with thrombolytic use (OR 0.67 per catheter; 95% CI 0.51 to 0.88).

**Discussion**

This study demonstrated that catheter sheaths significantly influence catheter patency and function. Patients who have a catheter sheath that is not actively disrupted will experience reduced patency, lower clearance, and a higher frequency of thrombolytic use than patients who do not have sheaths. Dis-
rupting the sheath modestly improves blood flow and clear-
ance and may reduce thrombolytic requirements. This pilot study suggests that the effect of disruption on catheter patency may be large and clinically relevant, but we did not demon-
strate that disruption prolongs patency because of the small sample size. Sheath disruption seems safe with no increase in postprocedure symptoms compared with guidewire exchange without disruption. Left-sided internal jugular placement and reversal of catheters independently reduced catheter function, in agreement with other studies (5,25,27).

Fibrin sheaths were first described by Hoshal et al. (21). Subsequent animal and human studies found that central ve-
nous catheters cause intimal injury, endothelial denudation, and adherent thrombus (15,17,18,28,29). Over time, smooth muscle cells proliferate and the vein wall thickens, leading to focal areas of attachment to the catheter forming a sheath composed of thrombus (in various stages of organization), collagen, and endothelial cells. Seventy percent of patients with refractory catheter dysfunction in this study had sheaths. Pre-
vious studies (12,19,20,22,30–33) reported a prevalence be-

![Figure 1. Time to repeat catheter exchange to treat dysfunction (patency) in patients with no sheaths, sheath with disruption, and sheaths/no disruption. The no sheath group had longer patency that the sheath/no disruption group ($P = 0.04$). The difference in patency between the sheath disruption group (median patency 411 d) and the sheath/no disruption group (median patency 198 d) did not reach statistical significance ($P = 0.17$).](image-url)

| Table 2. Catheter function after guidewire exchange according to presence of sheath and use of disruption$^a$ |
|-----------------|----------------|-----------------|-----------------|
| Outcome         | No Sheath      | Sheath/No Disruption | Sheath Disrupted |
| No. of patients | 14             | 12              | 18              |
| Follow-up days (median) | 123.5        | 132.5           | 182.0           |
| Follow-up HD sessions (median) | 75.0         | 39.5            | 81.5            |
| Blood flow (ml/min; mean [SD]) | 360 (2.0)   | 329 (3.2)$^b$  | 340 (1.9)$^{bc}$ |
| URR (mean)      | 73.0           | 66.0$^b$        | 72.0$^c$        |
| Blood flow <300 ml/min (%) | 7.1          | 22.0$^b$        | 15.0            |
| Recirculation (mean) | 12.0            | 8.6             | 12.0            |
| Lumen reversal (%) | 63.0           | 62.0            | 53.0            |
| URR <65 (%)     | 9.8            | 27.0$^b$        | 16.0            |
| Use of thrombolytic dwells (%) | 1.8          | 5.0$^b$         | 2.1             |

$^a$Follow-up days were calculated from the day of the exchange procedure to the day of catheter removal or termination of the study. Follow-up hemodialysis (HD) sessions were the number of HD sessions during which outcomes were prospectively measured (blood flow, lumen reversal, and use of thrombolytics). Recirculation and urea reduction ratios (URR) were measured weekly for the first month and then monthly thereafter. All means are least square means calculated using linear longitudinal models. The average percentages were calculated as proportions weighted for the number of observations in each patient.

$^b P < 0.05$ versus the no sheath group.

$^c P < 0.05$ versus the sheath/no disruption group.
between 47 and 82%. Prevalence may vary because studies use different enrollment criteria and diagnosed sheaths using different methods including the presence of contrast filling defects, retrograde tracking of contrast, and sluggish flow of contrast (19). This study diagnosed sheaths during catheter withdrawal, which may be a more sensitive diagnostic technique (34,35).

Methodologic strengths of this study included uniform inclusion criteria, randomization, and blinding. Enrollment was also based on mean blood flow over the duration of dialysis, which can be calculated using objective measures of blood processed and time on dialysis rather than peak blood flow, which can be subjective. Randomization reduced bias compared with a previous retrospective study (23) that compared disruption with no disruption. Patients could also be enrolled only once, so measurements of patency were truly independent compared with studies that used the procedure as the unit of analysis (22,23). Catheter performance was measured carefully over the duration of catheter use using longitudinal models, which adjusted for correlated measurements within patients.

Limitations of the study include the unbalanced randomization, which seemed to have occurred by chance but was not detected because of blinding. Future studies would benefit from a computerized randomization schedule and careful monitoring of randomization procedures by nonblinded coordinators. The study was also designed as a pilot, so it was not powered to detect differences but rather to determine feasibility and measure effect size. Nonetheless, a significant difference in patency between the no sheath group and the sheath/no disruption group was found because the difference was very large. The results also suggest that disruption may have clinically important effects on patency. The sample size was also adequate to detect differences in catheter function and dysfunctional events among the three groups.

This study, although small, provides a comprehensive view of catheter function over the duration of use. Mean catheter blood flow was well above the K/DOQI target, averaging 330 to 360 ml/min per group (4). Absolute differences between groups were small but were statistically significant because the standard deviation in blood flow within each group was remarkably low. The incidence of blood flow <300 ml/min and URR <65% ranged from 7.1 to 22% and 9.8 to 27%, respectively, indicating that dysfunction defined in this manner is common after guidewire exchange. It is interesting that even though blood flow <300 ml/min and inadequate clearance were common, the use of thrombolytics ranged from only 1.8 to 5.0% of treatments. Lumen reversal occurred in more than half of the treatments, increasing recirculation and lowering clearance.

Catheter patency after disruption was 373 d when measured as the time to refractory dysfunction and 411 d when measured as the time to repeat catheter exchange. These estimates are longer than studies of sheath stripping (9 to 126 d), infusions (42 d), and exchange (40 d), suggesting that catheter exchange with angioplasty balloon sheath disruption may produce a more durable patency (12,19,22,31,36).

The results of this study are relevant because 5 to 13% of patients who use catheters for vascular access are expected to require catheter exchange for dysfunction (9–11). These procedures are invasive, can cause damage to the central veins, and consume interventional radiology resources. The cost of a catheter exchange has been estimated at $2384 USD (22). The added cost of angioplasty disruption in this study was $180 USD, which may be justified if disruption significantly prolongs patency. Disruption of sheaths is also likely widely practiced because it makes intuitive sense not to insert a new catheter into an old sheath. This study provides preliminary outcome data to support this practice.

Conclusions

The presence of a sheath at the time of HD catheter exchange significantly reduces subsequent catheter function. Disrupting sheaths by angioplasty balloon modestly improves blood flow and clearance. Patency after disruption was approximately 1 yr, but larger studies are required to confirm whether angioplasty disruption significantly extends catheter patency.

Acknowledgments

This research was generously funded by the Kidney Foundation of Canada. R.R.Q. is supported by a Bristol-Myers Squibb Cardiovascular Fellowship.

This study was presented at the annual meeting of the Canadian Society of Nephrology: May 23–27, 2007; Halifax, Nova Scotia, Canada. We thank the patients and staff who participated in the study. We thank Norah Palmateer, Laura Lodberg, Bonnie Houghton, Dina Yee, James Kang, and Sherry Mariash for assisting with the study and Virginia Wooland and Lisa Thackeray for assistance in preparing the manuscript.

Disclosures

None.

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