

Metastatic infectious complications in tunneled dialysis catheter-associated infections: a single-center experience

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ABSTRACT

Aim: Although the guidelines recommend arteriovenous fistula (AVF) primarily as vascular access in hemodialysis patients, tunneled catheter (TC) use is gradually increasing. TCs are associated with an increased risk of infection. TC infections can cause many metastatic infectious complications such as infective endocarditis (IE), spondylodiscitis (SpD), and paravertebral abscess. This study aimed to determine the frequency, risk factors, and prognosis of metastatic infectious complications in patients admitted to our hospital with TC infections.

Material and Method: Patients with TCs hospitalized to the Nephrology unit of Ondokuz Mayıs University Hospital between January 1, 2015, and January 1, 2020, with catheter infection, were included in the study. Demographic, clinical, and microbiological information was obtained from the patients' medical records retrospectively. Metastatic infectious complications were defined as IE, SpD, paravertebral or epidural abscess, and septic embolisms in any focus. Binary logistic regression analyzes were used to identify risk factors for metastatic infectious complications.

Results: One hundred and forty-eight catheter episodes were included in the study. Eighty-seven (58.8%) of the patients were women. Metastatic infectious complications developed in 22 (14.9%) of the patients. Of these, ten patients had IE, ten patients had SpD, and two patients had both IE and SpD. Coagulase-negative staphylococci was obtained as pathogenic microorganism in most cases (9/22, 49%). Patients with infectious complications had higher length of hospital stay [46.5 (10-171) vs 18 (6-92); $p < 0.001$], and higher rates of sepsis (50% vs 16.7%; $p < 0.001$), need for intensive care unit (36.4% vs 12.7%; $p = 0.005$), and death (36.4% vs 11.9%; $p = 0.003$). In multivariate binary logistic regression analysis, diabetes mellitus (DM) [OR: 7,813; 95% CI (2.05–29,783); $p = 0.003$] and catheter duration [OR: 1.002; 95% CI (1-1,003); $p = 0.009$] were identified as risk factors associated with metastatic infectious complications.

Conclusion: Metastatic infectious complications are associated with significant morbidity and mortality in hemodialysis patients. Long catheter duration and the presence of DM are risk factors for infectious complications. As recommended in international guidelines, minimizing the use of catheters and preventing the development of catheter infection by paying attention to basic hygiene rules, especially in diabetic patients, will help prevent these serious complications.

Keywords: Hemodialysis, infective endocarditis, metastatic complications, spondylodiscitis, tunneled catheter

INTRODUCTION

Among the renal replacement therapy options for end-stage renal disease patients, hemodialysis is the most preferred modality both in our country and all over the world (1). Arteriovenous fistula (AVF), synthetic AV grafts, or central venous catheters can be used as vascular access in hemodialysis patients. Although the guidelines recommend AVF primarily as vascular access in hemodialysis patients, central venous tunneled catheter (TC) use gradually increases (2).

Unfortunately, TCs are associated with significant morbidity and mortality in hemodialysis patients. In

a meta-analysis, compared with persons with fistulas, those individuals using catheters had higher risks for all-cause mortality (risk ratio=1.53), fatal infections (2.12), and cardiovascular events (1.38) (3). Hospitalization rates for patients with TCs are more than twofold higher than those in patients with AVF (4). Infections are the most common cause of death in dialysis patients after cardiovascular causes (5). Local infections such as tunnel and exit site infections may occur in TCs, and bacteremia can also be seen. A Canadian study showed that during the first six months of dialysis, there is a high rate of bloodstream infection (BSI). In comparison to the AV

fistula, survival analysis revealed a relative risk of BSI of 8.49 (95% CI, 3.03–23.78) for TCs (6). Bacteremia can cause many metastatic infectious complications such as infective endocarditis (IE), spondylodiscitis (SpD), paravertebral abscess. These metastatic complications have also been shown to increase mortality and morbidity (7).

Our knowledge of metastatic complications in tunneled catheter infections is not sufficient. This study aimed to determine the frequency, risk factors, and prognosis of metastatic infectious complications in patients admitted to our hospital with tunneled dialysis catheter infections.

MATERIAL AND METHOD

The study was carried out with the permission of Ondokuz Mayıs University Clinical Researchs Ethics Committee (Date: 26.08.2021, Decision No: 2021/403). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study was planned retrospectively. Patients with TCs hospitalized to the Nephrology unit of Ondokuz Mayıs University Hospital between January 1, 2015, and January 1, 2020, with catheter infection were included in the study. Patients with a temporary catheter and individuals under the age of 18 were excluded from the study.

Catheter-associated infection was defined as positive blood cultures or catheter cultures and no source of infection other than the catheter.

Demographic, clinical, and microbiological information was obtained from the patients' medical records. Data included age, gender, etiology of chronic kidney disease, duration of dialysis, clinical symptoms, and inflammation parameters [C-reactive protein (CRP), procalcitonin, erythrocyte sedimentation rate (ESR), white blood cell count] and biochemical parameters. Microbiological data included the type of microorganism and antimicrobial treatments. In addition, the treatments applied for the infected catheter (withdraw or exchange of catheter, transition to AVF, AV graft, or peritoneal dialysis) were also determined.

Metastatic infectious complications were defined as IE, SpD, paravertebral or epidural abscess, and septic embolisms in any focus. When vegetation was detected by echocardiography, the presence of IE was clinically confirmed and used in the analyses. The diagnoses of SpD, paravertebral and epidural abscess, and septic embolism were accepted as definitive diagnose when supported by clinical findings and characteristic changes detected in radiological evaluation.

When there was more than one episode of catheter infection in the same patient, each episode was considered as a separate patient in the analyses. However, since the primary endpoint was the presence of metastatic complication if a patient with metastatic infection continued with a catheter and re-infection developed, these episodes were not included in the analysis.

Statistical Analysis

All analyzes were conducted using the Statistical Package for the Social Sciences for Windows, version 25 (SPSS Inc., Chicago, IL, USA). Normality distribution was evaluated with the Shapiro-Wilk and Kolmogorov-Smirnov tests. The continuous variables were expressed as mean±standard deviation in the variables showing normal distribution and median (minimum-maximum) in those that did not show normal distribution. Categorical variables are expressed as percentages. Independent Samples T-test was used to compare non-dependent non-parametric variables in those with normal distribution, and Mann Whitney U test was used in those without normal distribution. The comparison of parametric variables was made with the Pearson Chi-Square test. Binary logistic regression analyzes were used to identify risk factors for metastatic infectious complications. P values <0,05 were considered statistically significant.

RESULTS

One hundred and forty-eight catheter episodes were included in the study. The median and mean ages of the patients were 62.5 (20-80) and 58.26±15.61 years, respectively. Eighty-seven (58.8%) of the patients were women. Diabetic nephropathy was the most common etiological cause of chronic kidney disease in 57 (38.5%) of the patients, while urological causes were the second most frequent. While 105 (70.9%) patients had hypertension, 21 (14.2%) patients had malignancy. The majority of patients (67.6%) had a right jugular catheter. The left jugular catheter was present in 41 (27.7%) patients, whereas the femoral catheter was present in only 7 (4.8%) patients. Fever was the most common complaint (85.1%) at admission. Eight (5.4%) of the patients had low back pain or neurological symptoms. Among the microbiological agents, the most common causative agent was staphylococci (53.4%), gram-negative bacilli were the second most common (25%). The culture was negative in 12.8% of catheter infection episodes.

Metastatic infectious complications developed in 22 (14.9%) of the patients. Of these, ten patients had IE, ten patients had SpD, and two patients had both IE and SpD. Paravertebral abscess accompanied in 7 (63.6%) of the patients with SpD. Mitral valve vegetation was detected in most patients with IE (7/11; 63.6%). While the

causative agent was coagulase-negative staphylococcus (9/22, 49%) in most of the patients with infectious complications, *S. aureus* was the causative agent in 6 (27.3%) patients. While 73 (49.3%) of the catheter infections were treated without catheter withdrawal or exchange, the catheter was exchanged in 59 (39.9%) episodes. Transition to AV fistula or peritoneal dialysis was performed in 16 (10.8%) episodes. Sepsis was observed in 32 (21.6%) episodes, and the need for intensive care developed in 24 (16.2%). In addition, the mortality rate was 15.5% (23/148).

Compared to those without metastatic infection, patients with infectious complications had higher ESR and CRP values, a higher incidence of diabetes mellitus (DM),

longer catheter duration and length of hospital stay, and higher rates of sepsis, need for intensive care unit, and death. However, albumin levels were significantly low (Table 1). In multivariate binary logistic regression analysis, DM [OR: 7.813; 95% CI (2.05 – 29.783); p=0.003] and catheter duration [OR: 1.002; 95% CI (1-1.003); p=0.009] were identified as risk factors associated with metastatic infectious complications (Table 2). While 9 (40.9%) patients with metastatic infection were treated without catheter withdrawal or exchange, catheter exchange was performed in 6 patients (27.3%) with IE, 4 patients (18.2%) with SpD and one patient (4.5%) with IE and SpD. One patient was transitioned to AVF, and one patient to peritoneal dialysis.

Table 1. Comparison of demographic, clinical and laboratory characteristics of patients according to metastatic infectious complication status

	Metastatic infectious complication		t	p
	No (n=126)	Yes (n=22)		
Age, year	61 (20-80)	63.5 (28-80)	1182.5	0.272 ^b
ESR, mm/h	79.88±32.39	96.33±31.63	-2.148	0.034 ^a
CRP, mg/L	68 (0.3-482)	153.5 (17-306)	872	0.006 ^b
Procalcitonin, ng/mL	8.58 (0.2-234)	6.65 (0.31-100)	1227	0.944 ^b
ALT, U/L	9 (2-128)	9 (2-344)	1378.5	0.968 ^b
AST, U/L	15 (4-171)	13 (5-328)	1354.5	0.865 ^b
Albumin, gr/dL	3.34±0.73	2.91±0.57	2.634	0.009 ^a
WBC, µL	9660 (197.1-31700)	10550 (1050-39460)	1169	0.242 ^b
Hemoglobin, gr/dL	9.82±1.79	9.41±1.55	1.020	0.309 ^a
Platelet, ×10 ³ / µL	182 (16.1-602)	167.5 (37-540)	1185	0.279 ^b
Length of hospital stay, day	18 (6-92)	46.5 (10-171)	572	<0.001 ^b
Catheter duration, day	202 (5-1880)	387.5 (18-2706)	975.5	0.027 ^b
Dialysis vintage, month	15 (1-320)	13.5 (1-146)	1385	0.996 ^b
Gender (Female), n (%)	76 (60.3)	11 (50)	0.823	0.364
Diabetes mellitus, n (%)	43 (34.1)	14 (63.6)	6.887	0.009
Hypertension, n (%)	86 (68.3)	19 (86.4)	2.98	0.084
Cardiovascular disease, n (%)	50 (39.7)	11 (50)	0.823	0.364
Malignancy, n (%)	17 (13.5)	4 (18.2)	0.338	0.561
Microbiological agent, n (%)			5.503	0.358
<i>S. aureus</i>	24 (19)	6 (27.3)		
CNS	41 (32.5)	9 (40.9)		
Gram-negative bacilli	33 (26.2)	4 (18.2)		
Sepsis, n (%)	21 (16.7)	11 (50)	12.28	<0.001
ICU need, n (%)	16 (12.7)	8 (36.4)	7.72	0.005
Death, n (%)	15 (11.9)	8 (36.4)	8.537	0.003

a: Independent Samples T test, b: Man Whitney U test, ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; WBC: White blood count; CNS: Coagulase-negative staphylococcus; ICU: Intensive care unit.

Table 2. Univariate and multivariate binary logistic regression analysis of risk factors for metastatic infectious complication

Variables	Univariate		Multivariate	
	OR (%95 CI)	p	OR (%95 CI)	p
Age	1.023 (0.99-1.057)	0.180	1.001 (0.954-1.051)	0.955
Gender (Male)	1.52 (0.613-3.771)	0.366	2.378 (0.743-7.614)	0.145
Diabetes mellitus (Yes)	3.378 (1.315-8.678)	0.011	7.813 (2.05-29.783)	0.003
Hypertension (Yes)	2.946 (0.824-10.533)	0.097	1.783 (0.37-8.586)	0.471
Cardiovascular disease (Yes)	1.520 (0.613-3.771)	0.366	1.132 (0.343-3.734)	0.838
Malignancy (Yes)	1.425 (0.43-4.721)	0.562	3.185 (0.716-14.164)	0.128
Catheter localization				
Right jugular	Reference		Reference	
Left jugular/Femoral	0.967 (0.366-2.556)	0.947	0.852 (0.237-3.07)	0.807
Hemoglobin	0.869 (0.663-1.138)	0.307	0.873 (0.643-1.185)	0.384
<i>S. aureus</i> infection (Yes)	1.875 (0.657-5.351)	0.240	3.125 (0.917-10.643)	0.068
Catheter duration	1.001 (1.000-1.002)	0.014	1.002 (1-1.003)	0.009

OR: Odds ratio; CI: Confidence interval

DISCUSSION

Our study found the incidence of metastatic infectious complications in tunneled dialysis catheter infections to be 14.9%. We found long catheter time and the presence of DM to be risk factors for the development of metastatic infectious complications. We also showed that the length of hospital stay, sepsis, and mortality rates are higher in cases with complications.

International guidelines recommend AVF for long-term vascular access in hemodialysis patients. However, tunneled catheters are frequently used for reasons such as patient selection, initiation of dialysis under emergency conditions, and inability to open AVF to the patient. In a recent observational cohort study, the risk of developing catheter-related complications at one year was 30%, and the risk of bacteremia was 9%. In the second year, bacteremia increased to 11%. In the same study, bacteremia was found to be the most common cause of hospitalizations (73%) (8). A large meta-analysis showed that catheter use causes a 2-4 fold increase in the risk of fatal and non-fatal infections, with increased mortality (53%) and hospitalization (68%) compared to AVF (3).

Chronic kidney disease, hemodialysis, and especially a catheter as vascular access pose a risk for infectious complications such as IE and SpD (9-12). However, data on the frequency of infectious complications after bacteremia in hemodialysis patients are scarce. Mokrzycki et al. (13) found an infectious complication rate of 7% in their study. In our study, this rate was found to be 14.9%. However, since there is no other data in the literature, the necessity of new studies on its actual frequency is obvious.

On the other hand, although it is known that catheter use in hemodialysis patients increases the risk of infection, our information on the factors affecting complications is not sufficient. Mokrzycki et al. (13) reported that the only variable in a multivariate analysis that was significantly associated with the development of an infectious complication was infection with *S. aureus*. Similarly, the most common causative organism in developing IE or SpD in dialysis patients is *S. aureus* (10,14,15). Parallel to these, complications are common in *S. aureus* bacteremia developing in hemodialysis patients, and it has been shown that 17% of the patients develop IE, and 5.7% of them develop osteomyelitis (16). In our study, *S. aureus* was found to be the causative agent in 6 of the patients who developed complications, but it was not detected as a risk factor for the development of complications in the multivariate analysis. Most of our patients were found to be coagulase-negative staphylococcal factors. In other studies in the literature, similar to ours, it is noteworthy that staphylococci are the most common factor in cases that develop both IE and SpD.

In our study, the presence of DM and the catheter duration were determined as risk factors for complications. Diabetes creates susceptibility to infections by affecting both cellular and humoral immunity (17). In a study conducted on a large group of hemodialysis patients with catheters, DM increased the risk of developing catheter infection 2.37 times (18). On the contrary, some studies show that DM does not cause an increase in the risk of infection (8,19). However, there is no previous study showing that DM poses a risk for metastatic infectious complications. In our study, DM was found to be a severe risk factor for the development of metastatic infectious complications (OR:7.8). It is known that there is a relationship between the duration of the catheter and the development of catheter-related infections. Lemaire et al. (18) found that a catheter duration of >90 days increased the risk of infection. Shingarev et al. (20) determined that there was a serious increase in the rate of infected patients with the increase in the duration of the catheter (35% at the 3rd month vs. 79% at the 12th month).

Studies show that the catheter location (left internal jugular vein or femoral veins) is associated with an increased risk of infection (21,22). However, on the contrary, it has been shown in many studies that catheter location is not one of the risk factors associated with the development of infection (23,24). It has even been found that infection rates in femoral tunneled catheters are similar to those in jugular catheters (19,25). It is not known whether the catheter location poses a risk for metastatic infectious complications. However, in our study, we did not find a relationship between the catheter location and the development of complications.

Our study found both the length of hospital stay and mortality rate significantly higher in patients with complications than those without complications. In addition, the development of sepsis and the need for intensive care were higher in these patients. The median length of stay was 46.5 days, and the mortality was 36.4% in patients with complications. Considering that patients should receive intravenous treatment for an average of 6 weeks, the length of hospital stay was prolonged. Similar or even longer lengths of hospital stay are observed in other studies in the literature (14,15). The length of stay in hospital also differs significantly higher when compared with the non-dialysis population (26). Severe infections in patients with complications have led to sepsis, in parallel, to an increase in the need for intensive care. In addition, disease severity is also associated with increased mortality rates. Although the mortality rate was relatively high in our study, similarly, the mortality rate in other studies in the literature ranged between 20% and 46% (14,15,26-28).

Our study has some limitations. First of all, the most important limitations are that it is retrospective, and it was performed only in patients hospitalized in a single-center or even only in the nephrology unit. In addition, the fact that our patients were only patients with TCs may not reflect the incidence of infectious metastatic complications in all hemodialysis patients. However, since TCs are preferred in the long-term treatment of patients, we think that it is more accurate to determine the frequency in patients with TCs.

CONCLUSION

Our study showed that metastatic infectious complications (infective endocarditis and spondylodiscitis) are common in TCs related infections. The length of hospital stay and mortality rates increase in patients with metastatic infectious complications. Long catheter duration and presence of DM were identified as risk factors for metastatic infectious complications. As recommended in international guidelines, minimizing the use of catheters and preventing catheter infection by paying attention to basic hygiene rules, especially in diabetic patients, will help prevent these serious complications

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ondokuz Mayıs University Clinical Research Ethics Committee (Date: 26.08.2021, Decision No: 2021/403).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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