

Impact of percutaneous nephrostomy in South African women with advanced cervical cancer and obstructive uropathy

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Objectives: South Africa women with cervical carcinoma present at younger ages and the majority with advanced-stage disease. Certain patients may have a favourable outcome after placement of a percutaneous nephrostomy (PCN) for obstructive uropathy in cervical cancer.

Methods: A retrospective audit was conducted at the Gynaecological Oncology Unit, University of Pretoria. All patients with primary untreated cervical cancer with renal impairment secondary to obstructive uropathy were included. Urea, creatinine and potassium were recorded for patients receiving PCN before insertion and after treatment.

Results: In total, 54 patients were included. The mean age was 49.5 years. The number of patients receiving PCN was 28 (51.9%) and 26 (48.1%) women did not. Altogether, 25% of patients had improvement in renal function after insertion of PCN and in 10.3% renal function worsened. Some 50% of these patients received palliative radiotherapy, 7% started therapeutic chemo-radiation and 7% of patients completed treatment. Response to treatment was unknown for 21% of patients, 7% showed partial response and 10.7% died of their disease. In the control group, 15.4% of patients had severe renal failure; 7.7% of patients never started treatment and 7.7% received palliative radiotherapy; 11.5% died of their disease. Some 26.9% of patients without PCN fell in the renal failure group, of whom 19.2% received palliative radiotherapy.

Conclusion: PCN in patients with cervical cancer and obstructive uropathy, even if HIV positive, is safe with minimal complications. An improvement in renal function was shown after insertion. PCN improved the number of patients qualifying for initiation and completion of treatment.

Keywords: advanced cervical cancer, obstructive uropathy, percutaneous nephrostomy

Introduction

Cervical cancer is an important contributor to cancer mortality worldwide and is even more significant in less developed countries.¹ South Africa, in comparison with Western countries, has a high incidence of cervical cancer. The associated problem of infection with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) in our country contributes significantly to the burden of disease. Women are typically of younger age and at a more advanced stage of disease by the time they are diagnosed.²

Uraemia secondary to malignant ureteric obstruction is common in patients with advanced pelvic malignancy and specifically cervical cancer.³ As a result of uraemia, electrolyte imbalances and/or urinary tract infections patients may deteriorate quickly if the urinary tract obstruction is not overcome. These changes usually result in a decrease in the patient's level of consciousness and ultimately death if left untreated.⁴

Utilising ureteral stents or percutaneous nephrostomy (PCN) to relieve urinary tract obstruction may lead to improved, and even restoration of, renal function.⁵ Controversy exists regarding the benefit of PCN in treating patients with renal failure as a result of advanced cancer, and currently there are no universally accepted prerequisite criteria in predicting long-term outcome.⁶

In the case of failure or contra-indications to relieve renal tract obstruction through retrograde insertion of ureteric stents, PCN is used to provide decompression of the renal collection system by placing a catheter percutaneously at the level of the kidney.⁷

Inserting PCN is a relatively safe and simple procedure and provides time needed for patients with advanced disease to receive curative or palliative radiotherapy or chemotherapy.

The limitations of inserting PCN include renal failure not improving, lifespan limitations of around six weeks of the nephrostomy stomas and catheters, as well as secondary upper urinary tract infection, ranging from mild infection to severe sepsis. Possible dilemmas may include prolonging the patient's suffering and/or increased cost, without a survival benefit or improvement in quality of life.⁷

Although there are no universally accepted guidelines for the placement of PCN in patients with advanced cervical cancer, the most important factor is intention to treat. In our resource-restricted region there is a need to identify which patients will benefit from placement of PCN, proceed to radiotherapy and chemo-radiation (CRN) and how many can complete therapy. This information might assist in changing current treatment protocols of patients with advanced disease by identifying certain predictive factors.

This study primarily aimed to describe the outcomes of and then to identify which patients had a favourable outcome after placement of PCN for obstructive uropathy in cervical cancer. The second objective was to determine the effect that PCN has on renal function and obstructive uropathy. Lastly, we sought to determine the proportion and profile of patients who were enabled to proceed to chemo-radiation with curative intent, or to complete therapy.

Methods

A retrospective audit was conducted for the time period from 1 January 2007 until 31 December 2012. The study was performed at the Gynaecological Oncology Unit at the University of Pretoria, which is a referral unit serving a mixed urban, peri-urban and rural society living in two provinces in South Africa, namely Gauteng and Mpumalanga.

Patient selection included all patients with primary untreated cervical cancer with renal impairment, secondary to obstructive uropathy, at the Steve Biko Academic and Kalafong Hospitals. Renal impairment was defined as serum urea more than 10 mmol/l and/or serum creatinine more than 100 µmol/l. Patients who had previously received treatment in the form of surgery, radiation and/or chemo-radiation were excluded.

The records of these patients were reviewed to obtain the following information: age, FIGO stage, HIV status and CD4 count (if HIV positive), whether antiretroviral drugs (HAART) were being taken and whether nephrostomies had been inserted. The presence or absence of hydronephrosis was reported by the radiologists performing staging ultrasounds. Urea, creatinine and potassium levels were recorded and the values divided into different groups. For the purpose of this study, we defined 'renal failure' as urea between 10 and 30 mmol/l and/or creatinine between 100 and 1000 µmol/l, and 'severe renal failure' as a urea greater than 30 mmol/l and/or creatinine greater than 1000 µmol/l. Renal function was recorded before intervention and where available after intervention on days three, seven and more than one week later.

Treatment outcomes (if applicable and available) were divided into the changes in renal function and complications from PCN,

initiation and completion of therapeutic or palliative radiotherapy or chemo-radiation, and response to treatment.

The sample characteristics were described with frequencies, relative frequencies (%), confidence intervals and bar charts. Logistic regression analysis was done to investigate variables. Fisher's exact test or Pearson's chi-square test was used to analyse data. This study was approved by the Research Ethics Committee of the Faculty of Health Sciences of the University of Pretoria (172/2012).

Results

Demographics of the study population, HIV prevalence and cancer characteristics

Fifty-four patients fulfilled the inclusion criteria for the study. The number of patients who received PCN totalled 28 (51.9%), with the remaining 26 (48.1%) women not treated with PCN. The ages of the study population ranged from 32 to 73 years and the mean age was 49.5 years. The mean age in the nephrostomy group was 48.4 years and 50.7 years in the group who did not receive nephrostomies. Seventeen (31.7%) patients were HIV infected and the majority (70.3%) were stage IIIB cervical cancer. Table 1 tabulates the age, HIV status, CD4 cell count and HAART usage (if applicable) and FIGO stage of the study population. Significantly more patients in the group that did not receive nephrostomies were reported as stage IIIB.

Hydronephrosis and renal function at baseline

Unilateral hydronephrosis was noted in seven of the 54 (13%) patients, with the rest of the patients (46 women) reported to have bilateral hydronephrosis, except for one patient where it was unknown.

Of the patients who received PCN, 11 (39.3%) were classified as severe renal failure and 10 (35.7%) as renal failure. In the no-nephrostomy group four patients fulfilled the criteria for severe renal failure and seven patients had renal failure. Twelve (42.8%) patients had complications, which included blockage of the nephrostomy and falling out of the tube more than 40 days after insertion. In 15 (53.6%) patients complications were unknown. Renal functions at baseline for all patients were categorised and are included in Table 2. Significantly more patients in the no-nephrostomy group had urea levels of less than 10 and lower creatinine values. As these are factors used to decide whether to offer intervention, the differences were expected.

Changes in renal function

The urea, creatinine and potassium levels were recorded for the 28 patients who received PCN. These investigations were done before insertion of the PCN, on days three and day seven after insertion and after treatment or more than one week after nephrostomy insertion. Renal function changes in patients receiving PCN are charted in Table 3.

Interpreting the renal function of patients who did not receive percutaneous nephrostomies was difficult. Post-treatment results were not available for 16 (61.5%) patients. It appears as if the urea, creatinine and potassium levels remained somewhat similar after disregarding patients' results that were not known. Figure 1 illustrates the changes in overall renal function for patients with known results.

Table 1: Descriptive statistics at baseline

Characteristic	Total group (n) [%]	Nephrostomies (n) [%]	No nephrostomies (n) [%]	p-value
Total	54	28	26	
Age				
Mean [SD]	49.5 [10.1]	48.4	50.7	
Median	50.5	49.5	52	
HIV status				
Positive	17 [31.5]	7 [25]	10 [38.5]	0.38
Negative	34 [63]	18 [64.3]	16 [61.5]	1.0
Unknown	3 [5.5]	3 [10.7]	0	0.24
CD4 in positives				
< 200	4 [23.5]	2 [28.6]	2 [20]	1.0
≥ 200	12 [70.6]	5 [71.4]	7 [70]	1.0
Unknown	1 [5.9]	0	1 [10]	1.0
HAART				
No	7 [41.2]	4 [57.1]	3 [30]	0.35
Yes	10 [58.8]	3 [42.9]	7 [70]	0.35
Stage				
IIIB	1 [1.9]	1 [3.6]	0	1.0
IIIB	38 [70.3]	16 [57.0]	22 [84.6]	0.04
IVA	14 [25.9]	10 [35.7]	4 [15.4]	0.12
Unknown	1 [1.9]	1 [3.6]	0	1.0

Table 2: Hydronephrosis, renal function at baseline

Characteristic	Total group (n = 54)	Nephrostomies (n = 28)	No nephrostomies (n = 26)	p-value
<i>Hydronephrosis</i>				
Unilateral	7 [12.9]	1 [3.6]	6 [23.1]	0.04
Bilateral	46[85.2]	26 [92.8]	20 [76.9]	0.13
Unknown	1 [1.9]	1 [3.6]	0	1.0
<i>Urea</i>				
< 10	18 [33.3]	4 [14.3]	14 [53.8]	0.003
10–20	7 [13]	4 [14.3]	3 [11.6]	1.0
21–30	10 [18.5]	6 [21.4]	4 [15.4]	0.73
> 30	18 [33.3]	14 [50]	4 [15.4]	0.01
Unknown	1 [1.9]	0	1 [3.8]	1.0
<i>Creatinine</i>				
< 100	1 [1.9]	1 [3.6]	0	1.0
101–500	23 [42.6]	6 [21.4]	17 [65.4]	0.002
501–1000	12 [22.2]	7 [25]	5 [19.2]	0.74
> 1000	17 [31.4]	13 [46.4]	4 [15.4]	0.02
Unknown	1 [1.9]	1 [3.6]	0	1.0
<i>Potassium</i>				
< 3.5	3 [5.6]	2 [7.1]	1 [3.8]	1.0
3.5–5.5	35 [64.8]	18 [64.3]	17 [65.4]	1.0
5.4–8	14 [25.9]	7 [25]	7 [27.0]	1.0
Unknown	2 [3.7]	1 [3.6]	1 [3.8]	1.0

Table 3: Changes in renal function of patients (n = 28) who received nephrostomies

Biochemistry	Pre-intervention	Post-intervention (D3)	Post-intervention (D7)	Post-treatment/ > 1 week	Best value post-intervention
<i>Urea (mmol/l)</i>					
< 10	4	4	6	7	10
10–20	4	6	6	7	8
21–30	6	6	3	1	2
> 30	14	7	6	10	8
Unknown	0	5	7	3	0
<i>Creatinine (umol/l)</i>					
< 100	1	0	0	1	1
100–500	6	9	15	13	17
501–1000	7	7	3	4	3
> 1000	13	7	3	7	7
Unknown	1	5	7	3	0
<i>Potassium (mmol/l)</i>					
< 3.5	2	2	2	1	0
3.5–5.3	18	17	14	19	26
5.4–8.0	7	4	5	5	2
> 8.0	0	0	0	0	0
Unknown	1	5	7	3	0

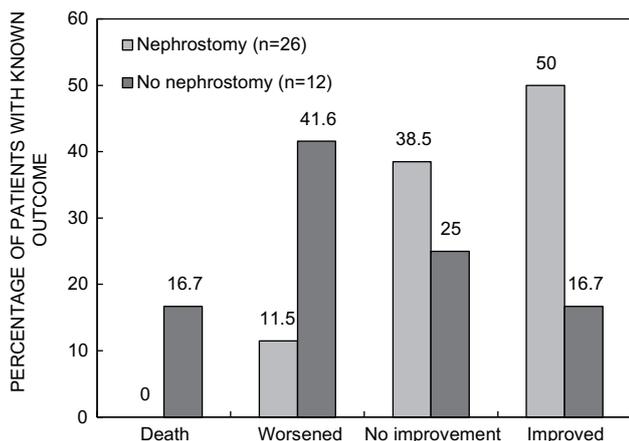


Figure 1: Renal function changes for patients with known results.

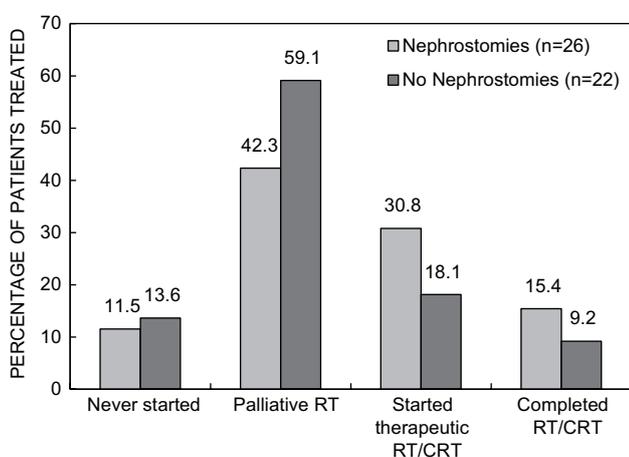


Figure 2: Cancer treatment outcome in patients with known treatment.

Treatment initiation, therapeutic intent and treatment completion

Comparing the two groups in relation to treatment of the primary cancer, in the nephrostomy group this information was not known for two (7.1%) patients and in the no-nephrostomy group for four (15.4%) patients. In the group of patients who received PCN, 11 of the 26 patients where information was available (42%) received and completed palliative radiotherapy. Five (19.3%) patients started therapeutic radiotherapy (RT) and three (11.5%) patients started CRT. Only four (15.4%) completed therapeutic RT/CRT.

In the group of patients where nephrostomies were not done, 13 (59.1%) of the 22 patients received palliative radiotherapy, four (18.1%) patients started CRT and two (9.2%) completed therapeutic RT/CRT. Three (13.6%) patients never started treatment (see Figure 2).

Disease outcome

Disease response was not known for 11 (39.3%) patients who received PCN and 15 (57.7%) patients who did not receive nephrostomies. In the nephrostomy group 12 (70.6%) of the 17 patients died from the disease. Five (29.4%) patients were reported to have a partial response. Ten (90.9%) of the 11 patients that did not receive nephrostomies died from the disease and one patient (9.1%) had a partial response to treatment.

Factors affecting the decision to offer PCN and curative intent

Through statistical analysis the following factors influenced the decision to offer a patient a nephrostomy: the FIGO stage of the disease ($p = 0.055$) and the urea ($p = 0.02$) and creatinine ($p = 0.01$) levels in deciding on this intervention. Age and HIV status were not significant and potassium levels also seemed to have no impact. Through applying logistic regression analysis, stage of the disease ($p = 0.09$) was a major factor affecting the decision to offer curative treatment.

Discussion

Ureteral obstruction with resultant renal failure is associated with poor survival of cervical cancer patients and is thus an ominous sign. Median survival duration of such patients ranges from three to 12 months. Urinary diversion has been used to bypass the ureteric obstruction.⁸ The reason for this intervention includes avoiding complications of renal insufficiency or allowing the opportunity of treatment to improve life expectancy or improve symptoms of disease progression.⁹

Socio-demographics

In this study the mean age of the entire study population was 49.5 years, which is comparable to two other studies where the mean age was 45.9 years and 48.2 years respectively.^{8,10} Some 22% of women in this study were younger than 40 years. Due to the high burden of HIV in South Africa, cervical cancer commonly affects younger women; however, half of the women below the age of 40 in this study with cervical cancer were HIV negative.

The importance of age in relation to successful PCN insertion was reported to be a significant factor. Better survival and lower hospital mortality rates were observed in patients aged 52 and less because of better metabolic reserve and response to treatment, whereas other studies failed to show statistical significance in survival outcome in patients below 65 years.¹¹

Renal function

In this study, 50% of patients who received PCN had an improvement in renal function. In a Serbian study in 2010, Plesina-Karapandzic *et al.* reported renal function completely normalising in 24.8% of patients and partial improvement in 68.8%.¹¹ A possible explanation for the lower rate of improvement in our study may be the fact that most of the patients already had severe renal impairment, whereas the Serbian study included patients who still had normal kidney function (20.1%). In the Serbian study, improved overall survival was seen in patients without abnormal renal function, which was statistically significant. Uraemia was the cause of higher mortality and, to avoid this, percutaneous nephrostomy should be placed prior to such complications.¹¹

Furthermore, in our study, the majority of patients had creatinine levels between 100 and 500 $\mu\text{mol/l}$ post-intervention, although the exact levels and day 3 post-intervention results were not completely recorded. A study done in Japan in 2011 by Lapitan and Buckley indicated an improved outcome with creatinine levels less than 150 $\mu\text{mol/l}$ at two weeks and three months after intervention. There was a statistically significant reduced risk of death within 12 months.⁸

The Serbian study indicated that the median survival time for patients with ureteric obstruction and normal renal function was 16 months, 12 months for patients with completely recovered renal function after percutaneous nephrostomy and five months

for patients with persistently raised creatinine levels. In patients without deterioration of renal function and initial azotaemia, higher overall survival was observed. It seems that there will be an improved outcome if ureteric obstruction is relieved prior to deterioration in renal function.¹¹

Complications

Although the percutaneous nephrostomy technique is known to be a safe and fast procedure with low complications, severe complications could occasionally occur, with financial implications and increased healthcare hours. Severe complications, although rare, include bowel injury and pneumothorax. Serious complications, also rare, include perirenal abscesses, pyelonephritis and urinoma.⁹

In this study, the complications of nephrostomies were not regularly reported on or documented. No infections or nephrostomies that fell out were reported and no major complications occurred. Due to the high incidence of HIV it would be expected that the resultant sepsis rate would be higher, but no cases of sepsis were reported. A possible explanation might be that the follow-up period of patients with nephrostomies was too short to detect this complication. Catheter blockage was the major problem in our setting.

Outcome

Outcome in terms of the primary cancer can be viewed by looking at the intention to treat the patient and the disease response to treatment. In both groups, just over 10% of patients never started treatment. The prognosis for patients with malignant obstructive uropathy is dismal at best and, despite alleviating the obstruction, the average survival duration is reported as 120 days.¹²

A Pakistani study by Jalbani and colleagues indicated a 24-month survival benefit in patients who have not yet been treated for the primary cancer.¹³ Different studies show varied results in correlation with survival following decompression of ureteric obstruction secondary to gynaecological cancers.^{10,12}

In the non-nephrostomy group, patients are clinically better before receiving radiotherapy/chemo-radiation in terms of stage of disease, renal function and presence of unilateral hydronephrosis. One would thus expect more patients receiving therapeutic radiotherapy/chemo-radiation, more patients completing therapy and overall better survival. But results indicate the opposite. The patients in the nephrostomy group are initially worse, but are advantaged by receiving the drainage procedure. So much so that they even have a better outcome than the 'control' group.

Limitations of the study

To our knowledge this is the first study of this nature in South Africa and definitely the first of its kind at our oncology unit. The study is limited by the retrospective nature of the audit and low patient numbers. Lack of short- and long-term follow up data was a major limitation. As information was retrieved from patients' records it led to non-response and selection bias in this study. The findings from our analysis only apply to patients from our unit and it is difficult to compare with other units where healthcare resources are more readily available and less of a challenge.

Conclusion

Nephrostomy insertion in patients with cervical cancer with obstructive uropathy, even if they are HIV positive, was shown to

be a safe procedure with minimal complications. An improvement in renal function was shown after insertion. It improved the number of patients qualifying for initiation of treatment and completing treatment.

Although our numbers are small in this study and the follow-up data poor, the group of patients with renal impairment who did not receive nephrostomies frequently had worsening in renal function. Many patients did not initiate or complete treatment and often received only palliative therapy with a resultant poor outcome. This is unexpected, since the patients in this group are clinically better in many aspects in comparison with the group that received nephrostomies. Studies are needed to investigate whether relieving obstruction through ureteric stents or percutaneous nephrostomies, in patients with obstructive uropathy and mild renal impairment, will improve disease outcome.

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