

Laparoscopic-Assisted Nephroureterectomy after Radical Cystectomy for Transitional Cell Carcinoma

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ABSTRACT

Objective: To report our experience with laparoscopic-assisted nephroureterectomy for upper tract transitional cell carcinomas after radical cystectomy and urinary diversion.

Materials and Methods: Seven patients (53-72 years-old) underwent laparoscopic-assisted nephroureterectomy 10 to 53 months after radical cystectomy for transitional cell carcinoma at our institution. Surgical technique, operative results, tumor features, and outcomes of all patients were retrospectively reviewed.

Results: Mean operative time was 305 minutes with a significant amount of time spent on the excision of the ureter from the urinary diversion. Estimate blood loss and length of hospital stay averaged 180 mL and 10.8 days, respectively. Intraoperative and postoperative complications occurred in two patients each. There was one conversion to open surgery. Pathology confirmed upper-tract transitional cell carcinoma in all cases. Metastatic disease occurred in two patients after a mean follow-up of 14.6 months.

Conclusions: Nephroureterectomy following cystectomy is a complex procedure due to the altered anatomy and the presence of many adhesions. A laparoscopic-assisted approach can be performed safely in properly selected cases but does not yield the usual benefits seen with other laparoscopic renal procedures.

Key words: carcinoma, transitional cell; cystectomy; laparoscopy; nephrectomy; recurrence; reoperation

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INTRODUCTION

Nephroureterectomy (NU) is the treatment of choice for high grade, invasive, or recurrent transitional cell carcinoma (TCC) of the upper urinary tract (UUT). Since the first laparoscopic NU was performed in 1991, (1) several series have demonstrated the safety and efficacy of the procedure, (2-6) with the benefits of decreased hospitalization, return to activity and pain

requirement. Nephroureterectomy following cystectomy is a very complex procedure due to the need for complete ureterectomy in the presence of many adhesions and an altered anatomy. This requires extensive enterolysis and dissection in a previously operated site to allow for removal of the ureter from the urinary diversion. There is limited data on open removal and no published data on laparoscopic NU for UUT TCC following cystectomy and urinary

diversion. The objective of this study is to report our experience with laparoscopic-assisted NU for UUT TCC after radical cystectomy.

MATERIALS AND METHODS

In 2003 and 2005, seven patients previously treated with radical cystectomy underwent laparoscopic-assisted NU for UUT TCC. Individual characteristics of the patients and the features of the primary bladder tumors are summarized in Tables-1 and 2, respectively. Cystectomy was performed for BCG-refractory carcinoma in situ (CIS) of the urinary bladder in four patients, recurrent superficial high grade TCC in two, and muscle-invasive disease in one.

Evaluation after cystectomy consisted of physical examination, chest X-ray, and urine cytology every 3-4 months in the first and second years, and at 6-month intervals for up to 5 years, followed by yearly exams. The upper tract was surveyed by intravenous urography (IVU), computed tomography (CT), conduitography and retrograde pyelography, and/or conduitoscopy and ureteroscopy every 6-12 months in the first year, and then yearly or when clinically indicated. Patients with a suspected upper tract tumor were biopsied, and in highly suspicious cases in which retrograde ureteroscopy was not possible were evaluated through nephroscopy, and antegrade pyelography and ureteroscopy.

Indications for NU in patients with a normal contralateral kidney included high-grade biopsy-proven TCC recurrences in three patients, and

Table 1 – Epidemiologic and clinical features of the patients.

Patient	Age	Sex	Predisposing Factors	Co-Morbidities	BMI
1	65	Male	Positive for tobacco	Asthma, atherosclerosis, status post-angioplasty	26.0
2	53	Male	Positive for tobacco	None	34.1
3	68	Female	Negative	Asthma, cardiac arrhythmia	26.0
4	71	Male	Positive for tobacco, benzidine, and components of the rubber making industries	Thyroid disease, urolithiasis, cardiac disease, status post-percutaneous nephrolithotomy, coronary artery bypass, cholecystectomy, appendectomy, and herniorrhaphy	25.9
5	72	Male	Positive for tobacco	Thyroid disease, and hypertension	32.4
6	69	Male	Positive for tobacco	Cardiac disease (status-post coronary artery bypass and repair of aortic aneurysm)	27.7
7	54	Female	Positive for tobacco	Thyroid disease, status post-cholecystectomy	30.6

BMI = body mass index.

Table 2 – Characteristics of bladder tumors treated with radical cystectomy.

Pt. N. Sex Age	Previous Intravesical Chemotherapy	Multifocality	Stage	Grade	Plus Ca In Situ	Prostatic Urethra Involvement	Ureteral Status	Margin Status	Urinary Diversion	Time from Initial Diagnosis to Cystectomy (Months)	Time from Cystectomy to UUT TCC (Months)
1 M 65	None	Multifocal	T2 N0	High grade	Yes	No	Ca in situ (left)	Positive (left ureter)	Ileal conduit	2	15
2 M 53	BCG	Multifocal	T1 N0	High grade	Yes	Yes	Ca in situ (bilateral)	Positive (right and left ureters)	Ileal conduit	8	22
3 F 68	BCG, Thiotepa	Multifocal	T1 N0	High grade	Yes	–	Ca in situ (right)	Positive (right ureter)	Ileal conduit	4	10
4 M 71	BCG, Mitomycin	Multifocal	T1 N0	High grade	Yes	Yes	Ca in situ (bilateral)	Negative	Orthotopic neobladder	3	17
5 M 72	BCG	Multifocal	T1 N0	High grade	Yes	Yes	Ca in situ (bilateral)	Positive (right ureter)	Ileal conduit	5	15
6 M 69	BCG, Mitomycin	Multifocal	Ta N0	High grade	Yes	No	Normal	Negative	Ileal conduit	25	53
7 F 54	None	Multifocal	T1 N0	High grade	Yes	–	Low grade TCC (left)	Negative	Orthotopic neobladder	2	28

persistent positive urinary cytologies in two patients - one who was non-responsive and another who recurred after mitomycin. Two patients had solitary kidneys. The first had been submitted to laparoscopic NU before radical cystectomy for primary UUT TCC, and developed contralateral UUT recurrence in a non-functioning renal unit. The second developed bilateral, extensive disease, not amenable to conservative resection, and underwent open NU followed by contralateral laparoscopic NU.

Laparoscopic-assisted NU was performed in all patients using a transperitoneal approach. Pneumoperitoneum was achieved through a Veress needle placed lateral to the rectus abdominalis, away from the lower midline incision. The Visiport optical trocar (United States Surgical Corporation, USSC, Norwalk, CT, USA) was used for initial access to the abdomen. Local adhesions from previous surgery were carefully taken down with sharp dissection. The colon was then mobilized medially and the kidney removed in a standard laparoscopic fashion (6). In summary, a plane was created between the ureter and the aorta or the vena cava (for left and right-side NU respectively), and this was carried up to the renal hilum. The renal artery and vein were dissected and sequentially transected with the use of an endovascular GIA stapler (USSC, Norwalk, CT, USA). The adrenal gland was routinely spared by entering the Gerota's fascia and dissecting it off the upper pole of the kidney. The remaining of the dissection was carried outside Gerota's fascia. Following complete dissection of the kidney and upper ureter, dissection of the remaining ureter was carried down as far distally as possible. On the left side, the ureter was dissected to the area where the ureter traversed the mesentery of the sigmoid colon. On the right, the dissection usually approached the urinary diversion. A low abdominal incision (in the previous cystectomy incision site) was then made when the complexity of the dissection was beyond the limitations of a safe laparoscopic approach. The ureteroenteric anastomosis was identified and completely excised with a cuff of normal bowel mucosa. The urinary diversion was closed with running 3-0 polyglactin suture, and repositioned in its usual anatomic position. In the two cases with

solitary kidney, urinary diversion was removed en bloc with the kidney and ureter.

Operative results and outcomes of all patients treated by this technique were retrospectively reviewed and analyzed.

RESULTS

Five male and two female patients with a median age of 68 years (range 53 to 72 years) developed multifocal recurrent UUT TCC after treatment with radical cystectomy for bladder cancer. The features of these recurrences are shown in Table-3.

All patients required extensive lysis of adhesions due to the previous open surgery, and multiple prior ureteroscopies and biopsies. One of the patients could not have his entire kidney dissected laparoscopically due to a prior abdominal aortic aneurysm repair that resulted in a fibrotic reaction around the renal hilum. The midline incision was extended and the renal dissection was completed through the extended open incision.

No intraoperative complications from the laparoscopic procedure occurred. Two patients had intraoperative complications during the open stage of the procedure, due to the intense adjacent reactive process. The first had an inadvertent bowel injury, which was managed with segmental enterectomy. In the second patient, transection of the contralateral ureter was recognized intraoperatively, requiring reanastomosis to the ileal conduit.

All patients had delayed return to bowel function beyond three days. Other minor post-operative complications occurred in two patients. One had colonic pseudo-obstruction that resolved with conservative management, and the other presented with a superficial wound infection treated with intravenous antibiotics. Two other patients developed anticipated end-stage renal disease due to previous contralateral NU. They were started on hemodialysis and required longer hospitalizations due to instituting dialysis in the setting of no renal function.

The mean operative time was 305.6 minutes (range 220 to 360 minutes), and estimate blood loss

Table 3 – Clinical-pathological features of upper urinary tract recurrences after radical cystectomy.

Pt. N. Sex Age	Symptoms	Positive Diagnostic Studies	Side of Recurrence	Site of Recurrence	Previous Treatments for UUT TCC	Final Treatment	Pathological Stage	Pathological Grade	Margin Status
1 M 65	None	Urine cytology, ureteroscopy with biopsy	Left	Renal pelvis, distal ureter	None	Left lap-assisted NU	T3	High grade	Negative
2M 53	None	Urine cytology	Left	Renal pelvis	None	Left lap-assisted NU	Tis	–	Negative
3 F 68	Gross hematuria	Urine cytology, CT scan, ureteroscopy with biopsy	Left	Renal pelvis	None	Left lap-assisted NU	T2	High grade	Negative
4 M71	None	Urine cytology, retrograde Pyelogram, ureteroscopy with biopsy	Left	Renal pelvis, proximal ureter	None	Left lap-assisted NU	T3	High grade	Negative
5M 72	None	Urine cytology	Bilateral	Distal ureter (bilateral)	Mytomicin	Right lap-assisted NU, distal ureterectomy (left)	Tis	–	Positive for carcinoma in situ (bilateral)
6 M 69	Gross hematuria	Urine cytology, ureteroscopy with biopsy	Left	Renal pelvis, distal ureter	Right lap-assisted NU, distal ureterectomy, Percutaneous resection (left)	Left lap-assisted NU	T1	High grade	Positive for invasive carcinoma
7 F 54	Gross hematuria	Urine cytology, IVP, nephroscopy with biopsy	Bilateral	Entire UUT (bilateral)	Left Mid/distal ureterectomy, bilateral percutaneous resection, right open NU	Left lap-assisted NU	T3	High grade	Positive for carcinoma in situ (left)

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was, in average, 180 mL (range 100 to 250 mL). Mean length of hospital stay was 10.8 days (range 5 to 25 days). Follow-up averaged 14.6 months (range 2 to 22 months), although two patients were lost to follow-up. The remaining five patients were regularly followed-up for more than 12 months. Table-4 gives an overview of the outcomes from each of the cases studied.

COMMENTS

TCC is a multifocal disease affecting the entire urothelium (7,8) and subsequent tumors may occur anywhere in the urinary tract after initial diagnosis (9). While primary UUT TCC is frequently followed by bladder recurrences, (7,10) and the cumulative incidence of UUT recurrence after bladder cancer is up to 28% in five years,(11) the incidence of UUT tumors after radical cystectomy is low (7-9). The incidence of post-cystectomy UUT TCC differs according to the stage of the bladder tumor. Patients submitted to radical cystectomy for superficial disease have a higher probability of developing UUT tumors than those with muscle-invasive disease (8). Other risk factors responsible for UUT recurrences in these

patients include histological grade, presence of distal ureteric carcinoma at cystectomy, associated CIS, multifocality, and involvement of the prostatic urethra (8,9,12).

The optimum method of surveillance of the UUT after cystectomy is questionable. Various regimens with annual or biannual imaging (IVU or CT), combined with urine cytology, have been reported (9). Since six (85.7%) of our patients had distal ureteral involvement by CIS or TCC, we adopted a more aggressive surveillance, similar to that for superficial bladder tumors, with urine cytology, imaging studies, and UUT endoscopy.

The role of urinary cytology in the diagnosis of UUT TCC is controversial, in particular for patients with intestinal diversions, because of the presence of small bowel cells (7). However, since most UUT TCC after cystectomy tends to be high grade, sensitivity is higher in these patients (9). Obtaining urine using ureteral catheterization further improves the diagnostic yield (13). IVU and CT scans increase the likelihood of early detection, and help in management decisions, but the key role in the diagnosis of recurrent UUT TCC is retrograde pyelography and ureteroscopy with biopsy, with a reported accuracy of 94% (13).

Table 4 – Oncological outcomes after laparoscopic-assisted NU for recurrent UUT TCC.

Pt. N. – Sex – Age	Recurrence	Local	Treatment	Follow-up	Status
1 – M – 65	No	–	–	3	No evidence of disease
2 – M – 53	No	–	–	20	No evidence of disease
3 – F – 68	Yes	Brain	Frameless stereotaxy	22	With disease
4 – M – 71	No	–	–	13	No evidence of disease
5 – M – 72	No	–	–	22	No evidence of disease
6 – M – 69	No	–	–	2	No evidence of disease
7 – F – 54	Yes	Pelvic	Chemo-therapy	20	With disease

The historic standard of care for high grade and stage UUT lesions has been open NU, with removal of a cuff of bladder around the ureteral orifice.(2-6,12-14) Several centers have replaced the open surgery for laparoscopic NU, given that it has well established advantages compared to the open approach, (2-6,8,14) and it is equally effective in terms of oncological outcome.(2-5,14) Following this trend, after performing over 80 laparoscopic NU at our department, we started performing laparoscopic-assisted NU for recurrent UUT TCC post-radical cystectomy in 2003. Surgical technique mirrors traditional open NU, including the removal of a cuff of bowel at the ureteroenteral anastomosis. All except one patient had the renal portion of the procedure successfully accomplished laparoscopically, and all surgeries were completed through the same previous incision performed for radical cystectomy, including the patient that required open conversion for marked hilar vessels fibrosis. In this patient, the incision was extended to the xiphoid process.

Mean operative time was long compared to standard NU but this was not due to the laparoscopic nephrectomy portion of the procedure but rather the complex dissection of the urinary diversion and necessity for complete removal of the ureter with a cuff of the bowel. In all cases, extensive and tedious lysis of adhesions was necessary to release the diversion and distal ureter from adjacent bowel. It is not surprising that delayed recovery of bowel function was seen in these patients, resulting in a lengthened hospital stay when compared to NU with no prior cystectomy. In addition, 2 patients had solitary kidneys removed and subsequently required postoperative dialysis, which made management and hospitalization more complex. These patients had failed prior attempts at organ sparing therapy.

The outcome of patients who develop UUT TCC after cystectomy is usually poor (1,7,12). So far, two of our patients presented recurrences, although the median follow-up is still limited. In addition, these patients are at higher risk of TCC in remaining sites due to the multifocal nature of their disease. Lifelong surveillance for recurrent disease in remaining urothelial surfaces and distant sites is necessary.

CONCLUSIONS

Our experience confirms that NU for UUT TCC after radical cystectomy is a complex procedure due to the altered anatomy and the presence of many adhesions. In the present series, a laparoscopic-assisted approach could be performed safely in properly selected cases but did not yield the usual benefits of decreased hospitalization seen with other laparoscopic renal procedures mainly due to patient co-morbidities and the delayed return to bowel function. We even still prefer this approach, as after many years of experience the majority of our surgeons regularly performing renal surgery feel more comfortable with the laparoscopic approach to the kidney. The distal ureter and bowel cuff, however, must still be extracted with open surgery. We recognize that advanced laparoscopic experience is required to achieve even comparable results to an open approach in this technically demanding procedure.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

Radical cystectomy with extended lymph node dissection is the gold standard treatment for invasive and/or refractory superficial bladder cancer (1). Although upper tract recurrence after radical cystectomy has a low incidence at 2% to 4%, it is associated with poor prognosis, and a short survival

(2). The disease specific-survival of patients with upper tract transitional cell carcinoma (TCC) and previous bladder cancer is worse when compared to patients with no bladder tumor, suggesting more aggressive pattern when the pan-urothelial disease is present (3). Laparoscopic nephroureterectomy is

routinely used to treat upper tract TCC with low morbidity and complication rate, and similar oncological outcomes comparable to the open procedure (4).

The authors are to be commended for this series of 7 cases of laparoscopic-assisted nephroureterectomy in patients with previous cystectomy for bladder TCC. In the cystectomy specimen, all patients had bladder carcinoma in situ (CIS), with 6 presenting ureteral CIS, and 4 of them presenting positive margin. These factors may increase the recurrence rate. During the follow-up, 3 patients presented with gross hematuria, but all had positive urinary cytology. A recent study by Raj et al. (2) showed the relevance of urinary cytology after radical cystectomy demonstrating not only the higher risk of recurrence but also the shorter survival; suggesting the need for closer follow-up and the potential for early adjuvant therapies.

The morbidity of the procedure in this group of patients was expectedly higher when compared to standard laparoscopic nephroureterectomy, with longer operative time, hospital stay, and bowel function recovery. One open conversion, one bowel and one intraoperative ureteral injury were reported in the study, with 40% positive margins in the pathological exam.

With the intention of minimizing the morbidity of the procedure, the retroperitoneal approach to the nephrectomy part of the procedure may be helpful in avoiding intra-abdominal adhesions due to the previous cystectomy site; the distal ureterectomy part of the procedure would be performed as described by the authors. These are surgically challenging cases in often unhealthy individuals.

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