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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Impact of anticoagulation and antiplatelet therapy on dialysis catheter fibrin sheath formation

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PURPOSE
Fibrin sheaths are a significant cause of dialysis catheter dysfunction. This study aimed to determine the role of anticoagulation, antiplatelet medications, and other factors in delaying fibrin sheath formation.

METHODS
An institutional review board-approved retrospective review of all patients treated for tunneled dialysis catheter fibrin sheaths from January 2014 to January 2020 was undertaken. All catheters were symmetric tipped, 14.5 F in diameter, and placed via the internal jugular vein. Seventy patients with venographically confirmed fibrin sheaths that developed after *de novo* catheter placement were identified. Recurrent fibrin sheaths were excluded. The impact of anticoagulation and antiplatelet therapy, as well as statin therapy, catheter side (right or left), hematocrit, platelet count, prothrombin time (PT), and international normalized ratio (INR), on the time to fibrin sheath formation was determined.

RESULTS
Patients on anticoagulation had a longer median catheter implantation time of 109.2 days (interquartile range (IQR): 29.3-178.5 days) compared to 80.7 days (IQR: 28.0-168.6 days) among patients not on anticoagulation. Catheter dwell time among patients taking antiplatelet therapy was 86.0 days (IQR: 31.5-160.7 days) versus 74.4 days (IQR: 27.5-202.4 days) for patients not on antiplatelet medication. Patients taking statins versus those not taking statins had median catheter dwell times of 97.5 days (IQR: 27.5-138.5 days) and 62.4 days (IQR: 29.9-259.6 days), respectively. Time to fibrin sheath formation was not significantly associated with hematocrit ($P = .16$), platelet count (0.12), PT ($P = .51$), or INR ($P = .74$).

CONCLUSION
Anticoagulation has no significant benefit in delaying sheath formation in patients with tunneled dialysis catheters. Hematologic and coagulation parameters at the time of catheter placement were also not associated with catheter dwell time.

Tunneled dialysis catheters are frequently the initial access for patients requiring dialysis.[1,2] According to the United States Renal Data System, 80% of end-stage renal disease patients require a catheter when starting dialysis. At 90 days after the start of dialysis, 68.5% of patients are still reliant on catheters.[3]

Fibrin sheaths are a significant cause of catheter dysfunction. Increased catheter infection risk and persistent bacteremia are also associated with fibrin sheaths.[4] Studies have demonstrated fibrin sheaths can develop within 24 hours of catheter placement and may affect up to 47% of catheters.[5,6] When thrombolytic treatment fails, patients have to undergo additional procedures to exchange the catheter, disrupt the sheath, or strip the sheath, which contribute to patient morbidity.[7-10]

Prevention of fibrin sheath formation would be expected to have a beneficial impact on satisfactory dialysis maintenance. Placing patients on anticoagulation is a potential strategy that may decrease the risk for catheter dysfunction secondary to fibrin sheaths.[11] The aim of this study is to determine whether anticoagulation, antiplatelet medication, or other factors

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may influence the rate of fibrin sheath development in patients with tunneled dialysis catheters.

Methods

This is an institutional review board (IRB)-approved Health Care Portability and Accountability Act-compliant study (IRB# 20-003224). A waiver for informed consent was approved by the IRB for this retrospective review. All patients treated for tunneled dialysis catheter fibrin sheaths from January 2014 to January 2020 were reviewed. Seventy patients with venographically confirmed fibrin sheaths that developed after *de novo* catheter placement were identified. All catheters were symmetric tipped, 14.5 F in diameter (Palindrome), and placed via the internal jugular vein.

The impact of anticoagulation and antiplatelet therapy, as well as statin therapy, catheter side (right or left), hematocrit, platelet count, prothrombin time (PT), and international normalized ratio (INR), on catheter dwell time was determined. Catheter dwell time, or time to fibrin sheath formation, was defined as the time between catheter placement and exchange. Only patients on anticoagulation, antiplatelet therapy, or statin therapy for the entire duration of time between catheter placement and fibrin sheath formation were analyzed. Laboratory parameters from the time of catheter placement were reviewed.

Statistical analyses were performed with JMP 13.0 (SAS). Parametric data were presented with mean and standard deviation. Non-parametric data were presented as median and interquartile (IQR) range. Linear regression analysis was used to determine the association between laboratory values and time to catheter malfunction. Mann–Whitney U test was used to compare dwell time among catheters placed in the right versus left internal jugular vein. Kruskal–Wallis test was used to compare catheter dwell time among patients taking anticoagulation, antiplatelets, and statins. A *P*-value less than or equal to .05 was considered statistically significant.

Main points

- Tunneled dialysis catheter dwell time was not significantly longer with anticoagulation, antiplatelet or statin therapy.
- There is no association between baseline coagulation profile and clinically significant fibrin sheath formation.

Results

Patient characteristics and baseline laboratory parameters are summarized in Table 1. Mean patient age was 61.2 ± 15.0 years. There were 39 males and 31 females. All patients had their catheter exchanged. Patients with recurrent fibrin sheaths were excluded from analysis.

The median catheter dwell time for the cohort was 85.1 days (IQR: 28.0-168.6 days). There were no procedural complications associated with catheter placement or exchange. There were 61 catheters placed in the right internal jugular vein and 9 placed on the left. Right-sided catheters had a longer mean dwell time of 88.4 days (IQR: 28.7-212.9 days) versus 51.6 days (IQR: 9.5-133.3 days) for left-sided catheters (*P* = .19) (Table 2).

Patients on anticoagulation had a longer median catheter implantation time of 109.2 days (IQR: 29.3-178.5 days) compared to 80.7 days (IQR: 28.0-168.6 days) among patients not on anticoagulation. Nine patients were on warfarin and 3 were on heparin. All patients taking warfarin were on standard intensity dosing with goal INRs of 2-3. The 3 patients on heparin were inpatients on prophylactic dosing. No patient was on direct oral anticoagulation.

A total of 38 patients were on antiplatelet therapy at the time of catheter placement; all 38 patients were taking aspirin, 5 of whom were on dual-antiplatelet therapy with the addition of clopidogrel. Patients on antiplatelet therapy had a median catheter dwell time of 86.0 days (IQR: 31.5-160.7 days), compared to 74.4 days (IQR: 27.5-202.4 days) for patients not on antiplatelet medication.

Median catheter dwell time among patients taking statins was 97.5 days (IQR: 27.5-138.5 days) versus 62.4 days (IQR: 29.9-259.6 days). There was no significant difference in dwell time among patients on anticoagulation, antiplatelet medication, or statins (*P* = .41). No statistically significant relationship was found between baseline laboratory parameters and catheter dwell time including hematocrit (*P* = .16), platelet count (*P* = .12), PT (*P* = .51), or INR (*P* = .74).

Discussion

The findings in this study suggest anticoagulation has a limited role in preventing fibrin sheath formation in patients with tunneled dialysis catheters. Other medications, including antiplatelet drugs, as well as hematologic laboratory parameters at the time of catheter placement, did not correlate with catheter dwell time prior to catheter exchange due to fibrin sheath. Right-sided catheters had longer time to fibrin sheath formation compared to left-sided catheters, which supports prior data favoring right internal jugular vein access.[12]

Table 1. Baseline patient characteristics

Characteristic	n = 70
Female, n (%)	31 (44.3)
Age, mean, years (SD)	60.5 (16.1)
Medication at time of catheter placement, n (%)	
Anticoagulation therapy	12 (17.1)
Antiplatelet therapy	38 (54.3)
Statin therapy	45 (64.3)
Catheter dwell time (days), median (IQR)	85.1 (28.0-168.6)
Hematocrit (%), mean (SD)	29.5 (4.8)
Prothrombin time (s), mean (SD)	12.8 ± 3.3
International normalized ratio, mean (SD)	1.1 (0.29)
Platelet count (10^9/L), mean (SD)	249.6 ± 100.0
Presence of additional central venous catheter or pacemaker, n (%)	13 (18.6)
Catheter laterality, n (%)	
Right	61 (87.1)
Left	9 (12.9)

SD, standard deviation; IQR, interquartile range.

Table 2. Impact of medications and catheter parameters on catheter dwell time	
	Dwell time median (interquartile range)
Anticoagulation therapy	
Yes	109.2 days (IQR: 29.3-178.5 days)
No	80.7 days (IQR: 28.0-168.6 days)
Antiplatelet therapy	
Yes	86.0 days (IQR: 31.5-160.7 days)
No	74.4 days (IQR: 27.5-202.4 days)
Statin therapy	
Yes	97.5 days (IQR: 27.5-138.5 days)
No	62.4 days (IQR: 29.9-259.6 days)
Catheter laterality	
Right	88.4 days (IQR: 28.7-212.9 days)
Left	51.6 days (IQR: 9.5-133.3 days)

IQR, iInterquartile range.

To date, there are limited data on the utility of anticoagulation for the prevention of fibrin sheath formation. In a prospective trial on cancer patients with totally implanted central venous catheters, 25 patients with fibrin sheaths detected by ultrasound at 6 months after catheter placement were placed on low-molecular-weight heparin.[11] Thirteen of these 25 patients had no detectable fibrin sheath by ultrasound at 6-month follow-up, while persistent sheaths were detected in 11 patients, and 1 patient developed subocclusive deep vein thrombosis. A prospective randomized control study by Mokrzycki et al.[13] investigated the potential benefit of minidose (1 mg) warfarin against placebo for late malfunction of tunneled dialysis catheters. The authors reported fewer fibrin sheath-stripping procedures in the warfarin group than in the placebo group, though the difference was not statistically significant ($P = .14$). There are no prior studies that have investigated therapeutic dose anticoagulation for the specific prevention of fibrin sheaths. Furthermore, anticoagulation and antiplatelet medications have not been shown to have consistent benefit for the prevention of catheter thrombosis.[14]

The limited efficacy of anticoagulants for deterring fibrin sheath formation may be attributed to the complex makeup of the sheaths. Fibrin sheaths are comprised of a heterogeneous composition of cells, thrombus, and proteinaceous material. Soujanen et al.[15] found that fibrin sheaths obtained from stripping dialysis catheters had several different histologic patterns with varying amounts of eosinophilic material, inflammatory cells, organized fibrous tissue, endothelial proliferation, and thrombus. Xiang et al.[16] reported the sleeve around central venous catheters in a rat model was composed of cellular-collagen tissue covered by endothelium formed by smooth muscle cells migrating from the injured vein wall into early pericatheter thrombus. The findings in the latter study suggest that if pericatheter thrombus can be mitigated, then there could be a lower likelihood of sleeve formation around catheters. Nevertheless, the terms "fibrin sleeve" or "fibrin sheath" inadequately recognize the complex composition of the material forming the sheath.

Catheters placed in the right internal jugular vein had longer implantation times compared to those placed on the left. This finding was not statistically significant, though this analysis was underpowered with only 9 catheters placed on the left. Right-sided dialysis catheter placements are associated with fewer early malfunction issues, including thrombosis, central venous stenosis, and infections.[12,17,18] However, the rate of fibrin development was previously shown to be equivalent among different access sites.[12] The higher rate of fibrin sheath development in left-sided catheters observed in the current study may be a result of the fact that fibrin sheaths are a result of smooth muscle cell migration from the injured vein wall.[16] Catheters placed on the left are associated with higher rates of vascular erosion, which is likely due to the more acute angle of the catheters as they pass through the left brachiocephalic vein into the superior vena cava.[19,20]

This study has several limitations as a result of the retrospective design. Clinical characteristics such as comorbidity and medications were not standardized. Given the variable follow-up inherent in retrospective designs, this study focused on patients with confirmed fibrin sheaths rather than all patients who had a catheter placed. Furthermore, only patients with catheters placed with new venous access were included. Patients with prior catheter exchanges from the same access site were excluded due to the potential for residual sheath material in the vein that could lead to premature dysfunction from sheath recurrence.[21]

This study found no statistical benefit of anticoagulation or antiplatelet medication in delaying clinically significant fibrin sheath formation around tunneled dialysis catheters. Hematologic and coagulation parameters at the time of catheter placement were also not associated with catheter dwell time suggesting limited benefit for optimization strategies from a fibrin sheath prevention standpoint.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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