Percutaneous nephrostomy in the management of advanced and terminal-stage gynecologic malignancies: outcome and complications

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Summary

Purpose: The goal of the study was to evaluate the outcome and complications after percutaneous nephrostomy (PCN) insertion in advanced and terminal-stage gynecological malignancies with ureteral obstruction (UO). *Materials and Methods:* We analyzed data of 117 patients with UO due to gynecological malignancies, who had undergone PCN between 1996.and 2006. Cervical cancer was evidenced in 108 patients, uterine carcinoma in six and ovarian cancer in three patients. Eighty-nine had UO at the initial manifestation of the disease, 22 had persistent or recurrent cancer, and six were disease-free after initial therapy. Oliguria was observed in 22.2% and creatine elevation in 79.5%. Mean follow-up was 11.43 months (range 0-112). *Results:* The median age was 51 years (range 28-85). Bilateral nephrostomy was performed in 36.7% and unilateral in 63.3%. Renal function normalization occurred in 24.8%. Overall two-year survival (OS) was 16.8%. Higher OS occurred in patients without initial azotemia versus those with azotemia (26.8% vs 13.9%). Median survival time for all the patients was seven months, eight in primary cases versus six in recurrent ones, and eight months in patients after initial therapy. Complications appeared in 53.85%. Most frequent were the loss of the nephrostomy catheter in 37.61% and urinary tract infections in 19.6%. Conclusion: Improvement of renal function after PCN can be of clinical benefit in patients who might be cured or for prolonged palliative care. Azotemia seems to be poor prognostic sign.

Key words: Gynecologic malignancies; Percutaneous nephrostomy.

Introduction

Advanced malignant disease localized in the organs of the pelvis and retroperitoneum (uterine cervix, prostate, urinary bladder, ovary) in a fourth of cases progresses to acute obstructive uropathy. Local spreading or pelvic metastases by extramural compression or direct ureter invasion has caused hydronephrotic atrophy, renal failure and secondary uremia. The diagnosis and level of UO may be confirmed by ultrasound, computerized tomography or other appropriate radiological procedures. If the UO was not immediately relieved, the final results would be water -electrolyte abnormalities and subsequent death of patients [1-5].

The most widely used techniques in relieving UO are endoscopic insertion of ureteral stents and percutaneous nephrostomy (PCN). Insertion of ureteral stents may be technically impossible in cases with anatomic deformities, compression or bleeding [2, 3]. PCN is a safe and effective method either as the primary option or an alternative procedure and can provide rapid, almost immediate renal function improvement [1, 6]. As a method of supravesicular urine derivation, since the time of Goodwin's description of this technique (1955), over a period of a few decades PCN has been the method of choice especially in the treatment of UO caused by gynecological malignancies [7-9]. Despite many benefits of the method, overall survival rate and quality of life in patients with advanced or metastatic disease are still subjects of investigations [10]. The total morbidity with prolonged agony caused by existing malignancy and exhausted treatment options has significantly increased treatment costs and consumed additional health care hours [6, 11]. These facts show the complexity of determining the indication for PCN and solving the problem from the point of an emotional, ethical and oncological dilemma.

The aim of this retrospective study was to evaluate the outcome and complications after PCN insertion in patients with advanced and terminal stage gynecological malignancies and ureteral obstruction.

Patients and Methods

We retrospectively analyzed 117 patients with UO due to advanced and terminal stage gynecological malignancies who had undergone unilateral or bilateral PCN between 1996 and 2006. The median age was 51 years (range 28-85). The diagnosis and the primary origin of the disease were confirmed by biopsy and were as follows: cervical cancer in 108 patients, uterine carcinoma in six and ovarian cancer in three patients. Eighty-nine patients had ureteral obstruction at the initial presentation of the disease, 22 developed UO secondary to persistent or recurrent cancer and six patients were without evidence

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of the disease following some initial therapy administered. Ureteral obstruction and hydronephrosis, the grade and side, were diagnosed mostly by means of ultrasonography, computerized tomography or intravenous urography. Routine laboratory tests were performed for evaluation of renal function in all the patients and included at least BUN (blood urea nitrogen) determination, serum creatinine and potassium levels. Azotemia and creatinine elevation were observed in 93 cases (79.5%) and oliguria in 26 (22.2%). Patient follow-up varied from 0 to 112 months, with a mean of 11.43 months. Patient characteristics including stage of disease and uni- or bilateral UO are given in Table 1.

Table 1. — *Patient characteristics*.

Characteristics	No. of patients
Age (years)	
Median	51
Range	28-85
Origin	
Cervical cancer	108
Uterine carcinoma	6
Ovarian cancer	3
Stage of disease	
Stage I	8
Stage II	15
Stage III	70
Stage IV	24
Ureteral opstruction (UO)	
Unilateral	40
Bilateral	77
Type of nephrostomy	
Unilateral	74
Bilateral	43
Presentation of ureteral obstruction	
Initial disease	89
Recurrent disease	22
Complication of initial therapy	6
Elevation of creatinine	
Present	93
Absent	24

Clinical indications for PCN included radiographic evidence of high grade UO, impaired renal function with azotemia or oliguria. Due to the emergency of progressive UO or/and uremic syndrome, the patients were referred to a urologist and aggressive elimination of UO by urgent PCN was done by an intervening radiologist.

PCN was performed under local anesthesia by a standard technique (Seldinger's technique) with fluoroscopic guidance with the patient in the prone oblique position. Kidney puncture was done with a Chiba needle at the posterior axillary line towards the lower or middle calices. All patients had undergone descending pyelography in order to confirm the proper position of the catheter. A drainage catheter was left in the renal pelvis or upper ureter to drain the kidney percutaneously and it was fixed to the skin by sutures. Antimicrobials (usually trimethoprime and sulfamethoxasole) were given as prophylaxis in case of subclinical infection for at least 48 hours after the procedure, or longer. If an infection coexisted, antibiotics were administered on the basis of urine cultures obtained at the time of the procedure. The catheter was changed every six to eight weeks and in case of permanent insertion or after additional specific oncological treatment, every three months.

Follow-up evaluations and monitoring included ultrasonography, urinalyses, blood laboratory tests and routine renal function tests. We assessed and evaluated the complications after the procedure.

In case of cervical carcinoma or corresponding recurrent disease when renal function improvement and normal renal function tests were obtained, additional complementary treatment for these malignancies was done. Radiotherapy at a dose according to the initial stage or palliative treatment intent were performed in patients who were able to receive it. Data such as survival status, complications and influence of some factor related to PCN were carefully assessed.

Statistical analysis was done by Statistical Package for the Social Science (SPPSS)* software, version 10.0. Comparison of continous data was performed using the log-rank test and Kaplan-Meier's method.

Results

Bilateral nephrostomy was performed in 43 patients (36.7%) and unilateral in 74 patients (63.3%). If bilateral UO was present, a single nephrostomy was usually done in less hydronephrotic kidney with thicker renal parenchyma and obvious better renal function. In case of bilateral PCN, the puncture was done first in the kidney with high-grade hydronephrosis when it was associated with uncontrolled pain and, as the second act, puncture was done in the other kidney.

Overall two-year survival (OS) for all the patients was 16.8% and the median survival time was seven months (Figure 1).

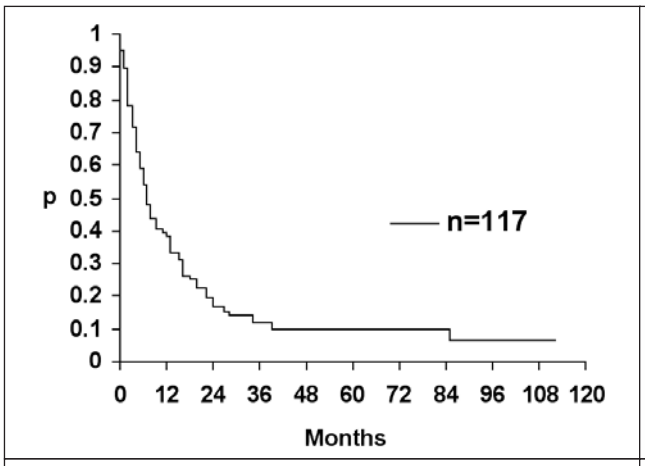
There was no statistically significant difference in survival (log-rank test, $p = 0.646$) among patients aged 65 years or less (Figure 2).

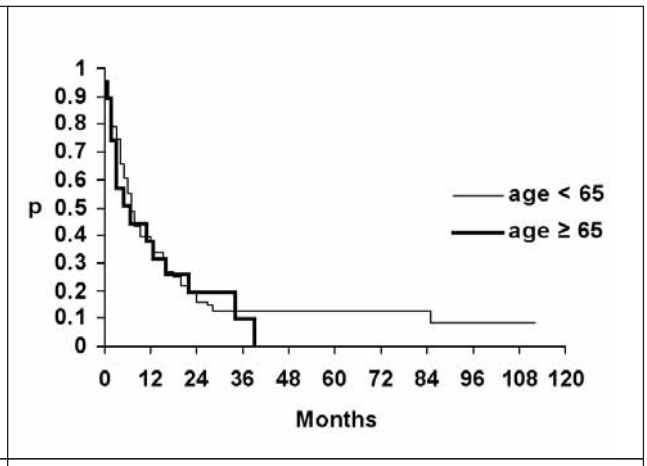
The median survival time for patients with initial primary disease was eight months versus six months in recurrent and eight months in patients after initial therapy. No statistically significant difference (log-rank test, $p = 0.256$) was found between these patient groups (Figure 3).

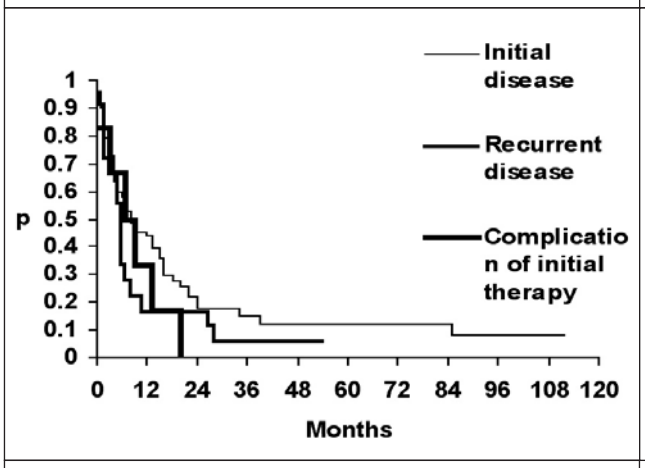
Complete normalization of renal function occurred in 29 patients (24.8%) and its improvement in the remaining 64 out of 93 patients with initial azotemia. Higher OS was observed in patients without deteriortation of renal function and initial azotemia versus those with azotemia (26.8% vs 13.9%) and the registered difference (log-rank test, $p = 0.017$) was statistically significant (Figure 4). The median survival time for patients with UO and normal renal function was 16 months and for those with completely recovered renal function after PCN, 12 months versus five months for patients with persistent azotemia.

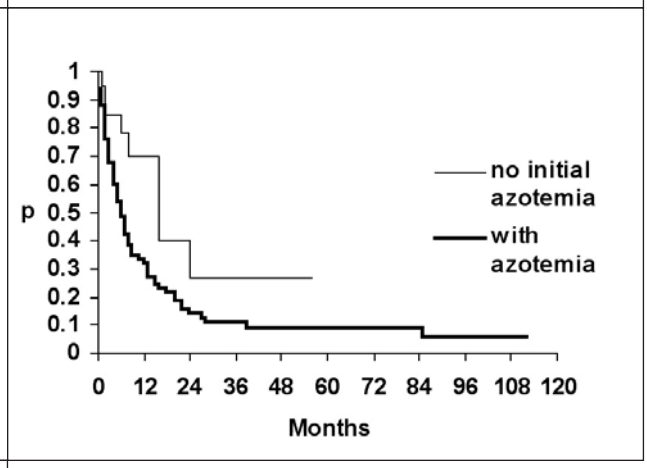
There is no advantage in performing bilateral PCN since no statistically significant difference in OS (log-rank test, $p = 0.23$) among the patients subjected either to bilateral or unilateral PCN was found (Figure 5). In the group of patients with persistent azotemia after the procedure, there was no statistically significant difference in OS after inserting either a bilateral or unilateral PCN (log-rank test, $p = 0.993$).

Complications associated with the procedure occurred in 53.85% of all the patients. Mild hematuria occurred in









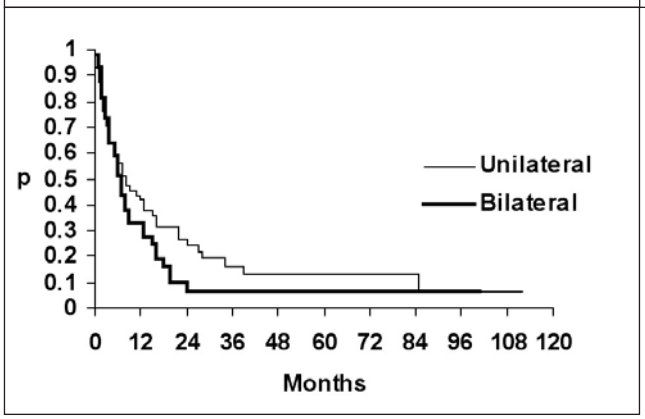


Figure 1. — Overall survival of patients with advanced gynecologic malignacies after PCN insertion.

Figure 2. — Overall survival of patients according to age.

Figure 3. — Overall survival of patients with PCN according to presentation of ureteral obstruction.

Figure 4. — Overall survival according to initial elevation of creatinine.

Figure 5. — Overall survival according to the type of PCN insertion.

all the patients but it was usually transient. Severe bleeding was not observed. The most frequent complication was the loss of the nephrostomy catheter, occurring in 37.61% of the patients and it was successfully solved by its simple replacement. Urinary tract infections were present in 19.6% and skin infections in 12.8%. These patients were treated medically by broad spectrum antibiotics. Serious complications such as perirenal abscess, pyelonephritis and urinoma were uncommon and occurred in 6.8%. Urologists participated in aggressive elimination and treatment depended on the patient's WHO performance status and life expectancy.

As a result of successful urinary diverging further definite or palliative radiotherapy was applied continously in 99 (84.6%) patients. Treatment interruption occurred in nine (7.7%) due to deterioration and progression of the disease. The treatment was applied according to the standard regimens required for stage and origin of the malignancies. Nine patients (7.7%) had no further treatment. The reasons for UO in six of them were severe complications caused by the primary treatment and in two patients no further treatment was feasible due to low performance status (PS).

Analyses of PCN outcome showed that in most cases

(71.8%), PCN remained as persistent. In 8.55% it was possible to replace it with a stent and only 19.66% of patients were without PCN.

At the time of analysis, 23 patients were alive without disease, in eight patients some signs of the primary disease were present and 86 patients died due to the primary disease.

Discussion

The experience of more than 20 years in performing PCN has made this method a world-wide accepted procedure in the treatment of gynecological malignancies related to UO. Many reports have demonstrated advantages of this method such as its simplicity (under ultrasound or radioscopic control), low price, minimal morbidity and acceptable complication rates [1, 12]. Performing this procedure improved the survival rate of these life threatened patients but at the same time uncritical application of the method was observed [10, 11, 13]. Patients with locally advanced or metastatic malignancies, quite often, even after PCN, were not considered for any further therapy. Fast progression and aggressive behavior of a tumor caused prolonged painful agony and diminished already poor quality of life [13-17].

Grabstald *et al*. reported that despite considerable selection of indications for PCN, a useful quality of life was not achieved in 32% of patients [18]. The patients with terminal stage cancer who had undergone successful PCN had a median survival time of 133 days (range 7-712), as was reported by Harrington *et al*. and an analysis of survival time showed that patients spent 50% of the time in the hospital [6, 19]. In a study by Hoe *et al*. a reasonable overall median survival of 19 weeks was reported. At the time of the review, seven out of 22 patients were alive. Seventy-seven percent of patients were able to leave the hospital after PCN, while 68% useful life [3].

In our study, two-year OS was 16.8%, with a median survival time of seven months. Better median survival time was associated with the primary presentation of the disease and in patients after initial therapy versus recurrent disease (8 vs 8 vs 6 months), but a statistically significant difference was not found. In a series of 40 patients. Barton *et al*. found that the median survival time in the primary disease was 12 months and it was similar to 9.5 months found in recurrent disease [2]. Baker *et al*. reported similar confirming survival results of six and three months for patients with primary and recurrent disease after PCN [1]. Other reports found a median survival time of seven months [20].

It was noted that the primary tumor location was a predictive factor in outcome following PCN [17]. Significantly better survival was associated with cervical and prostatic cancer and the increment was one year or more in 60% of patients [5, 21].

Patient age is quite often reported to be an important factor for successful PCN [20, 22]. Romero *et al*. observed lower hospital mortality rate and longer survival in patients younger than 52 years due to larger metabolic resources for recovery and better response to subsequent treatments [5]. In contrast, Barton *et al*. in their study found that age had no impact on survival [2]. In our cohort we did not find a statistically signifficant difference in survival among patients aged 65 years or less.

Although we have seen complete renal function recovery in only 29 patients, in all the remaining ones serum BUN and creatinine levels were improved. A statistically significant better OS was observed in patients without renal function deterioration and azotemia versus those with azotemia (26.8% vs 13.9%). Higher mortality was probably due to more severe uremic complications, and to avoid them PCN should be performed prior to development of such clinical conditions [23]. Perinetti *et al*. reported marked recovery in 13 ot of 15 patients [24]. More recent reports in the gynecological literature have demonstrated similar results [5, 22]. Renal function following PCN was improved in a cohort of Barton *et al*. in 76.9% [2]. Despite these results, Barton *et al.,* as well as some other authors, confirmed that the degree of renal failure was less important than expected [12,16].

Survival in our patients with bilateral PCN was not better and was associated with poor quality of life. In bilateral UO the side with less dilatation and greater parenchymal thickness should be considered. A similar finding and recommendations were found in other studies [2, 20, 22].

The PCN technique has been well recognized as a safe and fast procedure with low complication rates. In a few retrospective studies it was reported that, besides minimal morbidity, severe PCN-related complications could occasionally occur and, consequently, significantly increase treatment costs while consuming health care hours as well. A rare case of urinoma (usually reported to occur in less than 2%) and perirenal abscesses require more aggressive treatment and are often compromised by the patient's performance status [25, 26].

The common complications in PCN in a cohort of Dudley *et al*., were catheter blockade in 65% and infection in 70% [7]. Catheter loss and dislocation may occur in up to approximatively 40% of cases [27]. In the study of Soper *et al*. 62% of patients with antibiotic prophylaxis after the procedure had evidence of pyelonephritis [20]. Carter *et al*. did not use antibiotics in prophylaxis and IV application of antibiotics was required in 37% of patients [12]. Barton *et al*. reported only 7.5% of infections without prophylactic treatment [2].

We found that besides mild transitory hematuria, the most frequent complication was catheter loss at 37.61%. Although prophylactic antibiotic therapy was applied, urinary tract infections occurred in 19.6%. These complications were successfully treated by simple catheter replacement or antibiotic therapy.

The presence of a urinary bag as a permanent extrarenal drainage in PCN diminishes the comfort and quality of the patient's life [10, 11, 15]. In some cases, after PCN has been performed providing good biochemical response regarding azotemia and if possible to pass

ureteral compression, an internal ureteric stent can be placed [3, 28]. In our study, only in ten patients (8.55%) was PCN replaced by a stent. Dudley *et al*. found that percutaneous diverging or stent in most cases were in situ at the time of death. Similar findings have been reported by more recent studies [2,7].

The SCVIR (Society of Cardiovascular & Interventional Radiology Standards of Practice Commitee) represents the clinical practice guidelines for PCN for the purpose of improving performance, complication rates and results. It has been pointed out that the most important facts for a successful procedure are patient selection, technical performance rate, and monitoring complications [4].

Patients with advanced malignant disease and UO are mostly not suitable for radiation or other specific therapy curatively intended [16]. However, in our cohort of patients, definite and palliative treatment was mostly applied continuously in 99 (84.6%) patients. Although the complete irradiation dose was applied, the two-year survival rate of 16.8% was low thus supporting the palliative role of radiation therapy. Only 23 patients were alive without signs of the disease and eight were alive with the disease.

Tauber *et al*. retrospectively analyzed therapeutical and ethical problems after PCN in patients with persistent cancer and 42% of those patients experienced no benefit from the procedure [29]. Tumor progression in 17% patients was expected at the time of PCN. Patients who undergo PCN without improvement afterwards will have prolonged agony caused by progressive neoplasm [10, 30]. A few recent reports have indicated that the factors considered as an absolute contraindication for UO treatment are: disease progression during or immediately after the optimal therapy, inability to apply effective treatment, WHO performance status 2 or lower (3-4), presence of tumor-related problems, and uncontrolled pain during the optimal medicamentous therapy [4, 10, 11, 31]. A conservative approach in UO treatment allows peaceful dying of patients who are unsuitable for any therapy and the onset of uremia can be considered as a welcome event [23].

Finally, the active role of patients and their families in making the decision for PCN is essential. Proper information provided by physicians is necessary for the purpose of encouraging the patient to make a reasonable decision.

Conclusion

PCN is a safe and effective procedure. The improvement of renal function after PCN could be of clinical benefit for patients who might have a chance of being cured or undergoing prolonged palliation care. Azotemia seems to be a poor prognostic sign. The complexity of the matter requires that the decision about PCN should be made based on essential close cooperation and clinical assessment by a team of an oncologist, interventional radiologist and urologist. Physician responsibility in selection of cases is to establish appropriate indications concerning aggressive or conservative therapy according to the patient's characteristics. Patients with poor prognosis due to low PS, the presence of uncontrolled pain, and in whom all the primary treatment regimens failed, should be considered for the application of conservative treatment.

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