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ORIGINAL ARTICLE

# Obstructive Uropathy with Uremia due to Advanced Cervical Cancer

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## Abstract

**Purpose** Cervical cancer is a worldwide public health problem because of its high mortality rate in women with a particularly high burden in many low-income and middle-income countries because of its advanced stage at diagnosis. The aim of our study was to analyze and provide evidence on survival and complications of ureteral stent placement or percutaneous nephrostomy treatment modalities in patients with obstructive uropathy and uremia caused by advanced cervical cancer.

**Methods** A retrospective observational study including patients diagnosed with obstructive uropathy due to advanced stage of cervical cancer. The patients were divided according to the type of interventional treatment they received as follows: the ureteral stent group and the percutaneous nephrostomy group. The primary outcome is survival rates compared between groups.

**Results** A total of 28 patients were included, of whom the mean blood urea and creatinine was 86.76 ± 60 mg/dL and 6.9 ± 6.5 mg/dL, respectively. 53.3% of the patients underwent ureteral stenting and 46.4% required percutaneous nephrostomy. A total of 10 patients (35.7%) died, with an average survival of 6 (1–17) months.

**Conclusion** Patients with advanced cervical cancer and obstructive uropathy who develop uremia due to renal involvement had a poor prognosis in the disease spectrum, with an average survival of 6 months despite comprehensive management.

**Keywords** Cervical cancer · Uremia · Obstructive uropathy · Acute kidney injury · Percutaneous nephrostomy · Ureteral stent

## Introduction

Cervical cancer is a worldwide public health problem and a major cause of death, the second most frequent cause of women's death cancer in Mexico [1], 11 deaths per day are reported [2], mainly affecting 25–59-years-old females. As described, about 90% of the world's cervical cancer cases and related deaths occur in many low- and middle-income countries because of its advanced stage at diagnosis [3, 4]. The main cause of cervical cancer is human papillomavirus (HPV), which can be detected in 99.7%, particularly oncogenic subtypes such as HPV 16 and 18 [5].

Advanced cervical cancer affects regional structures causing obstructive uropathy. Rarely, obstructive uropathy can cause acute kidney injury (AKI) but leads to uremic syndrome. In these extreme situations, urgent treatments such as ureteral stent placement, percutaneous nephrostomy (PCN) and hemodialysis are required as lifesaving modalities.

We conducted a retrospective observational study to analyze and provide evidence on survival and complications of ureteral stent placement or percutaneous nephrostomy treatment modalities in patients with obstructive uropathy and uremia caused by advanced cervical cancer.

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## Methods

A retrospective observational study was carried out to analyze patients with obstructive uropathy and uremia caused by advanced cervical cancer who presented to the emergency department of the University Hospital, a tertiary center in Monterrey, Mexico, during January 2014–December 2019. Eligible patients were at > 17 years old, diagnosed with cervical cancer stage IIIB–IVA, with evidence of obstructive uropathy. Exclusion criteria were patients who did not give signed consent to participate in the study, those without any desire to receive treatment or palliative care, previous uropathy, lost to follow-up, and significant missing data in the records. Patients with obstructive uropathy were diagnosed by ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI). The patients were divided according to the type of interventional treatment they received as follows: the ureteral stent group and the PCN group. Demographic, clinical, biochemical, and radiological characteristics were recorded. The primary outcome is survival rates compared between groups. The study was approved by the ethics review board; and informed consent was obtained. The ureteral stent was placed using lidocaine gel as a local anesthetic in the form of Doble-J ureteral stent. Flexible cystoscopy was used in all procedures and, if unsuccessful, a PCN was performed. The PCN was performed by an interventional physician under ultrasound or radiographic guidance as per hospital protocol. All patients were treated according to international guidelines as advanced stage with cisplatin-based chemotherapy and external and internal radiation therapy.

All statistical analysis was performed using the Statistical Package for the Social Sciences, Version 21 (SPSS, Chicago, Illinois, USA). Student's *t* test and $\chi 2$ test were used to determine the significant difference between the groups. Differences with $p < 0.05$ were considered statistically significant.

## Results

We analyzed 28 patients with a mean age of 45 ± 11.36 years (Table 1). The main comorbidities identified were Type 2 Diabetes Mellitus and Hypertension, identified in 5 (17.7%) and 5 (17.7%) patients, respectively. The mean prior admission period of cervical cancer evolution was 22 ± 20.34 months. The most common presenting symptom was malaise and weight loss in 57% and 46% of patients, respectively. The mean blood urea and creatinine was 86.76 ± 60 mg/dL and 6.9 ± 6.5 mg/dL, respectively. Unfortunately, 60% of patients had metastatic disease on admission. The great majority of patients were having an Eastern Cooperative Oncology Group (ECOG) score of 2–3. 53.5% of the patients underwent ureteral stenting and 46.4% required PCN. The average hospitalization period was 6.64 ± 7.64 days. A total of 10 patients (35.7%) died, with a median survival of 6 (1–17) months, median follow-up was 12 months. The survival analysis showed no differences in mortality when comparing both types of treatment (long-rang test: 0.95, Fig. 1).

**Table 1** Clinical, laboratory and treatment characteristics

| Variable | Measurement |
|---|---|
| Age, years (SD) | 45.1 (± 11.36) |
| *Comorbidities* | |
| T2DM, n (%) | 5 (17.7) |
| HTN, n (%) | 5 (17.7) |
| Prior admission period, years (SD) | 22.16 (± 20.34) |
| Metastasis, n (%) | 17 (60) |
| ECOG score, median (Range) | 2 (1–3) |
| *Initial Symptom* | |
| General malaise, n (%) | 16 (57) |
| Weight loss, n (%) | 13 (46) |
| *Laboratory* | |
| BUN, mg/dL (SD) | 86.76 (± 60) |
| Creatinine, mg/dL (SD) | 6.9 (± 6.5) |
| *Treatment* | |
| Doble-J ureteral stent, n (%) | 15 (53.5) |
| Percutaneous nephrostomy, n (%) | 13 (46.4) |
| Hospitalization period, days (SD) | 6.64 (± 7.64) |
| Mortality, n (%) | 10 (35,7) |
| Survival, months, median (Range) | 6 (1–17) |

T2DM, Type 2 diabetes mellitus; HTN, hypertension; ECOG, Eastern cooperative oncology group; BUN, blood urea nitrogen

## Discussion

Obstructive uropathy is rarely caused by cervical cancer [6]; also, a late manifestation of advanced cervical cancer, a result of extrinsic ureteral compression, which can lead to AKI, uremia, or infection, with significant adverse effect on survival [7–9]. In our study, patients mainly presented with nonspecific symptoms, mean blood urea of 86 mg/dL and mean creatinine of 6.9 mg/dL. Accordingly, others have reported an increase in creatinine in 93% of patients [7]. Patients had a high frequency of metastasis.

In this report, patients affected by advanced cervical cancer and obstructive uropathy who develop AKI presents to the emergency services with a long previous period of evolution, on average 22 months. Cervical cancer is classified

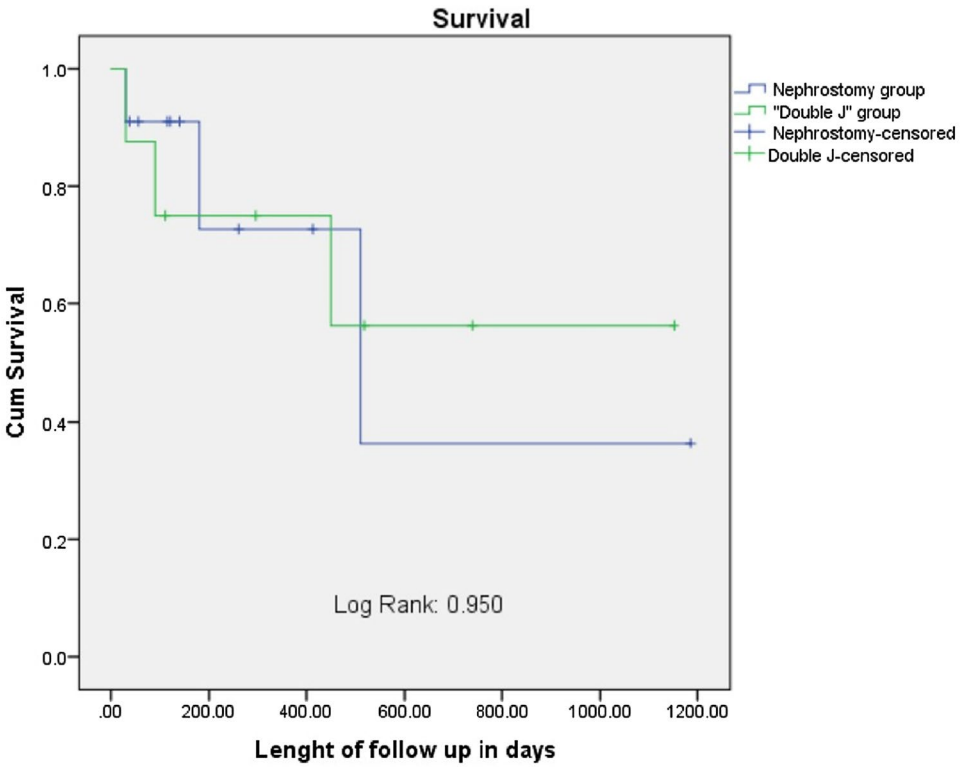


**Fig. 1** Survival analysis

in 4 stages accordingly to the International Federation of Gynecology and Obstetrics (FIGO) [10]. Specifically, cervical cancer stage IIIB is defined as tumor local extension to the pelvic sidewall or by the presence of hydronephrosis [10]. Hydronephrosis, if bilateral, may result in AKI caused by obstruction [11].

The treatment for cervical cancer includes surgery, radiation and chemotherapy, or combinations [12]. Early tumor stages (IB–IIA) generally require surgery or definitive radiotherapy; while, patients with advanced disease are usually treated with primary chemo-radiotherapy [13, 14]. Available therapies to advanced cervical cancer include ureteral stent placement, PCN, hemodialysis, and conservative treatment. Currently, placement of a ureteral stent is the treatment of choice in hydronephrosis secondary to advanced cervical cancer [15], due to a high successful stenting rate, reported as 82.6–97.5% [15]; also, less time and resource consuming [15, 16]. Factors associated with high success rate for ureteral stent placement are mild hydronephrosis and < 4-cm-long ureteral obstruction [15]. Evidence showed the PCN success rate is 100% [15]. Although the PCN method has a high success rate, patients need an external drainage bag, thus, quality of life is worse, management is less convenient compared to the ureteral stent placement and there is poor patient compliance. Complications associated with PCN occurred in 5–53.85% of all patients [6, 7]. The most frequent complications were the loss of the nephrostomy catheter and urinary tract infections [7].

Conservative treatment should be implemented to patients with poor prognosis such as low performance status, uncontrolled pain, failure to primary treatment regimens.

Unfortunately, in our study advanced cervical cancer patients with hydronephrosis and uremia had a high mortality (35.7%) rate; similarly, others have reported the overall 1- and 2-year survival was 22.2 and 16.8%, respectively [7]; with a median survival of 7 months [7], like our reported data of a median survival of 6 months. Accordingly, Alawneh et al. [17] reported that the median survival in patients with malignant ureteric obstruction was 5.05 months (95% CI 3.87, 7.11; range 2–963 days).

In our study, there was no difference in mortality between therapies; however, evidence is controversial. The 12-month survival in the diversion group was not greater than patients who did not receive diversion [8]; diversion was associated with 12-month survival of 22% [8]. In recent series, the 2-year survival rate in urinary diversion group (48.0%, 12/25) was better than hemodialysis group (0%, 0/20), but no statistical difference when comparing with the PCN group (21.7%, 5/23) ($P > 0.05$) [18]. Others have reported that advanced cervical cancer patients with obstructive uropathy had an overall survival of 21 weeks, and the 12-month survival rate is 22% [8]. Patients with risk factors, such as low serum albumin, presence of pleural effusion and bilateral hydronephrosis have a short survival time [17]. Similarly, Plesinac-Karapandzic and col. reported a 2-year overall survival of 16.8% and a mean survival of 7 months. In that case

series, 93% of the patients had renal injury; interestingly, higher overall survival was reported in patients without initial renal involvement versus those with uremia (26.8 vs 13.9%, log-rank test, $p = 0.017$) [7].

Interestingly, the presence of uremia is a poor prognostic factor in this clinical scenario [7]. Patients with ECOG scores > 1 and > 3 events related to malignant dissemination had poor prognosis when malignant obstructive uropathy appeared; when these two factors are present, they have an overall survival of < 10% at 1 year [19]. Quality of life scores seemed to not differ between the patients who underwent diversion than those who did not [8].

Our data have some limitations such as small sample size, its retrospective design, and data source from a single center. Thus, a multicenter prospective study should be conducted to include more patients.

In conclusion, patients with advanced cervical cancer and obstructive uropathy who develop uremia due to renal involvement had a poor prognosis in the disease spectrum, with an average survival of 6 months despite comprehensive management.

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## Declarations

**Conflict of interest** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

**Ethical Approval** The study was reviewed and approved by the Ethics Review Board of Hospital Universitario Dr. José Eleuterio González.

**Consent to Participate** Informed consent was obtained from all individual participants included in the study.

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