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ORIGINAL RESEARCH

Does percutaneous drainage of malignant obstructive uropathy improve renal function? A retrospective records review

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Background: Malignant conditions of the pelvis and/or abdomen can cause ureteric obstruction and associated impaired renal function, which can be managed by performing percutaneous nephrostomy (PCN) tube insertion. This is often in a palliative setting and the available literature is still divided on the benefit that these procedures provide. The main objective of this study was to assess the changes in estimated glomerular filtration rate (eGFR) over the first six months following PCN for malignant ureteric obstruction. We also explored the role of urinary tract infections (UTIs) in the changes of eGFR following PCN.

Methods: Retrospective folder review of patients who had PCN procedures at Groote Schuur Hospital for malignant obstructive uropathy from January 2015 to December 2017. For each included patient, eGFR was recorded at baseline pre-PCN, and at its best and worst value in the first six months after PCN, as well as the presence of confirmed UTIs.

Results: Fifty-four male and 36 female patients were included in the study, with a combined mean age of 56 years. The most common cancers in men were bladder (59%), while the most common cancers in women were cervix (64%). Pre-PCN eGFR, median (IQR), was 9 ml/min/1.73 m^2 (5, 26). Post-PCN eGFR improved to 48 ml/min/1.73 m^2 (30, 75) before deteriorating to 23 ml/min/1.73 m^2 (9, 44) within the six-month follow-up window. The patients who developed UTI post-PCN had 6.15 ml/min/1.73 m^2 (95% CI: 0.87, 11.43) lower eGFR at their worst measurement.

Conclusion: Most patients' renal function initially improved post-PCN, before deteriorating towards pre-PCN eGFR values within six months. Intercurrent UTIs are associated with a poor renal function response within six months post-PCN. These findings highlight the importance of shared decision making as to who will benefit from an intervention.

Keywords: percutaneous drainage, malignant obstructive uropathy, renal function

Introduction

Advanced or locally advanced malignant conditions of the pelvis and/or abdomen can cause ureteric obstruction and associated impaired renal function. This obstruction can be managed by performing percutaneous nephrostomy (PCN) tube insertion with or without antegrade double J stent insertion.[1] Having PCN tubes in situ is associated with prolonged hospital stay which affects quality of life.[1]

The available literature reports clearly on the complications and morbidity associated with PCN, as well as the immediate improvement in renal function post-PCN.[1-5] Complications causing morbidity include blockage of PCN-tube, displacement of PCN-tube, sepsis, pyelonephritis, haemorrhage, and pain requiring inpatient management.[1,2]

Some studies found that patients spend between 23% and 40% of their mean survival time in hospital due to complications associated with nephrostomy tubes.[2] Mean serum creatinine levels improved from 280 umol/L to 150 umol/L, post diversion in a large study of 208 patients.[1] There is limited data on the trend in renal function following the expected initial improvement post-PCN.

Deciding whether a patient needs PCN can be difficult. Various prognostication models[1,2,4] have been described to assist the clinician and patient with the decision-making process. None of these prognostication models have long-term renal function response or urinary tract infections (UTIs) post-PCN as factors affecting survival. Median survival post-PCN has been reported as being anything between 78 days[5] and 174 days.[2]

We aimed to describe the response in renal function following PCN for obstructive uropathy due to abdominal/pelvic malignant conditions at our institution. We hypothesised that UTI post-PCN is associated with poor response in renal function.

Methods

All patients who had percutaneous nephrostomy for malignant ureteric obstruction done at Groote Schuur Hospital between 1 January 2015 and 31 December 2017 were eligible for inclusion in the study. All malignant conditions were considered for inclusion. Patients had to be followed up for at least one week post-percutaneous nephrostomy. Each patient record was reviewed for relevant data recorded during the six months post-PCN.

Patients who had a failed PCN procedure and those who weren't followed up for at least one-week post-intervention, were excluded. No children under the age of 18 years were included in this study.

We performed a retrospective folder review of all patients with complete records identified during the specified time period. Data were extracted from the hospital radiology system and the National Health Laboratory Services (NHLS) laboratory system.

Renal function was recorded as per the chronic kidney disease (CKD) staging system,[6] according to estimated glomerular filtration rate (eGFR) values. eGFR was determined using the Modification of Diet in Renal Disease (MDRD) Study equation.[6] The chronic kidney disease (CKD) staging system we used is as follows (according to eGFR values): Stage 1: eGFR ≥ 90 ml/min/1.73 m^2; Stage 2: eGFR 60–89 ml/min/1.73 m^2; Stage 3: eGFR 30–59 ml/min/1.73 m^2; Stage 4: eGFR 15–29 ml/min/1.73 m^2; and Stage 5: eGFR < 15 ml/min.[6] CKD stages and eGFR pre-PCN were compared to the best CKD stage and eGFR post-PCN and worst CKD stage and eGFR within six months post-PCN. A poor response was defined as the worst CKD stage post-PCN being the same or worse than the pre-PCN CKD stage. A good response was defined as the worst CKD stage post-PCN being better than pre-PCN CKD stage.

UTIs were diagnosed if a patient had a documented positive urine microscopy and culture more than seven days post-PCN. UTI was defined as a single organism cultured in affected urine with a bacteria colony count of > 10 000 CFU/ml. UTIs identified within seven days post-PCN were assumed to be related to pre-existing infected urine or colonisation and were not included.

We collected data for six months post-PCN, as this represents the upper end of the range for median survival for our target population.[1]

We collected the following data: i) demographics, ii) type of malignancy, iii) laterality of the nephrostomy tube, iv) renal function, and v) UTIs. Demographics collected included the patient's age and sex. We grouped CKD Stages 1 and 2 together, since the laboratory we used for this trial did not offer specific eGFR values at levels ≥ 60 ml/min. If a patient had an eGFR ≥ 60 ml/min, we classified them as *at worst CKD Stage 2* and recorded their eGFR to be 75 ml/min (midway between CKD Stages 1 and 2).

Statistics

Continuous and interval data were described in terms of mean (standard deviation) or median (interquartile range) as appropriate for the data distribution. Categorical data were described as counts and proportions (*n/N* [%]). The student's t-test, Wilcoxon rank sum test and the Wilcoxon sign rank test were used to compare continuous and interval groups. Fisher's exact or chi-squared tests were used to compare categorical groups. The differences in eGFR pre- and post-PCN, were stratified according to presence or absence of UTI. Difference in CKD stage between timepoints was assessed with simple ordinal regression. Z-test for differences in proportions was used to compare proportions of patients with improved or deteriorated CKD stage following PCN between groups with and without UTI. We performed an exploratory multiple linear regression to evaluate the impact of UTI on worst eGFR outcome. The a priori level of significance for all analyses was 0.05. Statistical analysis was performed using RStudio (2016, RStudio Inc., Boston, MA. http://www.rstudio.com/).

Results

We identified 90 patients that fulfilled our inclusion criteria. Fifty-four (56%) were men. The most common cancers in men were bladder (59%; *n* = 32), prostate (20%; *n* = 11), lymphoma (7%; *n* = 4), and colorectal cancer (4%; *n* = 2). The most common cancers in women were cervix (64%; *n* = 23), bladder (19%; *n* = 7), lymphoma (6%; *n* = 2), colorectal (6%; *n* = 2) and endometrial cancer (6%; *n* = 2). Sixty-four per cent (*n* = 58) of patients had bilateral PCN procedures (as opposed to unilateral procedures). Fifty-two per cent (*n* = 47) of

Table I: Patient characteristics (*N* = 90), grouped by presence or absence of one or more post-percutaneous nephrostomy (PCN) urinary tract infection (UTI); mean (SD) or *n* [% for column]

	No UTI	≥ 1 UTI	Total
N =	**43**	**47**	**90**
Age (years)	55 (15)	58 (12)	56 (14)
Male sex	24 [56%]	30 [64%]	54 [60%]
Bilateral PCN	26 [60%]	32 [68%]	58 [64%]
Cancer type			
Bladder	16 [37%]	23 [49%]	39 [43%]
Cervix	14 [33%]	9 [19%]	23 [26%]
Prostate	4 [9%]	7 [15%]	11 [12%]
Lymphoma	3 [7%]	3 [6%]	6 [7%]
Colorectal	2 [5%]	2 [4%]	4 [4%]
Endometrial	1 [2%]	1 [2%]	2 [2%]
Other	3 [7%]	2 [4%]	5 [6%]

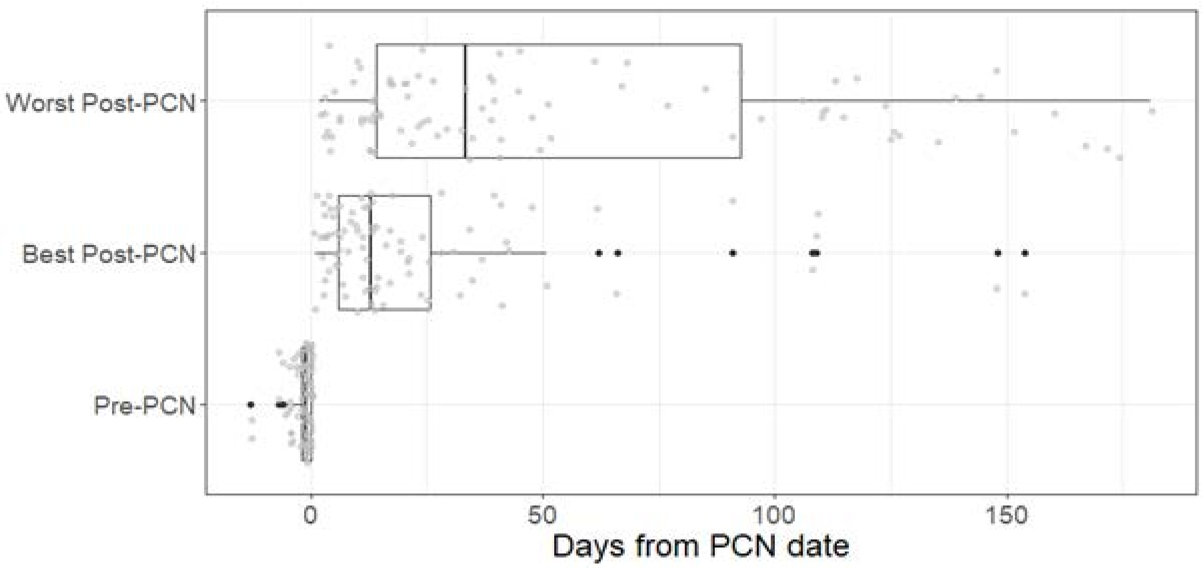

Figure 1: Boxplots of timing of eGFR measurement

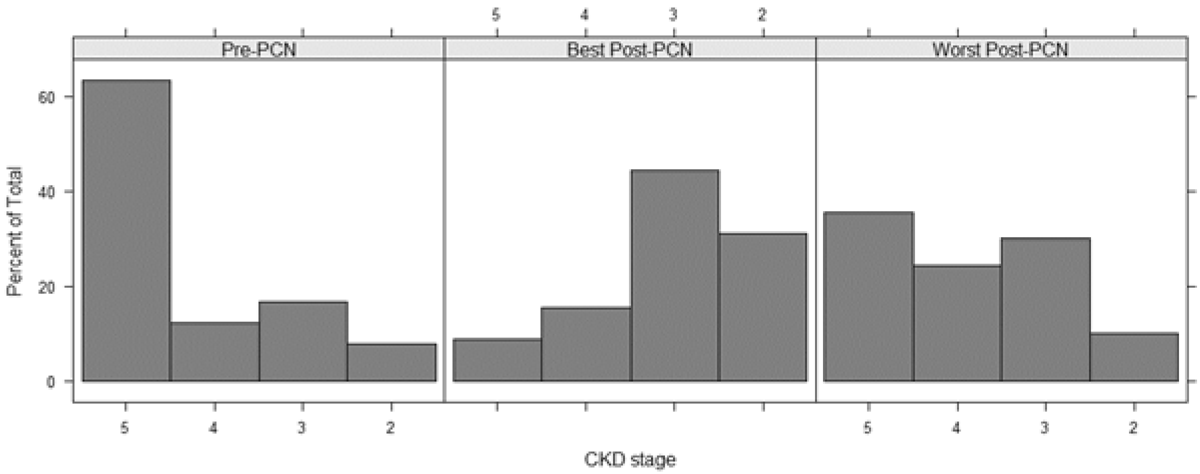

Figure 2: Histograms of CKD stages at three time intervals (pre-PCN, best post-PCN, and worst post-PCN)

patients developed at least one post-PCN UTI during the six-month observation period (Table I).

Post-PCN renal response

Median (IQR) timepoints at which baseline eGFR, best post-PCN eGFR and worst post-PCN eGFR were documented, were 1 (-2, 0) day pre-PCN, 13 (6, 26) days post-PCN and 34 (14, 93) days post-PCN (Figure 1). The worst eGFR measurement occurred a median 33 (20, 49) days after the best eGFR measurement (*p*-value < 0.001, Wilcoxon sign rank test).

Pre-PCN eGFR, median (IQR), was 9 (5, 26) ml/min/1.73 m^2. Post-PCN eGFR improved to 48 (30, 75) ml/min/1.73 m^2 before deteriorating to 23 (9, 44) ml/min/1.73 m^2 within the six-month follow-up window. The median difference (95% CI) between pre-PCN eGFR and best eGFR post-PCN was 30 (25, 26) ml/min/1.73 m^2. The difference between pre-PCN eGFR and worst post-PCN eGFR was 8.5 (4, 13.5) ml/min/1.73 m^2. The difference between eGFR from best to worst post PCN value was -25 (-20.5, -29.5) ml/min/1.73 m^2. Worst CKD staging post-PCN was consistently better than CKD staging before PCN (*p*-value 0.0008, simple ordinal regression) (Figure 2).

The effect of interval UTI on the response in renal function

The worst eGFR (95% CI) of those who experienced a post-PCN UTI was 5.1 (-11.5, 1.4) ml/min/1.73 m^2 lower than those who did not experience a post-PCN UTI (unadjusted association) (Table II). The estimated difference in worst eGFR is -6.2 (-11.4, 0.9) ml/min/1.73 m^2 when adjusted for baseline eGFR, magnitude of initial eGFR improvement following PCN, age, sex, laterality and cancer type. Apart from interval UTI, baseline eGFR and magnitude of initial eGFR improvement following PCN were significantly associated with the worst post-PCN eGFR value.

Alluvial plots report the CKD stages at pre-PCN, best post-PCN and worst post-PCN timepoints for each included patient (Figure 3). The median worst eGFR post-PCN for patients who did not have any UTI was 29 (14, 48) ml/min/1.73 m^2, compared to 19 (8, 38) ml/min/1.73 m^2 for the patients who had at least one post-PCN UTI.

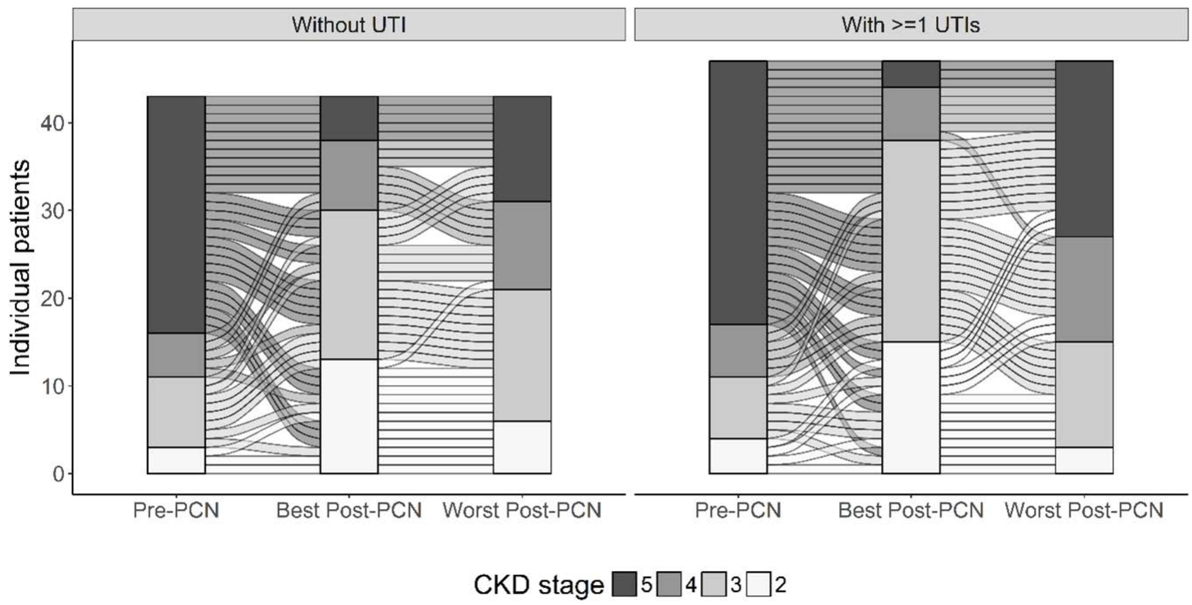

Figure 3: Alluvial plots of patient CKD stage at three intervals; comparing those with at least one postoperative UTI event to those without any postoperative UTI events; worst stage is dark grey at top of bars, best stage is light grey at bottom of bars

Table II: Patient outcomes grouped by presence or absence of post-PCN UTI

	No UTI	≥ 1 UTI	*p*-value	Total
N =	**43**	**47**		**90**
Timing of outcome measurement				
Preoperative value (day)	-1 (-3, 0)	-1 (-2, 0)	0.414†	-1 (-2, 0)
Best postoperative value (day)	11 (5, 18)	16 (10, 32)	0.018†	13 (6, 26)
Worst postoperative value (day)	18 (11, 40)	45 (25, 112)	0.0004†	34 (14, 93)
eGFR				
Preoperative (ml/min/1.73 m^2)	11 (6, 29)	7 (4, 24)	0.342†	9 (5, 26)
Best postoperative (ml/min/1.73 m^2)	41 (26, 75)	52 (36, 75)	0.158†	48 (30, 75)
Worst postoperative (ml/min/1.73 m^2)	29 (14, 48)	19 (8, 38)	0.128†	23 (9, 44)
CKD stage				
Preoperative				
≤ 2	3 (7%)	4 (9%)	0.213‡	7 (8%)
3	8 (19%)	7 (15%)		15 (17%)
4	5 (12%)	6 (13%)		11 (12%)
5	27 (63%)	30 (64%)		57 (63%)
Best postoperative				
≤ 2	13 (30%)	15 (32%)	0.213‡	28 (31%)
3	17 (40%)	23 (49%)		40 (44%)
4	8 (19%)	6 (13%)		14 (16%)
5	5 (12%)	3 (6%)		8 (9%)
Worst postoperative				
≤ 2	12 (28%)	20 (43%)	0.238‡	9 (10%)
3	10 (23%)	12 (26%)		27 (30%)
4	15 (35%)	12 (26%)		22 (24%)
5	6 (14%)	3 (6%)		32 (36%)

Median (IQR)
†Wilcoxon Rank Sum test, ‡Chi-squared test with continuity correction

In the group of patients who did not develop post-PCN UTI, only 42% (18/43) ended with a worse CKD stage after the best post-PCN CKD stage had been reached. This is in contrast to the group who did develop post-PCN UTI, where 72% (34/47) ended up with a worse CKD stage after the best CKD stage had been reached post-PCN. The difference (95% CI) in proportions of the two groups (with/without UTI) is 30% (9%, 52%), *p*-value = 0.007.

The effect of other variables on the response in renal function

Looking at age distribution and renal function response, the younger age-group (< 50 years) showed a good response in renal function up to six months post-PCN in 46% (13/28) of patients. In the age-group 50–65 years, a good response was found in 41% (14/34) of patients and in the group ≥ 65 years, a good response was found in 32% (9/28) of patients.

In the patients who had bilateral PCN (58 patients), 45% (26/58 patients) had improved CKD stage up to six months post-PCN, while in the group of patients who had unilateral PCN (32 patients), only 22% (7/32 patients) had improved CKD stage up to six months post-PCN. The incidence of UTI in the bilateral PCN patients was 55% (32/58 patients), while the unilateral PCN patients had an incidence of 47% (15/32 patients).

Comparing different cancers and percentage of good responders in renal function post-PCN [total]: bladder Ca 49% [19/39], cervical Ca 30% [7/23], haematological malignancies (seven lymphoma and one multiple myeloma patients) 86% [6/7] and prostate Ca 18% [2/11].

Discussion

To determine eGFR trends from pre-PCN to best and worst post-PCN eGFR, we evaluated the timing when the different values were obtained. The majority of patients (69%) had a best post-PCN eGFR measurement prior to worst post-PCN eGFR measurement. Only 8% of patients had their best post-PCN eGFR measurement after their worst eGFR measurement.

Patients in our study experienced a median early improvement in eGFR of 30 ml/min/1.73 m^2 around two weeks post-PCN followed by a median 25 ml/min/1.73 m^2 deterioration towards baseline around one month post-PCN. This is an important finding. The reason for this trend can be multifactorial, including cancer progression, drug/chemotherapy toxicity, blocked PCN-tubes and UTI. Half of our patients developed at least one UTI following PCN. UTI events were associated with worse eGFR outcome and worse CKD staging. Further investigation to assess if the prevention of UTI post-PCN, might improve renal function response, would be beneficial. UTIs are also one of the main factors of morbidity in PCN-patients,[1] leading to prolonged hospital stay, in patients who generally don't have a long life expectancy. UTI secondary to PCN, should almost always be treated as a nosocomial infection. This requires parenteral antibiotics in most cases, which again leads to prolonged hospital stay (and morbidity). Immunocompromised patients might be at a greater risk to develop UTI post-PCN, although this factor was not measured in this study. Better PCN-tube hygiene care can potentially decrease the amount of UTIs. The use of a closed drainage system directly into a bag (as opposed to the tube hanging free in a drainage bag stuck onto the patient's skin) might decrease the incidence of UTI. Our findings highlight the importance of appropriate counselling as well as multidisciplinary decision making as to who should be offered PCN for their obstructive uropathy secondary to malignant abdominal/pelvic conditions.

Despite the observed pattern of early improvement followed by deterioration during the first six months following PCN, renal function generally remained better post-PCN compared to pre-PCN values.

Limitations of our study

There was large variance in the time at which best and worst renal function values were recorded. Comparing best to worst values, instead of measures at standardised timepoints, inflates the observed renal responses. Prospective studies can overcome this problem by standardising timepoints for outcome assessment.

Another limitation is the fact that the laboratory service we used does not give specific values of eGFR for values > 60 ml/min. We therefore decided to use CKD Stage 2 and eGFR of 75 ml/min for all eGFR > 60 ml/min. The truncated nature of the eGFR variable complicates statistical modelling.

Interpretation

eGFR trends post-PCN

Our findings support the hypothesis that patients experience an initial improvement in renal function, followed by a deterioration in function towards pre-PCN values. Available literature is unclear on this topic. This is an important factor to acknowledge when counselling patients for PCN in this setting. Nariculam et al.[7] found that among prostate cancer patients who underwent either unilateral or bilateral PCN, no major differences in post-PCN creatinine levels were seen. Our patients' worsening renal function after initial improvement may be due to the aggressiveness of the malignancy present[7] or development of UTI (a risk factor for acute kidney injury [AKI]).[8] Our cohort had a higher incidence of UTI post-PCN when compared to available literature,[1,9] indicating higher risk for developing AKI.

eGFR and CKD stage response post-PCN

We investigated eGFR/CKD stage at three intervals (baseline, best and worst values post-PCN). CKD stage improved significantly following PCN with change from pre-PCN to best post-PCN CKD stage, and deteriorated again from best post-PCN to worst post-PCN CKD stage. Possible causes for this deterioration include progression of primary malignancy, dislodgement/blockage of nephrostomy tubes, pre-renal causes (excluding UTI) and acquiring UTI secondary to foreign body (nephrostomy tube) in situ.

Unlike similar studies on this topic, this study design sought to report best and worst values after baseline measurement (Figure 2).

Our results call in to question the role of PCN in advanced malignancy as we have shown that initial improvements in eGFR and CKD stage are short-lived.

There are few other studies which have investigated or shown this conclusively. Van Aardt et al.[3] did a retrospective audit of all patients with primary untreated cervical cancer with renal impairment secondary to obstructive uropathy. Patients receiving PCN had their serum urea, creatinine and potassium recorded pre-PCN, then again on days three and seven post-PCN. They included 28 patients who received PCN into their study. Of the patients, 11.5% ended with worse renal function, 38.5% had unchanged renal function and 50% had improved renal function post-PCN. A number of studies, including Maurício et al.,[1] Wilson et al.[10] and Misra et al.[5] all reported on a mean improvement in serum creatinine post-PCN, but failed to report follow-up renal functions once the mean improved levels had been reached post-PCN.

Interaction between renal function and development of UTI post-PCN

The incidence of UTI in our study (52%) was higher than the reported literature, with reported incidences of UTI/sepsis post-PCN between 15%[9] and 22.7%.[1]

Our secondary objective was to analyse the association between eGFR response and the development of post-PCN UTI. Our study population has multiple factors that contribute to the development of UTI, including renal dysfunction, obstructive uropathy, compromised immune systems and foreign material in the collecting system (PCN tube). Multiple linear regression showed that patients who develop one or more post-PCN UTIs have a 6.15 ml/min/1.73 m^2 lower eGFR at their worst eGFR measurement than those who do not. This has the potential to be a predictor of worse outcome and future prospective studies should investigate if this is indeed a modifiable risk factor to preserve renal function post-PCN.

The prognostication models available do not include UTI as a factor affecting survival.[1,2,4] Maurício et al.[1] established that the number of events related to malignancy (≥ 4) and Eastern Cooperative Oncology Group (ECOG) index (≥ 2) were associated with short survival on multivariable analysis. They only use these two factors in their prognostication model, however the presence of UTI was not part of this analysis. Another group, Alawneh et al.,[4] used serum albumin (< 3.5 mg/dL), pleural effusion, and bilateral hydronephrosis to stratify patients into four prognostic groups: zero risk factors, one risk factor, two risk factors, and three risk factors. Median survival for each group was 17.6 months, 7.7 months, 2.2 months, and 1.7 months, respectively. UTI was not a factor considered in this model.

Proportional breakdown of the worst CKD stage is better in the group without UTI (Figure 3). There were also markedly fewer deteriorations in CKD stages between best and worst post-PCN interval in the patients without UTI. These findings support our hypothesis that UTI is associated with poor renal function response post-PCN. The poor response in patients who developed UTI post-PCN also applies to patients who initially responded well. This finding warrants further investigation in a prospective trial environment.

Other considerations

It appears that older patients had worse renal function response and more UTIs.

A total of 64% of our patients had bilateral PCN. This is in line with the reported literature of incidences ranging from 22%[2] to 72%.[7] The patients who had bilateral PCN showed a higher percentage of improved CKD stage up to six months post-PCN, when compared to the patients who only had unilateral PCN. Interestingly, the incidence of UTI in the bilateral PCN patients was higher compared to the patients with unilateral PCN (55% vs 47%). This is contrary to our hypothesis that a higher incidence of UTI is associated with poorer renal function response.

When comparing renal function response up to six months post-PCN between type of malignancies, the lymphoma group had the best response with six out of the seven patients (86%) still maintaining their improved renal function at six months. This might be due to the nature of the disease and good responses to chemotherapy. Only two out of eleven (18%) prostate cancer patients included in the study had a good renal function response up to six months post-PCN.

Conclusion

Although most patients' renal function initially improved post-PCN, the general trend for the majority of patients was to deteriorate towards pre-PCN eGFR and CKD stage values.

UTIs appear to play and important role in poor renal function response within six months post-PCN.

Other factors that appear to have an influence on renal function response post-PCN include type of malignancy, age and laterality of PCN, and these might require further investigation in future.

In our study, the only potential modifiable risk factor associated with poor response in renal function post-PCN, seems to be UTIs. This finding can however be just a confounder and warrants further prospective research in trying to prevent UTIs (potentially with prophylactic antibiotics). Should lower rates of UTI lead to improved renal function response post-PCN, it can be practice-changing to preserve maximum renal function and potentially increase life expectancy.

This study showed that doing PCN for advanced malignancies, only has the desired outcome in a small percentage of patients and might actually cause more morbidity and prolonged hospital stay. The importance of informed shared decision making between the treating physicians and the patient with/without the family involved, cannot be overstated.

Conflict of interest

We have no conflict of interest to disclose.

Funding source

This was an unfunded project.

Ethical approval

Human research ethics committee approval was obtained from the University of Cape Town, Faculty of Health Sciences (HREC REF: 097/2019). The requirement for informed consent was waived.

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Units of measurement

Renal function: Measured by estimated glomerular filtration rate (eGFR) in ml/min per 1.73 m^2 according to the MDRD formula.

UTI: Measured in CFU/ml (colony-forming units per millilitre)

Serum creatinine: Measured in umol/L