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CLINICAL INVESTIGATION

Comparison of Heparin-Coated and Conventional Split-Tip Hemodialysis Catheters

Timothy W. I. Clark · David Jacobs · Hearns W. Charles · Sandor Kovacs · Theresa Aquino · Joseph Erinjeri · Judith A. Benstein

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Abstract Catheter coatings have the potential to decrease infection and thrombosis in patients with chronic dialysis catheters. We report our midterm experience with a heparin-coated dialysis catheter. This retrospective, case-control study was approved by our Institutional Review Board. A total of 88 tunneled dialysis catheters were inserted over a 13-month period via the internal jugular vein. Thirty-eight uncoated split-tip catheters and 50 heparin-coated catheters were inserted. Primary catheter patency was compared between the two groups using the log rank test, with infection and/or thrombosis considered as catheter failures. Dialysis parameters during the first and last dialysis sessions, including pump speed, actual blood flow, and arterial port pressures, were compared using unpaired *t*-tests. Primary patency of the uncoated catheters was 86.0 ± 6.5% at 30 days and 76.1 ± 8.9% at 90 days. Primary patency of heparin-coated catheters was 92.0 ± 6.2% at 30 days and 81.6 ± 8.0% at 90 days ($p = 0.87$, log rank test). Infection requiring catheter removal occurred in four patients with uncoated catheters and two patients with heparin-coated catheters ($p = 0.23$). Catheter thrombosis requiring catheter replacement or thrombolysis occurred in one patient with an uncoated catheter and two patients with heparin-coated catheters ($p = 0.9$). No differences in catheter function during hemodialysis were seen between the two groups. In conclusion, the heparin-coated catheter did not show a significantly longer patency compared to the uncoated catheter. The flow characteristics of this device were comparable to those of the conventional uncoated catheter. A demonstrable benefit of the heparin-coated catheter in randomized trials is needed before a recommendation for routine implementation can be made.

Keywords Catheter · Hemodialysis · Heparin

T. W. I. Clark (✉) · D. Jacobs · H. W. Charles · S. Kovacs · T. Aquino · J. Erinjeri
Section of Vascular and Interventional Radiology, Department of Radiology, New York University School of Medicine, 560 First Avenue, HE-221, New York, NY 10016, USA
e-mail: timothy.clark@nyumc.org

J. A. Benstein
Division of Nephrology, Department of Medicine, New York University School of Medicine, New York, NY 10016, USA

Introduction

Dialysis catheter function is determined by intrinsic catheter characteristics determining flow rates, recirculation, and wall apposition to endothelial venous surfaces. Long-term catheter function is additionally hampered by infection and thrombosis [1]. These are interdependent phenomena relating to the formation of thrombus and a biofilm which can become secondarily infected [2]. Strategies to reduce the risk of chronic dialysis catheter dysfunction include coating catheter surfaces with agents to reduce thrombus deposition and antimicrobial coatings to reduce infection. We report our initial experience with a chronic dialysis catheter with a covalently bound heparin coating.

Patients and Methods

Institutional Review Board approval was obtained for this retrospective study, which was performed in compliance with the Health Insurance Portability and Accountability Act. Over a 13-month period, we identified 80 patients who underwent placement of 88 chronic hemodialysis catheters from an electronic quality assurance database. During this period, our division made a consensus decision to transition to a heparin-coated device (Decathalon Gold; Spire Biomedical, USA) for patients receiving a tunneled dialysis catheter. Prior to this transition, our division utilized uncoated dialysis catheters for patients receiving chronic catheters (Ash Catheter; Medcomp, Harleysville, PA, USA). Both catheters are split-tip devices with similar lumen and tip configurations.

Patients who underwent catheter exchange for bacteremia or malfunction were not included, except as evidence of catheter failure among those patients who underwent prior de novo catheter placement during the study period. Patients who had tunneled catheter removal who underwent placement of a new tunneled dialysis catheter were considered as independent events. The study group consisted of 49 men (one catheter $N = 46$; two catheters $N = 3$; three catheters, $N = 1$) and 31 women (one catheter, $N = 29$; two catheters, $N = 2$).

All catheters were placed in the interventional radiology suite from an internal jugular approach, using ultrasound and fluoroscopic guidance, by five experienced, fellowship-trained operators. Seventy-four catheters were placed from a right jugular approach and 14 catheters were placed from a left jugular approach. Preprocedure antibiotics were not administered. All skin surfaces were prepared with a 2% chlorohexidine solution and allowed to dry prior to puncture. Catheters were placed by conventional radiologic technique, using peel-away sheaths with aerostatic valves. Venotomy incisions were closed in layers with a single absorbable suture and tissue adhesive.

Primary patency was defined in accordance with the Recommended Reporting Standards of the Society of Interventional Radiology [3]. Catheter patency failure occurred for infection, thrombosis, or both. Catheter patency was censored (removed from subsequent patency calculations) at the last dialysis session prior to recovery of renal failure, death, termination of hemodialysis due to functioning renal allograft, or catheter removal due to functioning vascular access. Catheter function was measured by actual blood flow, pump speed, arterial port pressure, and duration of dialysis session. Most dialysis treatments were performed using the Prisma dialysis machine (Gambro, Lakewood, CO, USA). The machine is equipped to provide a measurement of pump speed, which is set by the operator, and actual blood flow achieved, which is determined by the access characteristics. Initial postinsertion and last dialysis session function parameters were obtained from existing dialysis facility data.

Catheter patency was estimated with the Kaplan–Meier technique, and the two groups of patients (uncoated and heparin-coated catheters) were compared with the log-rank test. Intergroup comparisons of continuous variables of catheter function were compared with two-sample unpaired t-tests. Infection and thrombosis events were compared between the two groups with Fisher's exact test. A p-value of 0.05 was considered the threshold of statistical significance.

Results

Primary patency (±SE) of the 38 uncoated catheters was 97.0 ± 3.0% at 7 days, 86.0 ± 6.5% at 30 days, and 76.1 ± 8.9% at 90 days. Primary patency of the 50 heparin-coated catheters was 97.4 ± 2.3% at 7 days, 92.0 ± 6.2% at 30 days, and 81.6 ± 8.0% at 90 days (Fig. 1). No statistically significant difference in catheter patency was observed ($p = 0.87$, log rank test). The mean duration of observation was 74 days in the uncoated catheter group and 48 days in the heparin-coated catheter group ($p = 0.08$). Overall catheter days were 2795 days in the uncoated catheter group and 2404 days in the heparin-coated catheter group.

Clinically suspected infection requiring catheter removal occurred in four patients with uncoated catheters; one of these infections was confirmed by concordant blood and catheter tip cultures and three had positive blood cultures but no growth of catheter tips. The rate of infection was 0.14 per 100 catheter days. Among patients with heparin-coated catheters, clinically suspected infection requiring catheter removal occurred in two patients; one patient had concordant cultures. The rate of infection among patients with heparin-coated catheters was 0.08 per 100 catheter days. No significant difference in infection events was observed between the two catheter types ($p = 0.23$).

Catheter thrombosis requiring catheter replacement or thrombolysis occurred in one patient with an uncoated

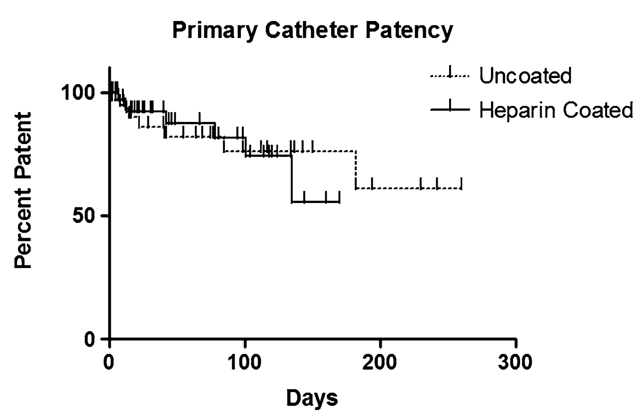

Fig. 1 Kaplan–Meier estimate showing primary unassisted patency between conventional (*dotted line*) and heparin-coated (*solid line*) split-tip catheters ($p = 0.87$, log rank test)

catheter and two patients with heparin-coated catheters ($p = 0.9$). The rates of thrombosis were 0.04 per 100 catheter days among patients with uncoated catheters and 0.08 per 100 catheter days among patients with heparin-coated catheters.

Catheter function during hemodialysis was compared between the two groups. Mean pump speed during the initial dialysis session after catheter placement was 344 ± 20.4 ml/min for patients receiving uncoated catheters and 327 ± 21.7 ml/min for patients receiving heparin-coated catheters ($p = 0.56$). Actual pump speed was 302 ± 17.0 ml/min for patients with uncoated catheters and 298 ± 16.1 for patients with heparin-coated catheters ($p = 0.86$). Arterial pressure was −130 ± 24.1 mmHg for patients receiving uncoated catheters and −157 ± 14.0 mmHg among patients with heparin-coated catheters ($p = 0.37$). The duration of the initial dialysis session was 160 ± 6 min among patients with uncoated catheters, compared to 161 ± 7 min among patients with heparin-coated catheters ($p = 0.92$).

Because the initial dialysis session following catheter placement may not be representative of day-to-day catheter function, we also compared catheter function during the last dialysis session for which data were available. The mean interval from initial dialysis session to last dialysis session for the entire study cohort was 71 days.

Mean pump speed during the last dialysis session after catheter placement was 406.2 ± 18.1 ml/min for patients with uncoated catheters and 365.5 ± 15.8 ml/min for patients with heparin-coated catheters ($p = 0.15$). Actual pump speed was 381 ± 17.5 ml/min for patients receiving uncoated catheters and 355 ± 17.7 for patients receiving heparin-coated catheters ($p = 0.35$). Arterial pressure was −187 ± 8.9 mmHg for patients receiving uncoated catheters and −167 ± 20.5 mmHg among patients with heparin-coated catheters ($p = 0.29$). The duration of the last dialysis session was 201 ± 6 min among patients with uncoated catheters, compared to 202 ± 8 min among patients with heparin-coated catheters ($p = 0.92$).

Discussion

Due to their higher rates of infection and dysfunction, chronic dialysis catheters are the least optimal form of hemodialysis access [4]. However, they remain widely utilized. Following the introduction of the K/DOQI guidelines by the National Kidney Foundation, the prevalence of fistulas among hemodialysis patients increased from 28% in 1998 to more than 45% in 2005. However, this increased prevalence of fistulas has resulted in the need for longer periods of catheter use during access maturation. As a result, catheter utilization has remained relatively constant over the last several years despite the goals of K/DOQI to minimize catheter utilization. In 2005, more than 81% of new hemodialysis patients in the United States initiated therapy with a catheter and 19% of prevalent patients had a catheter [5]. Similarly, the rates of catheter replacement, removal, and thrombolysis have not decreased. Clearly, there is a continued need to improve catheter performance and decrease catheter-related morbidity.

Current strategies to improve catheter longevity include surface coatings with antithrombotic and/or antimicrobial agents. Catheter malfunction and infection are interdependent events, related to formation of catheter thrombus which becomes secondarily infected [1]. Fibrin sheath formation also exacerbates this process [6].

Strategies to decrease the infectious and thrombotic complications of central venous and dialysis catheters have included surface coatings with silver [6], chlorhexidine and silver sulfadiazene [8], rifampin and minocycline [9], and heparin [10, 11].

Heparin is a polysaccharide anticoagulant which exerts its anticoagulant effect through binding to antithrombin, which then forms a complex with thrombin. This heparin-antithrombin-thrombin complex inactivates thrombin, inhibiting its ability to convert fibrinogen to fibrin [12, 13]. Recently, an FDA-approved hemodialysis catheter with a heparin-coating has become available (Decathalon Gold; Spire Biomedical, Bedford, MA, USA). The catheter has a split-tip configuration similar to that of the Ash catheter. Heparin is coated on both the luminal and the abluminal surface of the catheter and is covalently bound to the polyurethane surface of the catheter material through an end-point linkage mechanism which does not affect the antithrombin binding surface of the heparin molecule. The inactivated antithrombin-thrombin complex detaches from the heparin molecule, providing sustained bioactivity of the catheter-bound heparin without systemic heparinization effects.

Based on available preclinical and clinical reports describing the efficacy of heparin-coated catheters in potentially reducing catheter-related thrombosis and infection, we elected to transition to heparin-coated catheters from our conventional uncoated catheters. As a quality assurance initiative, we tracked available dialysis catheter performance data from dialysis sessions, monitored catheter infection rates from our division's quality assurance data, and studied data from the Infection Control service of our hospital.

We compared flow characteristics between the uncoated and the heparin-coated catheters, since a decline in catheter function can be secondary to the accumulation of catheter tip thrombus. There was no significant difference in flow rates, actual pump speeds, or pressures required for the "arterial" lumens of the catheters between patients receiving uncoated and those receiving heparin-coated catheters. The mean duration of the initial and last recorded dialysis sessions was nearly identical between the two groups. Within each of the two groups, we did not find a significant difference in individual catheter function parameters when comparing the initial and last dialysis sessions.

This study has several limitations. The sample size was small and data were captured retrospectively. Although we did not observe a difference in catheter patency among patients who received a heparin-coated catheter in this study, the retrospective nature of this analysis may have been inherently biased in favor of the conventional uncoated catheters, since patients receiving those catheters were observed for a longer period of time. Therefore, early catheter failures due to infection and/or thrombosis would be expected to have a greater decrease in Kaplan–Meier survival estimates among patients receiving heparin-coated catheters. We did not record Kt/V or other common parameters of dialysis access performance which may have shown differences between the two types of catheters. Kt/V is a valid metric of dialysis adequacy only among stable patients receiving chronic maintenance dialysis therapy. Because our patient population was heterogeneous, the dialysis orders varied depending on the clinical situation. The patients in our study included those with acute renal failure, those beginning maintenance hemodialysis, and others who were critically ill. Therefore, there was no standard target Kt/V and no opportunity to compare dialysis efficacy between the two groups.

The covalent binding of heparin to the catheter surface is a proprietary technology and it is unknown what the therapeutic range of heparin bioactivity is for dialysis catheters. We also do not know what decease in heparin activity, if any, occurs over time.

Although both of the split-tip catheters in this study were very similar, there were subtle differences in tip design, sidehole configuration, and catheter diameter (Spire, 15.5 Fr; Ash, 14.5 Fr). One or a combination of these might incur significant differences in overall catheter performance which could be masked in a small study such as this, i.e., a Type II statistical error.

In summary, a heparin-coated catheter did not show a significant increase in catheter patency compared to an uncoated catheter in this retrospective series of hemodialysis patients. The flow characteristics of the heparin-coated device were comparable to those of conventional uncoated catheters. This warrants comparison of heparin-coated and uncoated catheters in a prospective, randomized trial.

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