Cancer Association of South Africa (CANSA)

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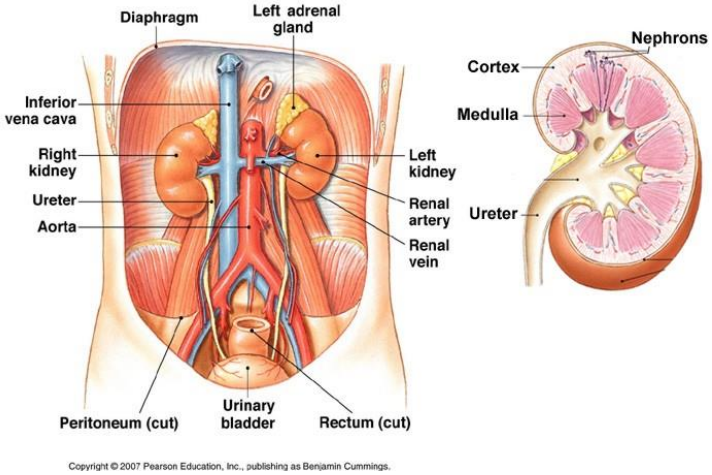
Fact Sheet
on
Ureteral Cancer

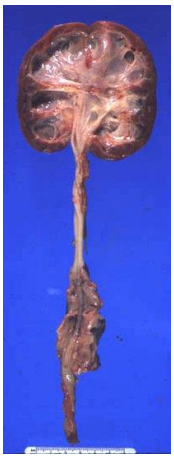
Introduction

The ureters are tubes consisting of smooth muscle fibres that propel urine from the kidneys to the urinary bladder. In the adult, the ureters are usually 25 to 30 cm long and ~3 to 4 mm in diameter. Histologically, the ureter contains transitional epithelium and an additional smooth muscle layer in the more distal one-third to assist with peristalsis.



[Picture Credit: Ureters]

The ureters arise from the pelvis of each kidney, and descend on top of the psoas major muscle to reach the brim of the pelvis. Here, they cross in front of the common iliac arteries. They then pass down along the sides of the pelvis, and finally curve forward and enter the bladder from its left and right sides at the back of the bladder. At the entrance to the bladder, the ureters are surrounded by valves known as ureterovesical valves, which prevent the backflow of urine into the ureters. In females, the ureters pass through the mesometrium (the mesentery of the uterus) and under the uterine arteries on their way to the urinary bladder.



[Picture Credit: Ureteral Cancer]

Ureteral Cancer

"Ureteral cancer is cancer of one or both ureters, the muscular tube(s) that propel urine from the kidneys to the urinary bladder. It is also known as ureter cancer, renal pelvic cancer, urothelial cell carcinoma, and rarely ureteric cancer or ureteral cancer. Cancer in this location is rare. Ureteral cancer is usually transitional cell carcinoma. Most patients with this condition are older (above the age of 60) and the disease is much more common in men (by a ratio of 3 to 1). However, the incidence is

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increasing, probably as a result of the increase of smoking among women". (Froedtert & Medical College of Wisconsin).

Incidence of Ureteral Cancer in South Africa

The National Cancer Registry (2014) does not provide any information regarding the incidence of ureteral cancer in South Africa.

Types of Ureteral Cancer

Renal cell carcinoma (RCC) is the most common type of kidney and ureter cancer in adults (85%). In RCC, cancerous (malignant) cells develop in the lining of the kidney's tubules and grow into a mass.

Transitional Cell Cancer of the Renal Pelvis and/or Ureter - about 6% to 7% of kidney and ureter cancer does not arise in the kidney itself, but in the renal pelvis, the point where the kidney joins the tube that carries urine from the kidney to the bladder (ureter). These tumours are called transitional cell carcinomas (TCC) and are made up of cancer cells different from those that characterise Renal Cell Carcinoma.

Causes and Risk Factors of Ureteral Cancer

The disease appears to be caused by carcinogens excreted in the urine. Inhaled tobacco is the most common source of these carcinogens, but occupational exposure to certain industrial chemicals can also play a role. In addition, there may be a link between vitamin D deficiency and incidence of ureteral cancer (Colin, *et al*., 2009; Korke*, et al*., 2006)).

People who have been exposed to certain chemicals used in dye factories and chemical industries are also at a slightly increased risk.

People who have kidney damage from long-term use of certain painkillers may also have a higher risk of developing cancer in the renal pelvis. This risk is highest in people who were overexposed to painkillers containing phenacetin. Although the use of phenacetin as a painkillers has now been discontinued, phenacetin may be added to some illegal recreational drugs, such as cocaine, so regular users could still be at risk.

Individuals with a rare condition called Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), have an increased risk of developing TCC of the renal pelvis and ureter.

Ureter and renal pelvis cancer, like other cancers, is not infectious and cannot be passed on to other people. It is not caused by an inherited faulty gene, so other members of one's family are not likely to develop it.

Hu, J., Deng, J., Guo, J. & Fu, B. 2019.

"Ureteral metastases from other primary cancers are very rare. Treatment of these metastases is difficult and outcomes are poor. A thorough literature review was done with the aim of finding

characteristics that may influence survival rates of patients with ureteral metastases. Systematic literature searches of PubMed and Web of Science were performed in Jan 2019. A total of 79 papers that included 265 patients with cancer metastases to their ureters were finally considered for evidence synthesis. Prostate, bladder, breast, gut cancer and lymphoma were the predominant primary tumors. The median interval time from primary tumor diagnosis to ureter metastasis was 28.5 months. The median survival time after diagnosis of ureter metastasis was 18 months. Risk factors of survival were analyzed. Age, sex, hydronephrosis, ureter side, and segment were not associated with survival. Interval time and treatment were associated with overall survival. Further analysis indicated that patients who underwent surgery had better outcomes."

Symptoms of Ureteral Cancer

The most common symptom of ureteral cancer is visible (or microscopic) blood in the urine. Occasionally, bladder irritability and frequent urination can be symptoms of these malignancies. People who notice blood in the urine or other symptoms should be evaluated by a physician immediately, because outcomes are correlated with the length of time between symptom onset and treatment. Ureteral cancer arises in the cells that line these organs.

Diagnosis of Ureteral Cancer

To diagnose or rule out transitional cell carcinoma, the doctor will ask about medical history and symptoms, perform a physical examination and order blood tests, urine tests and radiologic imaging studies such as a CT scan or MRI.

If transitional cell carcinoma is suspected, the doctor may recommend a ureteroscopy in order to determine the best way to surgically manage the disease. During a ureteroscopy, a thin, flexible tube is passed through the urethral opening and threaded up through the bladder into the ureters. Fibre optic cable within the tube allows doctors to view any lesions in the ureteral or renal pelvic wall. In this way, doctors can count the lesions and determine their precise location. During ureteroscopy, a biopsy of the lesions may also be taken for further examination by a pathologist, who can confirm the grade of the cancer. X-rays, radiologic imaging and urine cytology (examining the size and shape of cells found in the urine) may also be used in diagnosing transitional cell carcinoma.

Staging of Ureteral Cancer

The doctor usually performs a staging exercise. This information is used to determine how far the cancer has evolved and to assist in deciding on the most appropriate treatment.

Treatment of Ureteral Cancer

Surgery is usually the primary treatment option for caner of the ureter. Treatment depends on the type, size, stage and location of the lesion. Removal of the entire kidney and ureter is the most common procedure. However, surgeons may use nephron-sparing procedures to save kidney function. These include the use of delicate telescopes to target the ureteral cancer tumours without removing the kidney.

If the ureteral cancer tumour is large, it may be possible to remove the affected portion of the ureter without removing the kidney itself.

For a tumour in the middle of the ureter, surgeons remove the tumour and rebuild the ureter. When the tumour is located in the bottom third, surgeons may remove that section of the ureter. The rest is reconnected to the bladder. This procedure is called a ureteroneocystomy, or reimplantation.

If the entire kidney and ureter need to be removed, surgeons often can do this laparoscopically (minimally-invasive) with better results.

If the tumour is located in the upper third of the ureter, a nephroereterectomy may be performed, removing the entire kidney and remainder of the ureter.

Haifler, M., Shvero, A., Zilberman, D., Ramon, J., Winkler, H., Margel, D. & Kleinmann, N. 2020.
Objectives: Malignant ureteral obstruction (MUO) is a devastating complication of cancer, and it is commonly treated by drainage via percutaneous nephrostomy (PCN). The objective of this study was to determine the efficacy, safety, and functional outcome of tandem ureteral stents (TUS) in the management of MUO.
Materials and Methods: The medical records of all patients with MUO who underwent balloon dilation and TUS insertion in Sheba Medical Center between 2014 and 2018 were retrospectively analyzed. Safety was measured by intra- and postoperative complications, efficacy by time to event analysis, and failure by the requirement of PCN attributable to renal failure or infection. Independent risk predictors of TUS failure were determined by a multivariable Cox regression analysis.
Results: A total of 103 procedures were performed on 81 patients during the study period. The median follow-up was 32 weeks (interquartile range [IQR] 24-67). Fifty-nine (72.9%) patients remained with TUS while 22 patients required PCNs. The median time to procedural failure was 4 months (IQR 2-8). Complications developed after 18 (22.2%) procedures. Two patients requested stent removal due to lower urinary tract symptoms. Independent predictors for TUS failure were metastasis (hazard ratio [HR] 3.03, 95% confidence interval [CI] 1.27, 7.23, $p = 0.013$) and prior PCN (HR 3.38, 95% CI 1.40, 8.13, $p = 0.007$).
Conclusions: TUS is an efficient and safe management option for patients with MUO. It can alleviate renal failure without the need for an external PCN. Metastasis and prior PCN are associated with TUS failure.

Chen, YH., Liu, C-Y., Zhang, Z-H., Xu, P-C., Chen, D-G., Fan, X-H., Ma, J-C. & Xu, Y-P. 2019.
Background: To study the outcome and experience of using metallic stents in treating patients with malignant ureteral obstruction (MUO).
Methods: Seventy-six patients with MUO were assigned to the metallic stent group (MSG) or the ordinary polymer stent group (OPSG) according to the different materials. The success rate of the operation, duration of operation, patency rate serum creatinine values ,postoperative complications and QOL scores were compared between the two groups.
Results: In the OPSG and MSG, the success rates of the operation were 95.5% and 96.9%, respectively, and the durations of the operation were 20.6 ± 2.2 min and 50.9 ± 10.3 min ($P < 0.01$), respectively. There was no significant difference between the groups in serum creatinine values at 3 days after the operation ($P > 0.05$); however, the creatinine values at 3 days after the operation

decreased significantly compared with those before the operation (P < 0.01). In the OPSG, there was no significant difference in creatinine values between 3 days and 6 months after operation, while the creatinine values 1 year after operation were increased significantly compared to those at 3 days after the operation (P < 0.05). In the MSG, there was no significant difference among creatinine values at different intervals (P > 0.05). The total rate of post-procedural complication was lower in the MSG than that in the OPSG(P < 0.05). There was no significant difference in the QOL score between the two groups before the operation (P > 0.05); however, the QOL scores at 6 months and 1 year after the operation were higher in the MSG than that in the OPSG(P < 0.05). In the MSG, there was no significant difference in the QOL score between preoperation and 6 months after surgery. Similarly, there was also no difference in the QOL score between 6 months after surgery and 1 year after surgery(P > 0.05). On the contrary, the differences of QOL score in the OPSG group were much significant between disparate time intervals (P < 0.05).
Conclusions: For patients with MUO who require long-term retention of the stent, metallic stents with longer indwelling time are superior to ordinary polymeric stents.

Huang, Z., Zhang, X., Zhang, X., Li, Q., Liu, S., Yu, L. & Xu, T. 2019.
Purpose: To determine if segmental ureterectomy (SU) could be chosen for wider oncological indications than low-risk ureteral carcinoma, given the difficulties in accurate preoperative risk stratification determination and kidney-sparing needs for successive therapy.
Methods: Data from ureteral carcinoma patients who underwent open SU or laparoscopic radical nephroureterectomy (RNU) between 2011 and 2016 were retrospectively reviewed. Kaplan-Meier survival analysis and Cox regression model with patients' baseline characteristics (age, bladder cancer history, hydronephrosis), procedure type, and tumor characteristics (site, size, pathological features) as covariates were used to evaluate oncological outcomes. Life quality parameters including preoperative renal function, Karnofsky performance status, pain score, and surgical complications were set as second endpoints.
Results: Sixty-three patients (24 in SU group, 39 in RNU group) who had at least one high-risk factor were enrolled. In the mean follow-up time of 24.67 months, no significant difference was found in recurrence-free survival (66.7% and 69.2%, $p = 0.798$), overall survival (79.2% and 84.6%, $p = 0.453$), and cancer-specific survival (83.3% and 89.7%, $p = 0.405$) between SU and RNU groups. The Cox regression demonstrated that procedure type was not associated with oncological outcomes. Patients in SU group experienced significant mean estimated glomerular filtration rate (eGFR) increase by 4.60 ml/(min·1.73 m^2) ($p < 0.001$). Proportion of patients having poor eGFR also decreased postoperatively in SU group. Mere tendency in physical performance status improvement and serious complications reduction was detected in SU group.
Conclusion: SU is acceptable for high-risk ureteral carcinoma comparing to RNU with satisfying tumor control efficacy and advantage in renal function preservation.

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers

- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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