

Laparoscopic Radical nephroureterectomy for Upper Renal Excretory Tract urothelial Carcinoma: Results from a single Center in Douala Cameroon

Research Article

Volume 4 Issue 1- 2023

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Article History

Received: February 8, 2023 Accepted: February 14, 2023 Published: February 15, 2023

Abstract

Background and aim: Upper Tract Urothelial Carcinoma (UTUC) which represent 5-10% of urothelial tumours are tumours that develop in the urothelium of the pyelocalical cavities or the ureters. The standard surgical treatment is total open radical nephroureterectomy with excision of the bladder collar. The development of minimally invasive surgery, such as laparoscopic surgery and its contribution to the management of renal pathologies has allowed the adaptation of this technique in the treatment of tumours of the upper excretory tracts. We present the epidemiological, clinical, paraclinical, therapeutic and evolutionary characteristics of patients with upper excretory tract tumours treated by laparoscopic nephroureterectomy.

Methods: This prospective single-center study included 5 patients with UTUC treated at the Centre medico-chirurgical d'urologie in Douala, Cameroon between 2016 and 2021.

Results: We included 4 men and 1 woman, with a mean age of 62.4 ± 3.85 years. Four (80%) patients had a history of tobacco and 3(60%) had a history of repeated urinary tract infections. The main reasons for consultation were gross haematuria and renal colic-type lumbar pain. In all cases, the diagnosis was made by the triad of thoracic and abdominal CT scan, cystoscopy and semi-rigid ureteroscopy. Four (80%) patients had tumours in the ureter and 3(60%) patients had an associated bladder tumour. The treatment consisted of transperitoneal laparoscopic nephroureterectomy with resection of the bladder collar via a double lumbar and iliac approach. The median surgery duration was 300[270-330] minutes and there were no major immediate post-operative complications. Histopathology confirmed that all 5 cases were urothelia carcinomas. Recurrence was observed in 4(80%) patients and 3(60%) patients died from disease progression, with a median survival time of 17.93 months.

Conclusion: Laparoscopic total nephroureterectomy with resection of the bladder collar is an important alternative to open surgery in the treatment of tumours of the upper excretory tract as it reduces operating time, length of hospital stay, and the occurrence of complications. The prognosis of these tumours depends on the stage and grade with a significant potential for recurrence indicating the need for regular and prolonged monitoring.

Keywords: Gross Haematuria; Tumour; Upper Excretory Tract; Nephroureterectomy; Laparoscopy; Chemotherapy



Introduction

The excretory tract of the kidneys consists of the pyelocaliceal system, ureter, urinary bladder, and urethra, with the pyelocaliceal system and ureter forming the upper excretory tracts [1]. Cancers of the urinary tract occur frequently, representing the second most common class of genitourinary cancers [2]. It has been reported that 90% of all urinary tract cancers are urothelial carcinomas, and Upper Urinary Tract Urothelial Carcinomas (UTUC) account for 5-10% of all urothelial carcinomas [1,3]. UTUC are malignancies that arise from the urothelial lining of the urinary tract, from the pyelocaliceal system to the distal ureter, with pyelocaliceal tumours being approximately twice as common as ureteral tumours. These malignancies, with an estimated annual incidence of 1-2 cases per 100,000 accounted for 5-7% of all renal tumours and 5-10% of all urothelial tumours in the United States in 2020 [4]. UTUC occurs more in men than in women with a male-to-female ratio of 2:1, with a peak incidence in individuals aged 70-90 years [5,6].

The Tumour, Node, Metastasis (TNM) classification with histological or cytological confirmation can be used to grade UTUC, with the hilar, the retroperitoneal, and the pelvic nodes being the regional lymph nodes [7]. Diagnosis of UTUC can be made through imaging (computed tomography urography or magnetic resonance urography), Urethroscopy and urinary cytology, or diagnostic ureteroscopy [8-12]. The management option for UTUC depends on the degree of spread of cancer. The European Association of Urology (EAU) Guidelines Panel on UTUC recommends kidney-sparing surgery for patients with low-risk tumours (localized nonmetastatic disease) and patients with solitary kidney and/or impaired renal function, provided it will not compromise survival. On the other hand, Radical Nephroureterectomy (RNU) is the standard treatment for patients with high-risk UTUC regardless of tumour location, with open, laparoscopic, and robotic approaches having similar oncological outcomes for organ-confined UTUC. RNU should be accompanied by the removal of the bladder cuff in its entirety, postoperative systemic platinum-based chemotherapy to patients with muscle-invasive UTUC, and postoperative single-dose bladder instillation of chemotherapy to lower the intravesical recurrence rate [13]. Complete excision of the ipsilateral bladder cuff was proposed by Kimball and Ferris in 1933 after the authors found a high incidence of tumours in the remaining ureter following a radical nephrectomy for upper tract urothelial carcinoma [14]. Some 40 years later, Strong and Pearse in 1976 quantified an average of 30% recurrence rate of urothelial carcinoma in the ureteral stump when incomplete nephroureterectomy was performed [15]. In the open approach, the kidney is removed along with the ureter and its bladder cuff. The surgery can be performed with one large midline incision to remove the kidney, the ureter, and the bladder cuff. Alternatively, two separate incisions can be made (a flank or subcostal incision and a Gibson incision).

Laparoscopic nephroureterectomy is becoming increasingly common, especially in the treatment of localized renal cell carcinoma [16]. Laparoscopic RNU done by an experienced surgeon with strict adherence to oncological principles offers equivalent oncological outcomes to open RNU [17]. Minimally invasive approaches in the treatment of upper tract urothelial carcinomas have been promoted by advances in technology and endoscopic and laparoscopic skills. In an international multicentre study by El Fetouh et al. [18], laparoscopic RNU was shown to be an effective minimally invasive treatment for some patients with UTUC [18]. Some advantages of laparoscopic RNU, like laparoscopic nephrectomy, include less intraoperative blood loss, less postoperative pain, faster recovery, and better cosmetics [19]. However, in resource-limited settings such as sub-Saharan Africa, laparoscopic procedures are not commonly performed. Thus, our study aims to present the experience of laparoscopic RNU in the management of UTUC in a single urology center in Douala, Cameroon.

Methods

Study design and study participants

This was a 5-year retrospective study between January 2016 and January 2021 carried out at the Centre medico-chirurgicale d'urologie, which is located in Bali, Douala. We studied the medical records of 5 patients with UTUC who were treated through laparoscopic radical nephroureterectomy. We excluded files with incomplete records. Using pre-tested data extraction forms, we collected data on patients' ages, genders, clinical profiles, relevant medical history, tumour parameters, and outcomes of surgery. All patients benefitted from a pre-operative cystoscopy, ureteroscopy, and abdominopelvic CT scan to localize and stage the tumour.

Pre-operative and intraoperative procedures

All 5 patients benefited from an anaesthesiologist consultation and did a pre-operative workup, which included a full blood count, urea and creatinine, clotting profile, and urine analysis with culture and antibiotic susceptibility profiling. A third-generation cephalosporin (single dose of Ceftriaxone 2g intravenous) was administered to all patients as a prophylactic antibiotic. All surgical procedures were performed under general anaesthesia. After induction of general anaesthesia, a nasogastric tube and transurethral Foley catheter (16Fr for women and 18Fr for men) were placed to decompress the stomach and the bladder respectively. The patient was then placed in a lateral decubitus position at the edge of the operating, at 90° to the table. The upper leg was kept straight while the lower leg was flexed at the knee joint (Figure 1). Pneumoperitoneum to a pressure of 14mmHG was created using standard percutaneous Veress needle insertion. After creating the pneumoperitoneum, 4 trocar ports were placed in a consecutive manner (Figure 2). A first 10mm trocar port was inserted 10mm above the umbilicus in the mid-clavicular line, a second trocar port of 5mm was inserted in the lower intercostal space, anterior axillary line, a third trocar port of 12mm was inserted above the iliac crest, anterior axillary line, and a fourth trocar port of 5mm was inserted midway between the umbilicus and the pubic symphysis. The colon was mobilized by incising along the Toldt's line. For left-sided procedures, this mobilization started from the pelvic brim, extending towards the spleen while for right-sided procedures, it was more ergonomic to start from the liver and move caudally.



Figure 1: Positioning of the patient during surgery (patient placed in lateral decubitus position at 90° to the table with the upper leg extended and the lower leg flexed at the knee joint).

The psoas muscle was then identified and the kidneys and gonadal vessels were isolated. The renal hilum was opened and the renal artery and vein were dissected and cut off. The ureter was identified, dissected, and clipped with hem-o-lok at the pelvic brim. The kidney was then completely dissected and excised while preserving the perirenal fascia and adrenal gland. Following nephrectomy, the procedure was switched to an open midline suprapubic laparotomy to perform the distal ureterectomy using the extravesical approach. During this stage, the patient was placed in a supine position. Following access



to the abdominal cavity, an anterolateral subperitoneal detachment was performed up to the level of the iliac vessels, widely opening the internal iliac fossa where the kidney was lodged. The ureter was dissected down to the bladder exposing the ureterovesical junction. A 10 mm bladder cuff around the ureteral meatus was cleared and clamped with right-angled forceps, and then the distal ureter and bladder cuff were resected. The resulting bladder wall defect was closed with a continuous 3-0 absorbable suture holding muscle and mucosa together and the resected tissue was extracted en bloc (Figure 3). Two suction drains were respectively placed in the perivesical space and the perirenal space.



Figure 2: Trocar arrangement during laparoscopic RNU.

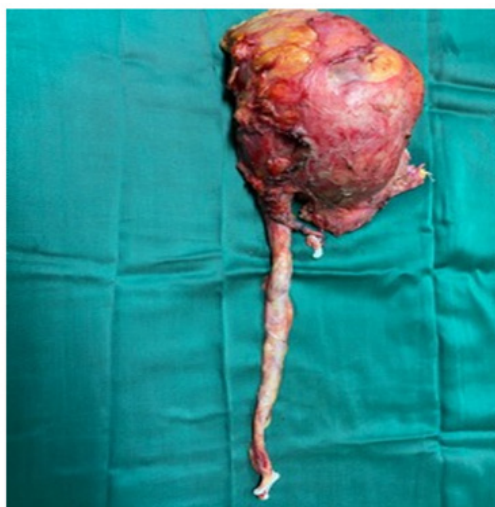


Figure 3: Extracted kidney and ureter bloc following laparoscopic RNU.

Postoperative Follow-up

All patients benefitted from clinical follow-up and cystoscopy at 3 months and 6 months and 9 months following surgery, then every 6 months thereafter for 2 years then yearly. Abdominopelvic CT scans were also performed at 3 months, 6 months, and 9 months following surgery, and then every year.

Data Management

The data extracted from patients' clinical records were entered into Microsoft Excel 2016 and then exported to SPSS version 25 for analysis. Continuous data are presented as mean values and standard deviations (for normally distributed data) and medians with interquartile ranges (for skewed data). On the other hand, categorical data are presented as frequencies and percentages. This study was approved by the institutional review board of the Faculty of Medicine and Pharmaceutical Sciences (FMPS) of the University of Douala and by the

ethical committee of the Centre medico-chirurgical d'urologie in Douala, Cameroon. The requirement for patients' informed consent was waived due to the retrospective nature of the study.

Results

The laparoscopic RNU procedures were successfully performed with no major immediate postoperative complications. Of the 5 patients we recruited in our study, 4(80%) were males and 1(20%) was female. The ages of the patients ranged from 58 years to 68 years, with a mean age of 62.4 ± 43.85 years. The baseline characteristics of the patients are shown in (Table 1). All 5 patients were hospitalised and underwent laparoscopic RNU. The duration of the surgery ranged from 260-340 minutes with a median duration of 300 [270-330] minutes. The duration of hospitalization of the patients ranged from 4-7 days, with a mean duration of 4.8 ± 1.3 days. Of the 5 patients treated with laparoscopic RNU, 2(40%) had adjuvant chemotherapy and 2(40%) had adjuvant TURT. Overall, 4(80%) patients had a recurrence of their tumours and 3(60%) patients died. The details of the surgical procedure and outcomes are presented in (Table 2).

The maximum follow-up period was 33.57 months and by the last follow-up, 3 (60%) patients had died from all causes. The overall estimated 1-year and 2-year cancer survival rates were, 60% and 40%, respectively. In total, 66.6% of all the deaths occurred before the end of the first year post-surgery (Figure 4). The lone female in this study died during follow-up while the mortality rate among males was 50%. The mortality rate among patients with multifocal tumours was 66.67% compared to 50% among patients with unifocal tumours, while patients with ureteral tumours had a mortality rate of 75% compared to 0% among patients with pyelocaliceal tumours (Table 3).

Discussion

This study aimed to evaluate the oncologic results and the place of laparoscopic nephroureterectomy in the management of upper urinary tract urothelial carcinoma in a single urology centre in Douala, Cameroon. We recruited five patients (4 males and 1 female) over a 5-year period, with a mean age of 62.4 ± 43.85 years. UTUC has been reported to have a peak incidence in individuals aged 70-90 years and is more likely to occur in men [6]. Some patients with UTUC are diagnosed incidentally while others present with symptoms. Haematuria is the main symptom of UTUC followed by back pain. In the current study, all the patients presented with macroscopic haematuria and back pain, and 3(60%) patients presented with weight loss and irritative urinary tract symptoms. Of the 5 patients with haematuria, 3(60%) were urgently transfused due to the presence of massive bladder clots. Brant et al. [20] reported visible or nonvisible haematuria as the most common symptom of UTUC, occurring in 70-80% of cases [20]. Back pain in patients with UTUC may be due to a clot in the excretory pathway or obstruction of the pathway by the tumour itself or may arise following a loco-regional extension of the tumour. In a retrospective study conducted by Nandra et al. [21], 13.4% of patients with UTUC presented with flank pain, and 6% had systemic symptoms of weight loss and lethargy [21]. Unlike bladder tumours, the origin of UTUC remains unclear. Many hypotheses have been proposed but only a few etiologies have been indisputably identified. These factors are, however, non-specific to UTUC and include cigarette smoking, consumption of coffee, and exposure to certain occupational carcinogens. Cigarette smoking is by far the most important risk factor for UTUC. Rink et al. [22] in a retrospective study assessed the impact of cigarette smoking status, cumulative smoking exposure, and time from cessation on oncologic UTUC outcomes in patients treated with radical nephroureterectomy. In their study, 71.8% of patients diagnosed with UTUC were former or current smokers, similar to the 80% gotten in the current study. Rink et al. [22] concluded that cigarette smoking was significantly associated with advanced disease stages, disease recurrence, and cancer-specific mortality in patients treated with radical nephroureterectomy for UTUC [22].

Table 1: Baseline characteristics of the patients.

Variables	Males (%)	Females (%)	Total (%)
Number of patients	4(80)	1(20)	5(100)
Mean age(\pm SD)	62.5(\pm 4.44)	62	62.4(\pm 3.85)
Presenting symptoms			
Back pain	4(100)	1(100)	5(100)
Haematuria	4(100)	1(100)	5(100)
Weight loss	3(75)	0(0)	3(60)
Irritative urinary symptoms	2(50)	1(100)	2(60)
History of smoking	4(100)	0(0)	4(80)
Mean haemoglobin(\pm SD), mg/dl	10.75(\pm 3.60)	8	10.20(\pm 3.35)
Laterality of tumour			
Left	2(50)	0(0)	2(40)
Right	2(50)	1(100)	3(60)
Localisation of tumour			
Renal pelvis	10(55.56)	6(85.71)	16(64)
Ureter	1(5.55)	1(14.29)	2(8)
Tumour focality			
Unifocal	2(50)	0(0)	2(40)
Multifocal	2(50)	1(100)	3(60)
Presence of associated bladder tumour	2(50)	1(100)	3(60)
Pathological staging of the tumour			
T1	2(50)	0(0)	2(40)
T2	2(50)	1(100)	3(60)
Tumour grade			
G1	1(25)	0(0)	1(20)
G2	1(25)	1(100)	2(40)
G3	2(50)	0(0)	2(40)

Table 2: Surgical outcomes of patients.

Variables	Males (%)	Females (%)	Total (%)
Median duration of surgery (IQR), minutes	290 [265-315]	340	300 [270-330]
Mean duration of hospitalization (\pm SD), days	5.0 \pm 1.41	4	4.8 \pm 1.30
Mean blood loss (\pm SD), ml	327(95.35)	310	324(82.95)
Mean follow-up (\pm SD), m	22.04(9.71)	9.97	19.63(9.99)
Adjuvant Chemotherapy	1(25)	1(100)	2(40)
Tumour recurrence post RNU	3(75)	1(100)	4(80)
Mortality rate at end of follow-up	2(50)	1(100)	3(60)

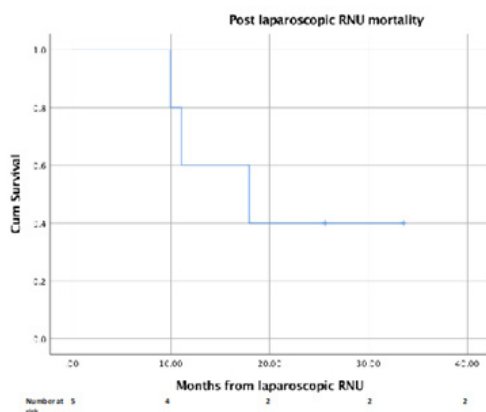
The diagnosis of UTUC can be made through imaging, cystoscopy and urinary cytology, or diagnostic ureteroscopy [13]. We used a combination of CT urography, cystoscopy and ureteroscopy, associated with biopsy to confirm the diagnosis and stage of UTUC in all the patients in the present study. The CT scan made it possible to highlight the location of the lesion within the upper excretory tract. We performed a cystoscopy systematically to exclude the presence of any associated bladder tumour and to verify the integrity of the ureteral meatus. Bladder involvement is not uncommon in cases of UTUC. In

fact, half of the time UTUC is associated with bladder lesions, particularly in the periorificial area [23]. In the current study, 3(60%) patients with UTUC had an associated Urothelial carcinoma of the bladder and underwent transurethral resection of the bladder at least 10 days prior to the laparoscopic RNU. Ureteroscopy using a semi-rigid ureteroscope, which permitted visualization of the tumour was performed in all patients (with associated biopsy in 3(60%) patients). Biopsy could not be performed in 2(40%) patients due to massive haematuria which limited visualization and accuracy of the biopsy.



Table 3: Multivariable Cox regression analyses predicting the risk of overall mortality in patients treated with laparoscopic RNU.

Variables	Frequency	Mortality Rate (%)
Gender		
Male	4	50
Female	1	100
History of smoking		
Yes	4	50
No	1	100
Localisation of tumour		
Renal pelvis	1	0
Ureter	4	75
Tumour focality		
Unifocal	2	50
Multifocal	3	66.67
Associated bladder tumour		
Yes	3	66.67
No	2	50
Pathological staging of the tumour		
T1	2	0
T2	3	100
Tumour grade		
G1	1	0
G2	2	50
G3	2	100

**Figure 4:** Kaplan-Meier survival analysis of overall mortality in patients treated with laparoscopic RNU for UTUC.

Muscle-invasive UTUC has a very poor prognosis. The 5-yr-specific survival is <50% for pT2/pT3 and <10% for pT4 [24-26]. In the current study, the overall 1-year and 2-year cancer survival rates were, 60% and 40%, respectively and two-thirds of all the deaths occurred before the end of the first year following surgery. In a population-based assessment of 6078 upper-tract urothelial carcinoma patients treated with nephroureterectomy from 17 registries of the Surveillance, Epidemiology, and End Results database, age, T, and N stages emerged as the most informative predictors of mortality [26]. The initial location of the UTUC is a strong prognostic factor. Faysal et al. [27] and Adil et al. [28] reported that after adjustment for the effect of tumour stage, patients with ureteral and/or multifocal tumours seem to have a worse prognosis than patients diagnosed with renal pelvic tumours [27,28]. In the current study, the mortality rate among patients with

multifocal tumours was 66.67% compared to 50% among patients with unifocal tumours, while patients with ureteral tumours had a mortality rate of 75% compared to 0% among patients with pyelocaliceal tumours in line with previous studies. The clinical implications of our present study are several-fold and uniquely highlight the need for close post-operative monitoring because of the high potential for tumour recurrence. Our study is limited by its small sample size, which is probably due to the lack of integration of laparoscopic surgery into daily medical practice in our setting. We recommend that more studies with larger samples be carried out on this topic in the future to further investigate our findings.

Conclusion

Laparoscopic total nephroureterectomy with resection of the bladder collar is an important alternative to open surgery in the treatment of tumours of the upper excretory tract as it reduces operating time, length of hospital stay, and the occurrence of complications. The prognosis of these tumours depends on the stage and grade with a significant potential for recurrence indicating the need for regular and prolonged monitoring.

Acknowledgements

The authors thank Health Search Association for critically reviewing the manuscript.

Author Contributions

Availability of data and materials

The data analysed in this study are available from the corresponding author upon reasonable request.

Conflict of interest statement

The authors have no conflicting interests to declare.



Funding

The authors did not receive any funding for this study.

Ethics statement

Ethical approval was obtained from the institutional review board of the Faculty of Medicine and Pharmaceutical Sciences and the ethics committee of the Centre medico-chirurgical d'urologie in Douala, Cameroon. The requirement for informed consent was waived due to the retrospective nature of the study.

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