Does Heparin Coating Improve Patency or Reduce Infection of Tunneled Dialysis Catheters?

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Background and objectives: Tunneled dialysis catheters are prone to frequent malfunction and infection. Catheter thrombosis occurs despite prophylactic anticoagulant locks. Catheter thrombi may also serve as a nidus for catheter infection, thereby increasing the risk of bacteremia. Thus, heparin coating of catheters may reduce thrombosis and infection. This study evaluated whether heparin-coated hemodialysis catheters have fewer infections or greater cumulative survival than noncoated catheters.

Design, setting, participants, & measurements: We retrospectively queried a prospective access database to analyze the outcomes of 175 tunneled dialysis catheters placed in the internal jugular vein, including 89 heparin-coated catheters and 86 noncoated catheters. The primary outcome was cumulative catheter survival, and the secondary outcome was infection-free catheter survival.

Results: The two patient groups were similar in demographics and clinical and catheter features. Catheter-related bacteremia occurred less frequently with heparin-coated catheters than with noncoated catheters (34 *versus* 60%, $P < 0.001$). Cumulative catheter survival was similar in heparin-coated and noncoated catheters (hazard ratio, 0.87; 95% confidence interval, 0.55 to 1.36; $P = 0.53$). On multiple variable survival analysis including catheter type, age, sex, diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease, catheter location, and previous catheter, only catheter location predicted cumulative catheter survival (hazard ratio, 2.03; 95% CI, 1.27 to 3.25, with the right internal jugular location being the reference group, $P = 0.003$). The frequency of thrombolytic instillation was 1.8 per 1000 catheter-days in both groups.

Conclusions: Heparin coating decreases the frequency of catheter-related bacteremia but does not reduce the frequency of catheter malfunction.

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The two major complications of hemodialysis catheters are thrombosis and infection (1). To prevent catheter thrombosis, an anticoagulant (heparin or citrate) is instilled into both catheter lumens at the end of each dialysis session (2). When a catheter clots despite the anticoagulant lock, a thrombolytic agent [tissue plasminogen activator (tPA) or urokinase] is instilled into the catheter lumens. If the thrombolytic agent is unable to restore catheter patency, the catheter is exchanged over a guidewire.

Because catheter thrombosis occurs despite instillation of an anticoagulant lock solution, an alternative approach is to coat the surface of the catheter with heparin. Preliminary short-term observations suggest that heparin-coated catheters are less thrombogenic than noncoated catheters (3). However, there are no published clinical studies comparing the long-term patency of heparin-coated and noncoated catheters in hemodialysis patients.

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Bacteremia is the second major complication of dialysis catheters. It arises from the bacterial biofilm that forms on the inner surface of the catheter after its insertion in the central vein (4). Catheter-related bacteremia is treated with systemic antibiotics in conjunction with catheter removal, guidewire catheter exchange, or instillation of an antibiotic lock into the catheter lumen after each dialysis session (1). The intraluminal thrombus acts as a nidus for the catheter biofilm, and *in vitro* studies have shown decreased adherence of bacteria to heparin-coated catheters compared with noncoated catheters (5). Moreover, two randomized clinical trials in hospitalized patients with short-term, nontunneled central vein catheters found a lower risk of catheter-related bacteremia in patients with heparin-coated catheters (5,6).

The goal of this study was to determine whether heparin-coated dialysis catheters reduce the risk of catheter dysfunction and infection compared with noncoated catheters.

Materials and Methods

About 500 hemodialysis patients receive their care at dialysis units affiliated with the University of Alabama at Birmingham. At any time, ~25% of our hemodialysis patients are catheter dependent (7). A tunneled dialysis catheter was placed in patients initiating dialysis without a permanent access or with an immature access. In addition, patients

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with permanent failure of their existing vascular access received a new, tunneled dialysis catheter. All catheters were placed by an interventional nephrologist or radiologist. During the 16-mo study period (November 1, 2006 to February 29, 2008), the patients received one of two types of tunneled dialysis catheters: a heparin-coated catheter (Decathlon Gold Spire Biomedical, Bedford, MA; coating by Carmeda, W. L. Gore & Associates, Flagstaff, AZ) and a noncoated catheter (Ash-split Medcomp, Harleysville, PA). Both catheters had a similar split-catheter configuration. The choice of catheter type was at the discretion of the operator. The dialysis nurses instilled heparin (5000 units/ml) in each catheter lumen at the end of each dialysis session.

Management of Catheter Complications

Catheter dysfunction was diagnosed when a catheter was unable to deliver adequate dialysis. This manifested as low dialysis blood flows (<300 ml/min) with excessively negative arterial pressures (< −250 mmHg). Catheter dysfunction was managed initially by changing the patient's position or reversing the arterial and venous lines. When these maneuvers were inadequate to correct the dysfunction, the dialysis nurse instilled tPA, 2 mg into each catheter lumen for 30 to 60 min. If the thrombolytic instillation did not restore adequate dialysis blood flow, the patient was referred for a guidewire exchange of the catheter.

Catheter-related bacteremia was diagnosed in patients with fever or rigors, positive blood cultures, and absence of an alternative source of bacteremia (1). Patients with catheter-related bacteremia received 3 wk of appropriate intravenous antibiotics after each dialysis session, in conjunction with an antibiotic-heparin lock solution (8). After completion of the antibiotic course, the use of standard heparin locks was resumed. Surveillance blood cultures were obtained 1 wk later. The catheter was removed in patients with persistent fever 48 h after initiation of antibiotics or in patients whose surveillance cultures showed recurrent bacteremia. Catheters were removed electively once a new fistula or graft had been cannulated successfully for dialysis.

Data Analysis

Two full-time access coordinators scheduled all catheter placements, removals, and exchanges and maintained the information in a prospective, computerized vascular access database (9). We queried this database retrospectively to identify all patients who underwent placement of a tunneled dialysis catheter during a 16-mo period (November 1, 2006 to February 28, 2008).

The radiology records were reviewed to identify the type of dialysis catheter placed and its insertion site. The patients' existing electronic medical records were reviewed to collect demographic and clinical information. We included only *de novo* placements of tunneled catheters in the right or left internal jugular vein. Catheters placed as a guidewire exchange of an existing catheter were excluded. Femoral catheters were also excluded, because they are known to have inferior patency to that of internal jugular catheters (10). If a patient had two or more catheters placed during the study period, only the first catheter was included in our analysis. A total of 175 patients received a first new, tunneled catheter during the study period, including 89 heparin-coated catheters and 86 noncoated catheters. We received approval from the local Institutional Review Board to perform this retrospective analysis.

Statistical Analysis

The primary outcome was cumulative catheter survival, defined as the time from initial placement to nonelective catheter removal or exchange, regardless of the need to instill a thrombolytic agent or an antibiotic lock. Patient follow-up was censored at the time of elective catheter removal because of use of a mature fistula or graft; patient death, kidney transplant, or transfer to an outside dialysis facility; or the end of study follow-up (July 31, 2008).

Survival analysis techniques were used to model catheter survival time and the log rank test to compare the survival of patient subgroups. Hazard ratios and their 95% confidence intervals (CIs) were calculated. Preliminary analysis showed that there was no violation of the proportional hazards model. Finally, multiple variable Cox proportional survival analysis was used to model the association between the clinical variables and catheter survival.

The secondary outcome was the proportion of patients diagnosed with catheter-related bacteremia. Additional outcomes included the frequency of tPA instillation and mean dialysis blood flows. The blood flows obtained during the last three dialysis sessions of each month after catheter placement were averaged. The mean blood flows were compared between the two catheter groups with unpaired *t* tests. All analyses were performed with the Statistical Analysis Software (SAS) version 9.0.

Results

Of the 175 study patients, 89 received a heparin-coated tunneled catheter, and 86 received a noncoated catheter. The mean patient age was 53 ± 15 yr. About one half of the patients were women, and 85% were black, reflecting the demographic distribution of our hemodialysis population. Diabetes was present in 53%, hypertension in 99%, coronary artery disease in 57%, peripheral vascular disease in 37%, and cerebrovascular disease in 34%. About three fourths of the catheters were placed in the right internal jugular vein and one quarter in the left internal jugular vein. About 40% of the patients had had a previous dialysis catheter. The demographic and clinical features were similar in patients receiving a heparin-coated catheter and in those with a noncoated catheter, except that a previous dialysis catheter was less frequent in patients receiving a heparin-coated catheter (Table 1).

The primary study outcome, cumulative catheter survival, did not differ significantly between the two study groups (Figure 1). The hazard ratio for catheter failure was 0.87 (95% CI,

Table 1. Clinical features of the study population

	Heparin Coated	Noncoated	*P* Value
Number of patients	89	86	
Age (yr)	54 ± 16	52 ± 15	0.28
Sex [*N*, (%) male]	50 (56%)	39 (45%)	0.17
Race [*N*, (%) black]	72 (81%)	76 (88%)	0.21
Diabetes [*N* (%)]	49 (55%)	43 (50%)	0.54
HTN [*N* (%)]	88 (99%)	86 (100%)	1
CAD [*N* (%)]	46 (52%)	53 (62%)	0.22
PVD [*N* (%)]	29 (33%)	35 (41%)	0.27
CVD [*N* (%)]	27 (30%)	32 (37%)	0.34
Catheter site			0.76
Right IJ vein	65 (73%)	61 (68%)	
Left IJ vein	24 (27%)	25 (32%)	
Previous catheter [*N* (%)]	29 (32%)	42 (49%)	0.03

HTN, hypertension; CAD, coronary artery disease; PVD, peripheral vascular disease; CVD, cerebrovascular disease; IJ, internal jugular.

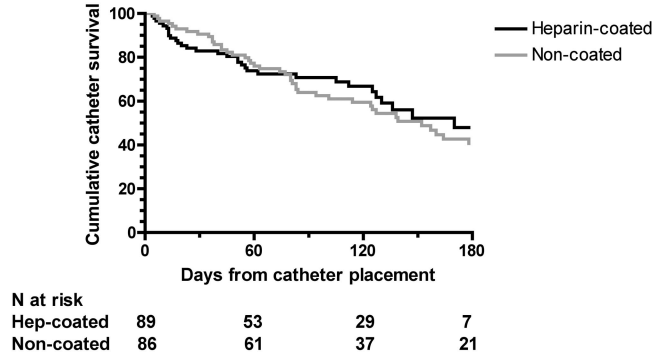

Figure 1. Cumulative catheter survival (time from catheter placement to permanent failure). $P = 0.53$ for heparin-coated *versus* noncoated catheters.

0.55 to 1.36; $P = 0.53$). Cumulative catheter survival for the heparin-coated and noncoated catheters was 74 *versus* 76% at 60 d, 67 *versus* 59% at 120 d, and 48 *versus* 41% at 180 d. The median cumulative catheter patency was 170 and 152 d, respectively. Multiple variable survival analysis was performed to evaluate which clinical factors were associated with catheter survival, with catheter type, patient age, sex, diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease, catheter location, and previous catheter included in the model. Catheter location was the only significant factor associated with cumulative catheter failure (HR, 2.03; 95% CI, 1.27 to 3.05; with the right internal jugular location being the reference group, $P = 0.003$ for the overall model).

We also categorized the frequency of catheter outcomes, with particular attention to catheter-related bacteremia (Table 2). Catheter malfunction requiring catheter exchange occurred with a similar frequency in patients with heparin-coated catheters and those with noncoated catheters. However, catheter-related bacteremia was substantially less common with heparin-coated catheters (34 *versus* 60%, $P < 0.001$). Conversely, patients with heparin-coated catheters were more likely to have elective catheter removal because of a mature vascular access or continue dialyzing with their original catheter (47 *versus* 25%). Finally, the frequency of tPA instillation for catheter dysfunction was 1.8 per 1000 catheter-days in both study groups.

The dialysis blood flows were significantly higher (by ~11%) in the heparin-coated catheters compared with the noncoated catheters (Table 3). This difference may be a consequence of the slightly larger inner diameter of the heparin-coated catheters, which is approximately 7% greater than that of the noncoated catheters (15.5 *versus* 14.5 F). For each catheter group, there was no significant change in dialysis blood flows measured at 30, 60, and 90 d.

Discussion

Dialysis catheter-related thrombosis occurs despite prophylactic anti-coagulant instillation into the catheter lumens. Pilot studies with short-term catheters have shown a smaller thrombus burden in heparin-coated catheters compared with noncoated catheters (3). In contrast, this study in hemodialysis patients observed no significant difference in the frequency of thrombolytic instillation, catheter malfunction, or cumulative catheter patency between the heparin-coated and noncoated dialysis catheters. Although patients receiving a heparin-coated catheter were less likely to have had a previous dialysis catheter, a history of a previous catheter was not associated with cumulative catheter survival in the multiple variable analyses. Why might heparin coating not reduce the frequency of catheter thrombosis? One possibility is that heparin coating is less effective in preventing thrombosis at the catheter tip compared with the rest of the catheter lumen. Alternatively, the heparin lock is sufficient to prevent most episodes of catheter thrombosis.

Catheter thrombus may serve as a nidus for biofilm formation (5). The clinical relevance of this observation was supported by two clinical trials showing a lower frequency of bacteremia with nontunneled heparin-coated catheters compared with noncoated catheters (5,6). The frequency of catheter-related bacteremia was substantially lower with heparin-coated dialysis catheters compared with noncoated catheters in this study. However, infection-free survival was a secondary endpoint of this study, and the study was retrospective. Thus, a randomized clinical trial would be required to determine whether heparin coating truly reduces catheter-related bacteremia. Why might the infection rate be lower in heparin-coated catheters? One hypothesis is that heparin coating prevents thrombus formation in most of the lumen except for the catheter tip. If the thrombus is a nidus for catheter biofilm formation, this may explain how heparin coating could reduce infection without affecting thrombosis.

Table 2. Catheter outcomes in the study population

	Heparin Coated	Noncoated
Number of patients	89	86
Catheter malfunction [*N* (%)]	17 (19%)	13 (15%)
Catheter-related bacteremia [*N* (%)]	30 (34%)[a]	52 (60%)
Elective removal [*N* (%)]	31 (35%)	17 (20%)
Remained patent [*N* (%)]	11 (12%)	4 (5%)
tPA instillations per 1000 catheter-days	1.8	1.8

[a]$P < 0.001$ *versus* noncoated catheters.
tPA, tissue plasminogen activator.

Table 3. Dialysis blood flows in the study catheters

	Heparin Coated	Noncoated	*P* Value
Number of patients	89	86	
Blood flows at 30 days (ml/min)	426 ± 47	380 ± 43	<0.001
Blood flows at 60 days (ml/min)	425 ± 49	383 ± 57	<0.001
Blood flows at 90 days (ml/min)	432 ± 47	390 ± 58	<0.001

We attempted to salvage the catheter in patients with catheter-related bacteremia by using an antibiotic lock. This strategy is successful in our hands in approximately 70% of cases (8). Because most infected catheters were salvaged with an antibiotic lock, and the frequency of catheter dysfunction was similar in both catheter groups, the cumulative catheter survival was similar with heparin-coated and noncoated catheters (Figure 1).

The dialysis blood flows were approximately 11% higher in patients with heparin-coated catheters compared with noncoated catheters. However, the inner diameter of the heparin-coated catheters was about 7% greater than that of the noncoated catheters (5.17 *versus* 4.83 mm). The blood flow rate in a rigid tube is proportionate to the fourth power of the luminal radius. Using this relationship, one would predict a 31% higher flow rate in the heparin-coated catheters [$(1.07)^4 = 1.31$]. Thus, the higher flow rate measured in heparin-coated catheters is attributable to the large diameter rather than the heparin coating.

This study has a number of limitations. First, the analysis was retrospective. However, the relevant information was collected prospectively in a computerized database by two dedicated access coordinators. Thus, it is unlikely that we missed any catheter events. Second, the study was not randomized, and there may have been clinical differences between the two study groups. However, the patients in the two groups appeared to be closely matched in terms of their demographic, clinical, and catheter characteristics (Figure 1). Finally, the study was performed at a single dialysis center, and the results may not generalize to all dialysis patients.

In conclusion, heparin-coated catheters have similar cumulative patency to that obtained with noncoated catheters, as long as an anticoagulant is instilled into the catheter lumen after each dialysis session. There was a lower frequency of catheter-related bacteremia with the heparin-coated catheters than with noncoated catheters. A randomized clinical trial would be required to confirm this potential benefit of heparin-coated dialysis catheters.

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Disclosures

None.

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