



# Risk factors for recurrent percutaneous nephrostomy catheter-related infections

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Received: 18 June 2018 / Accepted: 30 October 2018 / Published online: 7 November 2018  
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## Abstract

**Purpose** Percutaneous nephrostomy (PCN) catheters are mainly indicated for urinary tract obstructions. Unfortunately, the rate for infection and recurrence remains elevated. Our objective was to identify the risk factors leading to recurrent PCN-related infections (PCNI) in cancer patients.

**Methods** We retrospectively reviewed 571 patients who underwent initial PCN catheter placement at our institution. Of these, we identified patients with a definite PCNI and catheter exchange, with a minimum 30-day follow-up. We defined PCNI as presence of a urine culture positive for bacteria ( $\geq 10^4$  CFU/mL) plus symptoms of urinary tract infection. A PCNI was considered recurrent if the same organism was isolated. Antibiotics were considered concordant if they were active against all identified organisms.

**Results** A total of 81 patients (14%) developed an initial PCNI. Of 47 patients with 30-day follow-up, 10 patients (21%) were identified as having a recurrent PCNI. In terms of demographic characteristics, clinical manifestations, and microbiological data, there was no statistically significant difference between the recurrent and non-recurrent groups. However, in multivariate logistic regression analysis, two factors were independently associated with a decrease in recurrent PCNI: concordant antibiotic use (OR 0.04;  $p=0.008$ ) and PCN catheter exchange within 4 days of infection (OR 0.1;  $p=0.048$ ).

**Conclusions** To decrease the high rate of recurrent infections, associated costs, and potential delay in further chemotherapy, we recommend that once antimicrobial susceptibility test results are available and the patient is known to be receiving concordant antimicrobials, clinicians proceed with immediate PCN catheter exchange, ideally within the first 4 days of the infection.

**Keywords** Device · Nephrostomy · Percutaneous · Urinary catheters · Urinary tract infection

## Introduction

Goodwin et al. [1] were the first to describe a trocar needle technique for placement of percutaneous nephrostomy (PCN) catheters in patients with hydronephrosis caused by a urinary tract obstruction. This technique has been improved over time, and the indications for PCN catheters have since

expanded to include, among others, diagnostic testing, access for therapeutic interventions, and urinary diversions by providing temporarily relief for ureteral damage and fistulas [2]. However, relief of an extrinsic or intrinsic urinary obstruction has remained the main indication for placement (85 to 90% of cases) [3]. In patients with cancer, PCN catheters can be used until the obstruction is eventually relieved by surgery, chemotherapy, or radiation treatment, preventing further kidney damage and allowing for recovery of renal function. PCN catheters can also be used as a permanent palliative care option for patients with advanced and/or untreatable malignancy.

Similar to other foreign medical devices, PCN catheters are prone to multiple complications including infections. As soon as the PCN catheter is placed, the device readily becomes colonized by host microbial flora [4], leading to

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the development of a complex three-dimensional biofilm [5]. This structure contains a high concentration of microorganisms that are under relative protection from both the immune system and antimicrobials. Furthermore, the biofilm and intraluminal encrustations may lead to malfunction and clinical infection, which can range from pyelonephritis, perinephric and renal abscess, and bacteremia to septic shock [6]. Additionally, the biofilm acts as a reservoir of organisms that can perpetuate an episode of infection or facilitate its relapse. Treatments of these infections have been estimated to cost approximately \$40,000 per episode [7]. Therefore, as a standard preventive approach, many institutions perform regular PCN catheter exchanges every 2–3 months at an average cost of \$3000 [2, 7, 8].

Infectious Diseases Society of America guidelines for prevention, diagnosis, and treatment of catheter-associated urinary tract infection (CA-UTI) have not addressed percutaneous nephrostomy catheter-related infection (PCNI) [9]. Furthermore, due to lack of robust clinical evidence, the optimal diagnostic and therapeutic approaches for PCNI has not been well established. It is accepted that replacing a chronic indwelling bladder catheter, in cases of symptomatic CA-UTI, results in a more rapid defervescence and decreased short-term relapse [10]. Similarly, a PCN catheter exchange is often performed in patients with an active UTI. However, once a new PCN catheter is replaced, it may be exposed to actively proliferating organisms, resulting in new biofilm formation, leading to a recurrent device-related infection. These recurrences affect patients' quality of life, increase cost, delay further chemotherapy, and through the repeated use of antimicrobials, can be associated with increasing antimicrobial resistance and *Clostridium difficile* infection [11]. Therefore, to reduce the rate of recurrent PCNI, our objectives were to analyse the rate of these infections, as well as identify risk factors leading to recurrent infections after an initial PCNI.

## Methods

### Hospital setting and study population

We retrospectively reviewed the electronic medical records of 571 patients who had undergone an initial PCN catheter placement at our institution between July 2014 and February 2017. Those patients who had developed an initial episode of PCNI with catheter exchange as part of the treatment were subsequently followed for 100 days. We excluded all patients who were lost to follow-up, had a PCN removed or exchanged due to non-infectious causes, or were discharged to hospice or died within 30 days from PCN placement. We performed an incidence analysis for infection among all patients who had an initial PCN placement. Thereafter, those

patients who had developed a PCNI underwent a risk factor analysis for recurrent infection. This study was conducted at The University of Texas MD Anderson Cancer Center, Houston, TX, after approval by the Institutional Review Board.

### Definitions

There is no established definition of PCNI in the literature. Therefore, to avoid including cases of sterile pyuria or asymptomatic microbial colonization and to increase the specificity of our study population, we defined PCNI according to the following strict diagnostic criteria: (a) clinical symptoms of UTI including fever, chills, costovertebral angle tenderness, hypotension, and/or entry site cellulitis, not explained by an alternative diagnosis; plus (b) urine culture obtained from a PCN with  $\geq 10^4$  colony-forming units/mL bacterial growth. Recurrence was defined as a second PCNI with the isolation of the same organism as seen in the initial episode, while a new PCNI was defined as a second infection with the isolation of a different organism than that seen in the initial episode. Severity of illness was defined according to the presence of sepsis with organ failure or septic shock at diagnosis of initial PCNI [12]. Antibiotics were defined as concordant if they were active against all isolated organisms obtained from the PCN urinary culture, based on antimicrobial susceptibilities, and discordant if they were not active against all isolated organisms.

### Data collection

We collected information on patient demographics, underlying malignancy, comorbid conditions, and clinical manifestations, at the time of the initial PCNI. Additionally, we documented laboratory and microbiologic data, as well as time to infection after initial placement, total duration of antibiotic therapy, timing of concordant antibiotics, and total days from diagnosis of infection to PCN catheter exchange.

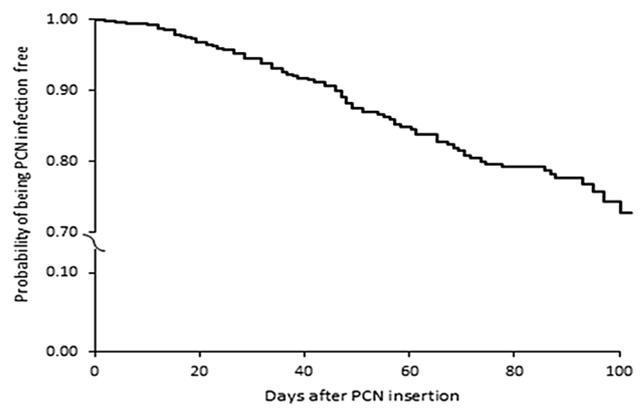
### Statistical analysis

Descriptive statistics were used to summarize patients' data. Categorical variables were presented as frequency and percentage and compared using the Chi square or Fisher exact test, as appropriate. Continuous variables were presented as median and IQR and compared using the Wilcoxon rank-sum test. The Kaplan–Meier method was used to estimate the probability of being PCNI-free in patients with initial PCN catheter placement. Logistic regression analysis was used to identify the factors that were independently associated with recurrence of PCNI. Only those variables with  $p$  value  $< 0.20$  in the univariate analyses were included in the initial multivariate logistic regression model, and the initial full model was reduced to the final model through backward

variable elimination procedure so that all the factors remaining in the model were statistically significant ( $p < 0.05$ ). All the tests were two-sided with a significance level of 0.05. The analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC).

### Results

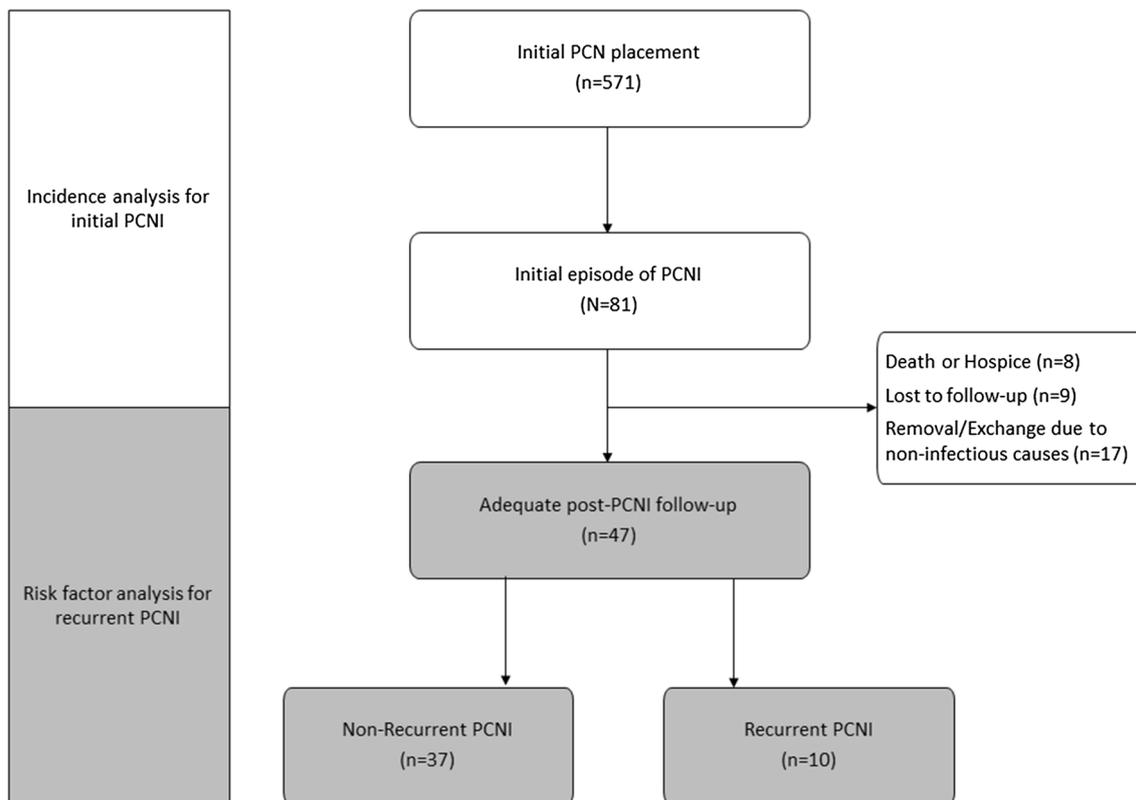
All 571 patients who underwent initial PCN catheter placement had received peri-procedure systemic antimicrobial prophylaxis with either ceftriaxone or ciprofloxacin. Of these patients, 81 (14%) fulfilled our strict PCNI definition, while the remaining had the PCN removed or exchanged due to non-infectious causes, were discharged to hospice, or died within 30 days from PCN placement, with no loss of follow-up (Fig. 1). The probability of remaining free of PCNI was 73% at 100 days (Fig. 2). This group had 30,577 follow-up patient-days, with an incidence density for PCNI of 2.65 per 1000 patient-days. Only 47 of these 81 PCNI cases had an adequate post-PCN exchange follow-up and were the subject of our risk factors analysis for recurrent infection. A total of 10 patients (21%) experienced a recurrent PCNI with a median time of 43 days (IQR 17–54), while 5 patients (11%)



**Fig. 2** Kaplan–Meier curve showing the probability of being infection-free from the time of initial PCN catheter placement. *PCN* percutaneous nephrostomy

had a new PCNI, and 32 patients (68%) remained infection-free (Fig. 1).

The demographic details of these 47 patients with an initial PCNI revealed a median age of 59 years (range 20–87), with most of the infections occurring in white patients (62%) with a similar gender distribution (Table 1). The most common underlying malignancies were urothelial bladder cancer



**Fig. 1** Flowchart of subgroups of patients with PCNI and recurrences. *PCNI* percutaneous nephrostomy-related infections

**Table 1** Characteristics of patients with PCN-related infections

Variables	Total (n=47)	Non-recurrence (n=37)	Recurrence (n=10)	p value
Age (years), median (range)	59 (20–87)	61 (27–87)	59 (20–80)	0.39
Male	24 (51)	18 (49)	6 (60)	0.72
Race				0.12
White	29 (62)	25 (68)	4 (40)	
Hispanic	8 (17)	4 (11)	4 (40)	
Black	7 (15)	6 (16)	1 (10)	
Other	3 (6)	2 (5)	1 (10)	
Underlying malignancy				0.96
Urothelial/bladder	21 (45)	17 (46)	4 (40)	
Cervix	8 (17)	6 (16)	2 (20)	
Prostate	7 (15)	6 (16)	1 (10)	
Other	11 (23)	8 (22)	3 (30)	
Comorbidities				
Active chemotherapy	33 (70)	25 (68)	8 (80)	0.70
History of urologic surgery	18 (38)	15 (41)	3 (30)	0.72
Diabetes	9 (19)	8 (22)	1 (10)	0.66
Presence of urinary stent	8 (17)	6 (16)	2 (20)	> 0.99
Presence of ileostomy/diversion	4 (9)	4 (11)	0 (0)	0.56
Kidney stones	3 (6)	3 (8)	0 (0)	> 0.99
Clinical manifestations				
Fever	33 (70)	28 (76)	5 (50)	0.14
Costovertebral angle tenderness	23 (49)	19 (51)	4 (40)	0.72
Chills	17 (36)	16 (43)	1 (10)	0.07
Exit site cellulitis	9 (19)	8 (22)	1 (10)	0.66
Sepsis with organ failure or septic shock	4 (9)	4 (11)	0 (0)	0.56
WBC K/ $\mu$ L, median (IQR)	6.8 (3.6–11.1)	6.8 (3.6–11.1)	6.8 (5.2–9.0)	0.96
ANC K/ $\mu$ L, median (IQR)	5.6 (2.9–8.9)	5.2 (2.9–9.8)	4.4 (2–5.7)	0.46
Microorganisms <sup>a</sup>				
<i>Pseudomonas</i> spp.	17 (36)	14 (38)	3 (30)	0.73
<i>Enterococcus</i> spp.	11 (23)	8 (22)	3 (30)	0.68
<i>Escherichia coli</i>	8 (17)	7 (19)	1 (10)	0.67
<i>Stenotrophomonas maltophilia</i>	7 (15)	5 (14)	2 (20)	0.63
<i>Staphylococcus aureus</i>	6 (13)	4 (11)	2 (20)	0.59
<i>Klebsiella pneumoniae</i>	5 (11)	4 (11)	1 (10)	> 0.99
<i>Candida</i> spp.	5 (11)	4 (11)	1 (10)	> 0.99
Monomicrobial infection	25 (53)	20 (54)	5 (50)	> 0.99

Values are N (%) unless otherwise indicated

ANC absolute neutrophil count, IQR interquartile range, PCN percutaneous nephrostomy, WBC white blood cells

<sup>a</sup>Of the 47 patients included, 47% had a polymicrobial infection, for a total of 59 organisms isolated

(45%), followed by cervical cancer (17%). The majority of patients were undergoing active chemotherapy (70%), and 38% had undergone a recent urologic surgical procedure. The most common clinical manifestations were fever (70%), followed by costovertebral angle tenderness (49%), chills (36%), and exit-site cellulitis (19%). The median absolute neutrophil count was 5.6 K/ $\mu$ L (IQR 2.9–8.9). The infections were almost equally distributed between mono- and polymicrobial. The most common bacterial organisms were

*Pseudomonas* spp. (36% of isolates), followed by *Enterococcus* spp. (23%), and *Escherichia coli* (17%). Overall, in terms of demographic characteristics, clinical manifestations, and laboratory data, there was no statistically significant difference between the 37 patients in the non-recurrent group and the 10 patients in the recurrent group that would help identify a risk factor for infection recurrence (Table 1).

All 47 patients had received antimicrobial therapy for a median of 15 days (IQR 13–16), with no statistical difference

among the non-recurrent and recurrent groups (15 vs 13 days;  $p=0.06$ ; Table 2). Of interest, we found that 34 of 37 (92%) patients in the non-recurrent group had a concordant antibiotic at the time of PCN catheter exchange, versus 5 of 10 (50%) patients in the recurrent group ( $p=0.007$ ). In addition, patients in the non-recurrent group had earlier PCN catheter exchange (within 4 days of infection; IQR 3–7) than did patients in the recurrent group (8 days; IQR 5–12;  $p=0.08$ ; Table 2). Of note, patient's severity of illness did not confound our results, as it had no significant association with either earlier catheter exchange ( $p=0.33$ ), or recurrent PCNI ( $p=0.56$ ). Multivariate logistic regression analysis identified two factors that were independently associated with a decrease in risk of recurrent PCNI: concordant antibiotic use (OR 0.04;  $p=0.008$ ) and PCN catheter exchange within 4 days of infection (OR 0.1;  $p=0.048$ ; Table 3).

## Discussion

The overall incidence for PCNI has been reported between 1 and 19%, while in our study it was 14% [13, 14]. The main reason for this broad range of results is likely the non-standardized definitions utilized to identify these neglected infections, including at times extrapolation from other well-known infections, such as CA-UTI [9]. To avoid including patients with a non-PCN-related infection (sterile pyuria, asymptomatic bacteriuria, or microbial specimen contamination), which could confound our results, and likely underestimating the true incidence, we only included those patients who fulfilled our strict clinical and microbiological definition of PCNI.

In a manner similar to CA-UTI [9], PCNI increases in prevalence the longer the device remains in place, until approximately day 90 when PCN catheters are routinely replaced because of progressive physiological intraluminal obstruction and encrustation of debris and solutes [15]. Sterile techniques, plus the use of systemic prophylactic antimicrobials targeting Gram-negative organisms provided at the time of initial PCN catheter insertion (clean-contaminated procedure) [16] will likely not provide long-term prevention, especially as these catheters are permanently exposed

**Table 3** Predictors associated with recurrent PCN infections by multivariate logistic regression analysis

Factor	OR	95% CI	<i>p</i> value
Concurrent antibiotics use for PCN infection	0.04	0.004–0.43	0.008
PCN exchange within 4 days of infection	0.10	0.01–0.98	0.048

95% CI 95% confidence interval, OR odds ratio

to the external cutaneous and internal urinary microbial flora [14]. Several strategies utilized in the prevention of other device-related infections may be extrapolated to PCN catheters upon further research studies. The use of closed urinary drainage bags with no internal urinary reflux, as well as maintaining the area “clean” with frequent soap, water, and antiseptics may assist in decreasing the high rate of infection [9]. The potential impact of utilizing chlorhexidine-impregnated dressings [17] at the entry site of the PCN, as well as creating an antimicrobial-coated PCN catheter for the provision of extended antimicrobial coverage [18], as utilized for infection prevention in central venous catheters and peripherally inserted central catheters [19], may also be considered for decreasing the high rate of recurrent PCNI.

Previously reported risk factors associated with PCNI and CA-UTI, include immunosuppression, diabetes, neutropenia, ureteral stents, nephrolithiasis, prior genitourinary surgeries, and UTI [9, 16]. However, in our study, we did not find that any of the above variables or even the diverse initial clinical manifestations were risk factors for recurrent PCNI. Furthermore, whether the infections were mono- or polymicrobial, the diverse microorganisms that cause PCNI have not been found to be risk factors for recurrent PCNI. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*, which were encountered in our study, are all well known to cause device-related biofilm infections [20]. These biofilm-embedded infections are often impossible to eradicate without removing the foreign medical device [20–24]. Therefore, the most likely reason these organisms have not been found to be a risk factor for recurrent PCNI is that, appropriately, these devices have been explanted and replaced with new ones in a timely manner.

**Table 2** Time to infection and therapeutic approach of patients with PCN-related infections

Variables	Total ( <i>n</i> =47)	Non-recurrence ( <i>n</i> =37)	Recurrence ( <i>n</i> =10)	<i>p</i> value
Days from PCN placement to infection, median (IQR)	44 (25–61)	44 (29–61)	43 (17–54)	0.64
Days from infection to PCN exchange, median (IQR)	5 (3–8)	4 (3–7)	8 (5–12)	0.08
Days of total antibiotic therapy, median (IQR)	15 (13–16)	15 (14–17)	13 (7–15)	0.06
Patients on concordant antibiotic at time of PCN exchange, <i>n</i> (%)	39 (83)	34 (92)	5 (50)	0.007

IQR interquartile range, PCN percutaneous nephrostomy

Of special interest, two key variables were found to be statistically significant in multivariate analysis: (a) the PCN catheter was exchanged within 4 days of PCNI diagnosis (OR 0.1;  $p=0.048$ ); and (b) the patient was receiving concordant antimicrobials at the time of PCN catheter replacement (OR 0.04;  $p=0.008$ ). Source control, by removing the microbial biofilm-embedded implant promptly, is key for a successful outcome [20, 23]. However, before the PCN catheter is removed and exchanged for a new device, the patient must have been receiving concordant antimicrobials. Otherwise, the new PCN would be implanted in an environment with actively proliferating microorganisms, not being appropriately treated, ultimately leading to recolonization and subsequent biofilm infection of the new implant.

The main limitations of our study are the retrospective nature of the data collection and the relatively small sample size for analysis on factors associated with recurrent PCNI. Also, our study population included only patients with cancer whom were not health care naïve and may have been colonized with hospital-acquired resistant pathogens, which may differ from the general population without underlying malignancy and limit the generalization of our results. Additionally, our definition of severity of illness as sepsis with organ failure or septic shock may have not captured all unmeasured confounders that could have influenced the timing of PCN exchange. Lastly, to avoid confounding our findings by including patients in whom the diagnosis of PCNI was questionable, we only included patients who fulfilled our strict PCNI definition, likely excluding patients with a mild subclinical presentation and underestimating the true prevalence of infection.

In conclusion, to prevent PCNI recurrences, we recommend that once antimicrobial susceptibilities are made available and the patient is receiving concordant antimicrobials, to proceed with immediate PCN exchange, ideally within the first 4 days of the infection, and to continue with appropriate antimicrobial coverage for a total course of 10–14 days. To validate our recommendations, we are proceeding with an interdisciplinary prospective quality improvement study, in which in addition to our internal standardized protocols, prior to PCN catheter exchange due to infection, all patients must be receiving concordant antimicrobials.

**Acknowledgements** UT MD Anderson's Department of Scientific Publications provided editorial assistance.

**Funding** This study was supported in part by funds from The University of Texas MD Anderson Cancer Center, Houston, Texas, and by the National Institutes of Health/National Cancer Institute, under award number P30CA016672.

## Compliance with ethical standards

**Conflict of interest** Dr. Issam I. Raad: financial interest and/or other relationship with Cook Medical. All other authors: no reported conflicts.

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