

## Clinical Presentation and Management of Urological Complications of Advanced Carcinoma Cervix

<sup>1</sup>L.S. Patil, <sup>2</sup>Gayatri L. Patil, <sup>3</sup>Veerendra H.S., <sup>4</sup>Rajashri Patil, <sup>5</sup>Vijayanath.V

**Author's Affiliation:** \*Professor, Dept of Surgical Oncology \*\* Professor, Dept of OBG,\*\*\* Associate Professor, Dept of Urology,\*\*\*\* Statistician, Dept of Community Medicine, S.S. Institute of Medical Sciences and Research Centre, Davangere, Karnataka,\*\*\*\*\* Professor, Dept of Forensic Medicine & Toxicology, Vinayaka Mission's Kiupananda Variyar Medical College & Hospital, Salem-636308, Tamil Nadu.

**Corresponding Author:** Dr. L.S. Patil, Professor, Deptt. of Surgical Oncology, S. S. Institute of Medical Sciences & Research Centre, Davangere-577005, Karnataka.

E-mail: ssimsr1@gmail.com

### Abstract

**Introduction:** Over 70% patients with cancer cervix present in advanced stages of the disease with coexisting urological complications like obstructed uropathy. **Objectives:** To determine the clinical profile of patients with urinary complications of advanced cancer cervix and the clinical outcome of the various therapeutic options administered. **Material and Methods:** In this study, 93 patients with advanced cancer cervix previously treated or untreated, who had obstructed uropathy were evaluated to know the type of urological complications, their management and their effect on the primary disease. Various methods of urinary reconstruction were tried and the clinical outcomes of these approaches were retrospectively analyzed. **Results:** A total of 93 patients included in the study, 37 (39.78%) were uraemic at presentation, majority of them being in stage II B of carcinoma cervix with 59 cases (63.44%) having bilateral obstruction. Of the 93 patients, 51 (54.83%) underwent surgical urinary diversion. Stenting was done in 86 (86.02%) cases, 15 (29.14%) had percutaneous nephrostomy, ileal conduit in 20 (39.21%), ureterosigmoidostomy in 8 (15.68%) cases, 8 patients had pelvic exenteration. 11 patients (11.82%) died before intervention. Outcome following urinary diversion procedure was poor, with 30 (58.82%) showing no clinical improvement. Complications following diversion procedures were detected late and were troublesome. **Conclusion:** Advanced cancer of the cervix leads on to obstructive uropathy, presenting as uraemia. Various urinary diversion procedures are useful in improving renal function, followed by definitive treatment options. At times they serve as life saving procedures.

**Keywords:** Obstructive uropathy; Advanced cancer cervix; Urinary diversion.

### Introduction

There is a high prevalence of urological complications among women with advanced cervical cancer, these complications are significantly correlate with the stage of cervical cancer.

Cervical cancers show locoregional invasion and metastasis. Tumor persistence or recurrence within the pelvis is the major cause of death in these patients. Patients with advanced or recurrent disease frequently develop infiltration of neighbouring organs like urinary bladder, ureter, intestines resulting in urinary complications including obstruction, fistula formation, uraemia or intestinal obstruction with ileus and fistula formation.

The most common presenting symptoms were anuria or oliguria, flank pain, dyspnea, leg edema and body malaise.

Urinary complications associated with advanced carcinoma cervix, lead on to uraemia and its debilitating effects pose a threat to the patient's life.

Predisposing factors for urinary tract complications include distorsion of the pelvic anatomy by adhesions due to previous surgeries, radiation therapy or pelvic inflammatory disease.

The stage of underlying malignancy, obesity, diabetes mellitus and postoperative infection

are other predisposing factors for urinary tract complications.

Anatomically, the terminal segment of the ureter is in close proximity to the cervix. So cervical cancer could lead on to initial hyperemia, later on compression or angulation of the ureter due to parametrial involvement. [1]

Involvement of the urethra, abdominal portions of the ureters and the kidneys is usually a secondary phenomenon, either due to infiltrating malignancy or back pressure changes. [1]

Patients can present clinically with incontinence of urine, dribbling of urine due to vesicovaginal, ureterovaginal or rectovaginal fistulae leading on to uraemia, lower urinary tract obstruction progressing to bilateral hydronephrosis, bilateral limb edema, recurrent urinary tract infections, bladder calculus, haematuria, pyuria, atonic bladder function and so on. [1]

Patients need to be investigated with basic renal function tests serum electrolytes, cystoscopy, abdominopelvic ultrasound, computed tomography and intravenous pyelography to diagnose the severity of the condition. Cystoscopy is crucial to locate the site, size of the fistula in the bladder. [2]

Various forms of diversions are tried to relieve urinary tract obstruction with rapid restoration and salvage of renal function.

Unilateral or bilateral ureteral stents have been used to relieve ureteral obstruction, inserted under cystoscopic guidance, retained for short or long term duration. Serious complications like catheter (stent) migration or dislodgement, penetration into the surrounding structures, coiling within the ureter are seen in 4% of patients while minor complications like bleeding, infection are seen in another 10% of patients. [2]

In cases where stenting is not possible, percutaneous nephrostomy is tried. During this procedure, a tube is placed through the skin at the back into the area of the kidney that collects urine. The tube may be connected to an external drainage bag.

Urinary diversion with an ileal conduit, uretero sigmoidostomy, or a neobladder formation is tried, followed by palliative chemotherapy would be the choice in vesicovaginal fistulas as repair of these fistulas can lead to poor healing. [3]

Partial or total cystectomy followed by urinary reconstruction by bladder flap repair, ileal ureter, ureterouterostomy is tried in selected cases.

Pelvic exenteration is a salvage procedure performed for centrally, recurrent gynaecologic cancers. The procedure involves en bloc resection of all pelvic structures including the uterus, cervix, vagina, bladder and rectum, with an operative mortality of 3.5% [2] with major perioperative morbidity rate of 30-44%. [2] It would be more of a palliative procedure for the control of local disease. However distant metastasis, bowel involvement are contraindications for the procedure. Determination of the extent of resection is based on sidewall involvement, infralevator versus supralevator and anterior versus posterior versus total exenteration with pelvic exenteration, with 5 year survival rates of 40% or more depending on the individual patient selection criteria. [4]

The clinical triad of leg edema, ureteral obstruction and leg pain, is almost pathognomonic for disease extending to the pelvic side walls. [4]

Reported complications of the various urinary diversion procedures include leakage of urine, pyelonephritis leading on to hydronephrosis. [5]

The management of advanced cancer cervix has to be individualized, taking into account the extent of bladder involvement, parametrial infiltration, renal function and patient performance. [5]

Chemotherapy or concurrent chemoradiotherapy, palliative radiotherapy/ chemotherapy followed by pelvic exenteration supported with a good palliative care would be the choice for patients who can tolerate the surgical procedure.

However, patients with poor general

condition, extensive local disease like fistulae, symptoms of uraemia etc., can be best offered supportive/palliative care.

A few patients do develop urinary complications following radiation therapy. These complications tend to occur 6-18 months after radiation therapy. Tissue injury can lead to direct mucosal necrosis, submucosal fibrosis, regional devascularization, ischaemia and fibrosis of surrounding connective tissue leading to fistula formation, ureteral stricture, periurethral fibrosis with secondary obstruction and contracted bladder.

### Material and Methods

This study was conducted at the surgical oncology department, SS Institute of Medical Sciences and research centre, Davangere, Karnataka, during a 6 year period (Jan 2006-Dec 2011).

A retrospective analysis of clinical records of in-patients with a primary diagnosis of advanced cancer cervix treated or untreated with coexistent obstructive uropathy were retrieved.

A total of 93 patients were included in the study.

#### *Inclusion Criteria*

- Women with advanced cancer cervix (by FIGO staging) treated or untreated with urological complications were included.
- Abnormal renal parameters.
- Structural abnormality on radiological investigations.
- Urinary symptoms with or without uraemia.

#### *Exclusion Criteria*

- With urinary stones.
- Diabetic neuropathic bladder with secondary vesicoureteric reflux.
- Ureteropelvic junction stenosis.

### Methodology

A total of 93 advanced cancer cervix patients were evaluated.

Proper history regarding duration of disease, treatment taken in the form of surgery, chemotherapy or radiotherapy was elicited in detail.

Patients were examined clinically for general condition, stage of disease, recurrent or residual disease as well as for any fistula formation.

Patients were then investigated with urine analysis, renal function tests, complete blood count, X-ray chest, ultrasonography of abdomen and pelvis to look for hydronephrosis, hydroureter and measure the tumor volume. Special investigations for urinary system evaluation were done as relevant, e.g. Intravenous pyelography, cystoscopy, CT scan, nephrocystogram.

Various treatment options were discussed with the attenders and then an informed consent was taken. Ureteral stenting, urinary diversion by percutaneous nephrostomy, cystectomy with neobladder formation or an exenteration procedure would then be decided depending on the clinical presentation and patient's condition. Following urinary reconstruction a few patients underwent definitive treatment. A small number of patients required dialysis following a ureteral stenting.

### Results

The different types and incidence of malignancy, laterality of ureteral obstruction, various urinary diversions used and the therapeutic outcome of each were summarized and tabulated. The cause of death of the patients who died after diversion were also noted. Finally, the complications encountered were analysed.

A total of 93 patients had metastatic ureteral obstruction. The mean age of patients in the study group was 30-65 years and urological complications were commonest in the 45-50 years age group.

**Tables 1: Laterality of Ureteral Obstruction**

Primary malignancy	No. of Patients		Total No. of Patients
	Bilateral (%)	Unilateral (%)	
Cervical	27 (33.75%)	53 (66.25%)	80

**Table 4: Causes of Death of Patients with Malignant Obstruction after Urinary Diversion**

Cause	No. of patients (%)
Pulmonary congestion	1 (5%)
Sepsis	12 (60%)
Liver metastasis	2 (10%)
Urosepsis	1 (5%)
Pulmonary metastasis	2 (10%)
Skin metastasis	2 (10%)

**Table 2: Various Types of Urinary Diversions Used**

No. of patients	Retrograde stenting (%) 80		Percutaneous nephrostomy (%) 15		Percutaneous nephrostomy + antegrade stenting (%) 6		Surgical diversion (%)		Percutaneous nephrostomy + retrograde stenting (%) 9		Exenteration procedures 8	
	Bilateral	Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Ileal conduit	Uretero sigmoido	Bilateral	Unilateral	Anterior	Total
	51	60 (75%)	20 (25%)	15 (29.41%)	0	6 (40%)	0	20 (39.21%)	8 (15.68%)	5 (55.55%)	4 (44.44%)	5 (9.80%)

**Table 3: Clinical Outcome of Patients Following Diversion Procedure**

No. of patients	Clinically improved (%)	Clinically unimproved (%)	Requiring dialysis % at presentation	Requiring dialysis postop	Died
51	21 (41.17%)	30 (58.82%)	15 (40.54%)	1 (0.51%)	11 (11.82%)

**Table 5: Complications of Urinary Diversions**

Type	Complications	Number of patients (%)	
1) Percutaneous nephrostomy	Dislodgement	3 (20)	
	Urosepsis	5 (33.33)	
	Urinary leak	2 (13.33)	
	Clogged tubes	3 (20.0)	
	Failed insertion of double J stent	0	
2) Retrograde stenting (n = 9)	Open nephrostomy	-	
	Ureterosigmoidostomy	-	
3) Surgical diversions (n = 28)	Ileal conduit	-	
	Hydronephrosis	2 (7.14%)	
	Prolonged ileus	-	
	Sepsis	-	
	Stoma necrosis	5 (17.85%)	
	Urinary leak	-	
	4) Exenteration procedure Anterior (n = 5)	Faecal peritonitis	2 (33%)
		Sepsis	1 (12.5%)
		Electrolyte imbalance	5 (62.5%)
		Leak	2 (33.33%)
Recurrence		1 (12.5%)	
Total (n = 3)			

Of these 93 patients, 37 (39.78%) were uraemic at the time of presentation and 56 (60.21%) had no uraemia on investigations.

Majority of the patients 37 (39.9%) belonged to stage IIB, (FIGO staging carcinoma cervix) while 33 (35.5%) were in stage IV and 23 (24.6%) belonged to stage III B.

The most common presenting symptoms were anuria or oliguria, flank pain, dyspnea and leg edema and body malaise. The mean admitting creatinine level was 6.2 mg/dl.

Patients diagnosed for the first time simultaneous with obstructive uropathy at admission were 37 (39.9%), while 56 (60.2%) cases were previously diagnosed cases who had received some form of treatment, be it surgery, radiotherapy or both.

About 59 cases (63.44%) and 34 cases (36.55%) had bilateral and unilateral obstruction respectively.

#### *Urinary Diversions*

Of the 93 patients, a total of 51 (54.83%) underwent urinary diversion. A preliminary cystoscopy with stenting was done in 80 (86.02%) of the total 93 cases, out of the 51 patients who underwent urinary diversion, 15 (29.14%) underwent percutaneous nephrostomy along with retrograde insertion of double J stents being successful in 9 (60%), of these patients, 5 (55.55%) had bilateral insertion and 4 (44.44%) had unilateral insertion.

Percutaneous nephrostomy along with antergrade stenting was successful in 6 (40%) of the 15 patients who had percutaneous nephrostomy.

Ideal conduit was performed in 20 (39.21%), ureterosigmoidostomy was done in 8 cases (15.68%), 5 patients (9.80%) underwent anterior pelvic exenteration, whereas 3 patients (5.88%) had a total pelvic exenteration.

Of the total 93 patients, 51 patients underwent some form of urinary diversion, 24 patients (25.80%) were not diverted due to various reasons and most of them just had a

stenting procedure done. 11 cases (11.82%) died before any intervention and 7 cases (7.52%) refused treatment, and finally 75 patients were eligible for analysis.

Of the 37 patients who presented with uraemic signs 15 (40.54%) needed dialysis support as they had signs of uraemia, pulmonary congestion, hyperkalemic or encephalopathy.

Of the 51 patients who underwent some form of urinary diversion procedure, only one patient (1.96%) needed dialysis support in the postoperative period.

On comparing the outcome, a total of 21 (41.17%) had clinical improvement, while 30 (58.82%) had no clinical improvement and later 21 (41.17%) succumbed to death.

Clinical improvement was manifested by good urine output from the nephrostomy tubes, decreasing creatinine levels and overall subjective relief of symptoms like loss of flank pain etc.

Among the 51 patients (54.83%) about 21 (41.17%) patients with obstructed uropathy were treated by urinary diversion procedure later received radiotherapy or chemotherapy and those unwilling for any definitive treatment just received symptomatic palliative treatment.

#### *Various Causes of Death*

Considering the 51 patients who underwent urinary diversion, 20 patients (39.21%) died of multiple organ failure secondary to complications of metastatic disease to the liver, lungs, mediastinum and intraabdominal carcinomatosis, of which 12 (60%) died of septicemia.

#### *Complications of Urinary Diversion*

Of those who underwent percutaneous nephrostomy (n = 15) dislodgement occurred in 3 (20%), urinoma in 5 cases (33.33%), leak in 2 (13.33%) clogging in 3 (20%), sepsis in 5 cases (33.33%), fistulae and stone formation in 3 cases (20%), incontinence in 5 (33.33%),

hydronephrosis and renal unit loss.

Patients were followed up once a month for symptoms and renal reconstruction method was reassured, though followup was possible for a 5 year duration, however many of them did not come for followup.

Patients (n=15) who underwent percutaneous nephrostomy along with antegrade (n=6, 40%) or retrograde stenting (n=9, 60%, of which 5(55.55% were bilateral and 4(44.44%) were unilateral procedures) done simultaneously.

## Discussion

Cervical carcinoma is the commonest genital malignancy in our country. Lack of proper screening procedures, poor literacy and ignorance do contribute to the delay in diagnosis of cancer cervix.

Close proximity of the lower urinary tract with the cervix, are prime factors for the early involvement of renal system in advanced cancer cervix.

Stage of the disease does play an important role, stage II B onwards risk of urological involvement definitely increases and various authors have found that advanced stage of the disease was significantly associated with urological complications.[6]

As spread to adjacent organs is related to the pathogenesis of cervical malignancy, 59 cases (63.44%) had bilateral involvement, as compared to Benito *et al*[3], 73% of cases had bilateral involvement.

In our study, urological complications were common in the 45 – 50 years of age group, as similar results are reported by Prajapati *et al*.[7]

About 39.78% of patients had uraemia at the time of presentation as compared to Atuhairwe *et al*, who had a 17% incidence of uraemia.[6]

A total of 51 (54.83%) underwent some form of urinary diversion procedures like 15

(29.14%) had percutaneous nephrostomy and 5 (55%) of them benefited with bilateral stenting. Hyppolite *et al*[8] in his study found bilateral nephrostomy superior to unilateral nephrostomy.

In our study, ileal conduit was done in 20 cases (39.21%), ureterosigmoidostomy in 8 cases (15.68%), urosepsis and prolonged ileus (7.14%) were troublesome complications following this surgery. Harade *et al*[9] has reported complications such as ineffective drainage (12.5%) and sepsis (10.5%) following similar procedures.

In the present study, 8 cases (15.68%) with locally advanced cancer cervix had an exenteration procedure. The procedure does carry morbidity risks and moreover the mean survival rates of patients with advanced malignancy are low. Fecal peritonitis (33%) and electrolyte imbalance (62.5%) were troublesome complications in our study group. Pawlik *et al*[10] and Houvenaeghal *et al*[5] have reported fewer complication rates, in their large series of cases. The role of the urological surgeon in extended surgical procedures is potentially important.

On analyzing the clinical outcome of patients following urinary diversion, about 41% of patients showed some improvement but 58.82% had poor improvement.

Although the various procedures help in improving the quality of life of the patients, allowing them to be eligible for subsequent definitive treatment and prolonging life. Palliative diversion should be the choice only after a reasonable expectation of prolonged survival is judged to be feasible.

## Conclusion

Advanced cancer of the cervix is commonly associated with a high prevalence of urological complications leading on to obstructed uropathy with uraemia with risk of impending irreversible renal damage. Urinary diversion

procedures help in improving the renal function and the quality of life for the patient.

### References

1. Hopkins MP, Morley GW. Prognostic factors in advanced stage squamous cell cancer of the cervix. *Cancer*. 1993; 72(23): 89-93.
2. Lau MW, Temperley DE, Mehta S. Urinary tract obstruction and nephrostomy drainage in pelvic malignant disease. *Br J of Urol*. 1995; 76(5): 565-9.
3. Benito J, Abraham, Abelardo M. Prodigalided. Palliative diversion for metastatic ureteral obstruction. *Urol J*. 1996; 1-6.
4. Marnitz S, Kohler C, Muller M. Indications for primary and secondary exenterations in patients with cervical cancer. *Gynaecologic Oncol*. 2006; 103(3): 1023-30.
5. Houvenaeghel G, Moutardier V, Karsenty G et al. Major complications of urinary diversion after pelvic exenteration for gynaecologic malignancies; a 23 year mono institutional experience in 124 patients. *Gynaecologic Oncol*. 2004; 92(2): 680-3.
6. Atuhairwe S, Busingye R, Sekikubo M. Urological complications among women with advanced cervical cancer at a tertiary referral hospital in Uganda. *Int J of Gynaecol and Obstet*. 2011; 1-6.
7. Prajapati K, Dave K, Doshi H. Obstructed uropathy in cancer cervix. *Indian J of Gynaecologic Oncol*. 2011; 10(1): 25-28.
8. Hyppolite JC, Daniels ID, Friedman EA. Obstructive uropathy in gynaecologic malignancy: Deterimental effect of intraureteral stent placement and value of percutaneous nephrostomy. *ASAIOJ*. 1995; 41(3): 18-23.
9. Harade K, Sakai I, Muramaki M. Reconstruction of urinary tract combined with surgical management of locally advanced non urological cancer involving the genitourinary organs. *Urol Int*. 2006; 76(1): 82-86.
10. Pawlik TM, Skibber JM, Rodrigues B. Pelvic exenteration for advanced pelvic malignancies. *Annals Surgical Oncol*. 2006; 13(5): 612-23.

**Red Flower Publication Pvt. Ltd,**

***CAPTURE YOUR MARKET***

**For advertising in this journal**

**Please contact:**

**International print and online display advertising sales**

E-mail: redflowerpppl@vsnl.net / tel: +91 11 22754205, 45796900

**Recruitment and Classified Advertising**

E-mail: redflowerpppl@vsnl.net / tel: +91 11 22754205, 45796900

**Disclaimer** The opinion in this publication is those of the authors and is not necessarily those of the Indian Journal of Cancer Education and Ressearch , the Editor-in-Chief and Editorial Board. Appearance of an advertisement does not indicate IJCER approval of the product or service.