Surgical Management of Upper Tract Transitional Cell Carcinoma

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Key Words
Transitional cell carcinoma, laparoscopic nephroureterectomy, kidney, ureter, upper tract

Abstract
Upper tract transitional cell carcinoma (TCC) accounts for approximately 5% of urothelial tumors. Surgical therapy for upper tract TCC is based on tumor grade, stage, location, and confounding factors of individual cases. Options for treatment range from minimally invasive procedures, such as ureteroscopy, to open nephroureterectomy. Laparoscopic nephroureterectomy is progressively eclipsing open nephroureterectomy in the surgical management of upper tract TCC. This article discusses the surgical options for managing upper tract TCC and their considerations for use. (JNCCN 2006;4:1015–1018)

Upper tract transitional cell carcinoma (TCC) accounts for approximately 5% of urothelial tumors. Ureteral tumors occur most often in the distal ureter (70%), followed by the mid-ureter (25%) and the proximal ureter (5%). The surgical therapy for upper tract TCC is based on tumor grade, stage, location, and confounding factors of individual cases. This article discusses the least-invasive to most-invasive surgical treatments, with a brief discussion of absolute and relative indications and contraindications for each.

Ureteroscopy
Ureteroscopy is most appropriate for low-grade, low-stage disease. It is also a reasonable treatment option for patients with bilateral upper tract tumors, anatomically or functionally solitary kidneys, severe renal insufficiency, palliative needs, or severe comorbidities that place them at high risk for other surgeries. The use of ureteroscopy for definitive therapy in patients with a normal contralateral kidney may be considered. Patients who elect for such treatment should have low-stage and low-grade disease, have tumors smaller than 1.5 cm, and be willing to undergo lifelong surveillance.

Several key steps should be observed in ureteroscopic treatment of upper tract TCC. Depending on tumor location and accessibility, either a semirigid or flexible ureteroscope can be used. If possible, both urine cytologies and pelvic or ureteral washings should be obtained. In addition, several biopsies of the tumor and tumor base should be obtained using either an endoscopic biopsy forceps or a basket. After biopsy, options for definitive tumor treatment include laser photocoagulation or ablation, mechanical tumor debulking, or fulguration with electrocautery.

Laser treatment can be accomplished using either an Nd:Yag or Ho:Yag laser alone or together. The Ho:Yag laser has a shallow depth of penetration (0.4 mm) and has the ability to coagulate tissue, making it useful for treating smaller lesions and ablating the thin-walled ureter. The Nd:Yag laser has a greater depth of penetration (5–6 mm) and can be used in a noncontact manner to treat larger tumors more efficiently. Charred superficial tissue is then removed using a basket or ureteroscopic forceps. Larger tumors may require staged resection.

After complete endoscopic treatment of an upper tract tumor, interval surveillance with cystoscopy, cytology, upper tract imaging, and ureteroscopy should be performed on a timeline similar to that for bladder TCC surveillance protocols. For example, an appropriate protocol would be cystoscopy and urine cytology every 3 months alternating with cystoscopy, cytology, retrograde pyelogram, and ureteroscopy every 6 months for the first...
Flexible ureteroscopy has been described as every 6 months and contralateral upper tract imaging annually.\(^2\) Flexible ureteroscopy has been described as every 6 months and contralateral upper tract imaging annually.\(^2\) Flexible ureteroscopy has been described as every 6 months and contralateral upper tract imaging annually.\(^2\) Flexible ureteroscopy has been described as every 6 months and contralateral upper tract imaging annually.\(^2\)

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2 years, followed by cystoscopy every 6 months and ureteroscopy and contralateral upper tract imaging annually.\(^2\) Benefits of laparoscopic ureteroscopy treatment include laser photocoagulation with electrocautery.\(^8\) Similar to retrograde ureteroscopy, operations for tumor treatment include laser photocoagulation with electrocautery.\(^8\) Similar to retrograde ureteroscopy, operations for tumor treatment include laser photocoagulation with electrocautery.\(^8\) Similar to retrograde ureteroscopy, operations for tumor treatment include laser photocoagulation with electrocautery.\(^8\)

The most common complications of ureteroscopic management of upper tract TCC are stricture and perforation. Ureteral stricture rates after ureteroscopic TCC treatment range from 5% to 14%. Treatment of larger tumors and tumors with a circumferential base increase this risk. Perforation is most common in the thin-walled proximal ureter and less common in the thicker-walled distal ureter. Perforation rates range from 0% to 10% in published series.\(^5\)–\(^7\)

Disease progression or worsening outcomes caused by either delayed nephroureterectomy or angiolymphatic spread from high pressures during ureteroscopy is a potential concern with ureteroscopic treatment. Kulp and Bagley\(^8\) reviewed the pathology of 13 patients who underwent nephroureterectomy after ureteroscopy and found no evidence of tumor cells in the vascular or lymphatic spaces. Limited studies on patients who underwent ureteroscopic treatment with delayed nephroureterectomy show no difference in clinical or pathologic outcomes.\(^9\)–\(^10\)

Percutaneous Endoscopy

Upper tract TCC can also be treated with antegrade endoscopy through percutaneous access. Indications for a percutaneous approach include tumor location and anticipation of postoperative topical immunotherapy or chemotherapy. Lower pole tumors are often more accessible from this approach. Concern exists regarding cancer seeding of the percutaneous access tract.\(^11\)–\(^12\) Similar to retrograde ureteroscopy, options for tumor treatment include laser photocoagulation or ablation, mechanical tumor debulking, or fulguration with electrocautery.

Partial Ureterectomy

Distal ureteral tumors can be managed with ureteroureterostomy, Boari flap, or psoas hitch as needed. Although the most appropriate tumors for this type of management are low-grade and low-stage, they may have characteristics not amenable to ureteroscopic treatment, including large size and configuration. For instance, a tumor with a circumferential base may result in stricture if resected ureteroscopically. In addition, patients without a second renal unit or with a high-risk second renal unit (i.e., chronic renal insufficiency, diabetes, hypertension, other renal disease, or contralateral tumor) may be good candidates for partial ureterectomy.

Laparoscopic Nephroureterectomy

The first laparoscopic nephroureterectomy was reported as a treatment option for upper tract TCC by Clayman et al.\(^11\) in 1991. Benefits of laparoscopic nephroureterectomy over open surgery include shorter convalescence, reduced pain and analgesic requirements, and faster return of bowel function. Hand-assisted and straight laparoscopic approaches offer similar benefits compared with open surgery. Hand-assisted laparoscopic nephroureterectomy may allow a smoother transition from an open surgical technique to laparoscopy with decreased initial operative times. In addition, hand-assisted surgery allows en bloc removal of the entire specimen, preserving the oncologic principles of open surgery.

In terms of technical aspects of the procedure, dissection of the kidney is identical to that described in laparoscopic radical nephrectomy. Importantly, the initial step of a laparoscopic approach is early identification and ligation of the ureter below the level of the tumor before manipulating and mobilizing the kidney. Either a retroperitoneal, transperitoneal, or hand-assisted approach may be used, depending on surgeon preference.

The bladder cuff and distal ureter can be managed through endoscopic and open excision using approaches such as the pluck technique. Transurethral cystoscopy and endoscopic resection of the ureteral orifice and bladder cuff with a Collins knife are performed. The distal ureteral is then “plucked” from its bladder attachment during the laparoscopic portion of the procedure and removed en bloc with the remainder of the specimen. One drawback of this technique is the possibility of tumor spillage and seeding.

However, this technique can be modified many ways. Cystoscopic resection can follow laparoscopic renal and ureteral dissection. Although it involves repositioning the patient, this approach is preferred because
laparoscopic occlusion of the distal ureter can be achieved with a clip, decreasing any chance of tumor seeding in the retroperitoneum. Some authors describe grasping the distal ureter with an endoscopic grasper that is introduced through a suprapubic intravesical trocar to place traction on the ureter and facilitate thorough intramural dissection. In this setting, if the bladder cuff is taken before renal and proximal ureteral mobilization, a 2-0 absorbable Surgi-Tie may be used to occlude the distal ureter and prevent tumor spillage.

Wong and Leveillee\textsuperscript{14} described another modification that avoids the need to reposition the patient, whereby the patient is placed in a modified dorsal lithotomy position in Allen stirrups with a 30° tilt. Early ligation of the ureter is performed laparoscopically with clips to prevent seeding of tumor cells. At the end of the operation, transurethral excision of the transmural ureter and bladder cuff is completed. The bladder defect is left to close by secondary intention with Foley decompression. A follow-up report on a series of 49 patients from the same group with a mean follow-up of 10.6 months showed no evidence of pelvic or peritoneal tumor recurrences.\textsuperscript{15}

A fifth approach is transvesical endoscopic resection of the bladder cuff. This involves establishing suprapubic bladder access with a transvesical trocar to perform endoscopic resection of the bladder cuff and distal ureter, allowing en bloc removal of the entire upper tract with the kidney specimen. This approach obviates the need to reposition the patient.

A sixth option is initial completion of the laparoscopic portion of the nephroureterectomy and dissection of the distal ureter to the level of the bladder. The bladder cuff and distal ureter are then excised with an endoscopic GIA stapler. In the initial description of this technique, the distal ureter is unroofed endoscopically before laparoscopic dissection and stapling of the distal ureter in the pelvis.\textsuperscript{16}

Another option is to complete the renal and proximal ureteral dissection laparoscopically with a formal open incision (modified Gibson, Pfannenstiel, or lower midline) to remove the distal ureter and bladder cuff. Open excision of the distal ureter and bladder cuff may also be achieved through an inferiorly located hand port incision. The detrusor is incised circumferentially and a 1- to 2-cm bladder cuff is removed with the distal ureter. The cystotomy is then closed in 2 layers with a 2-0 absorbable suture.

Some concern exists regarding tumor seeding if the distal ureter is left open to the retroperitoneum or pelvis during nephroureterectomy. Although reports of retroperitoneal recurrences exist,\textsuperscript{17–19} these reports originate from early experiences in which endoscope resection of the distal ureter was performed before open nephroureterectomy. Therefore, the authors advocate clipping the distal ureter before excising the bladder cuff to prevent spillage of cancer cells into the bladder and retroperitoneum.

Laguna and de la Rosette\textsuperscript{20} reviewed the different techniques for distal ureteral and bladder cuff management in open surgery and found similar outcomes among all options. Tan et al.\textsuperscript{21} performed a similar review of the literature for distal ureter and bladder cuff management in the setting of laparoscopic nephroureterectomy, and concluded that no technique was superior. However, efforts to minimize potential tumor seeding (i.e., early occlusion of the distal ureter) should become standard care. In addition, a recent series comparing several methods of bladder cuff management reported higher incidences of positive margins and bladder recurrences when laparoscopic stapling was used at the distal ureter.\textsuperscript{22}

**Open Nephroureterectomy**

Historically, open nephroureterectomy has been the gold standard of treatment for upper tract TCC. This technique involves 1 or 2 lengthy incisions and the expected associated morbidity. The salient steps of open nephroureterectomy include full mobilization of the entire kidney along with the perinephric fat and Gerota’s fascia; dissection and individual division of the renal vessels in a standard fashion; and removal of the entire ureter, including the intramural portion, ureteral orifice, and bladder cuff. The bladder wall defect is then closed with absorbable suture in 2 layers. As with laparoscopy, several options are available for managing the bladder cuff and distal ureter, including open and endoscopic approaches.

Although open nephroureterectomy is the historic gold standard, laparoscopic surgery is progressively eclipsing standard open techniques for treating upper tract TCC. After reviewing laparoscopic versus open nephroureterectomies in all published series between 1991 and 2004, Rassweiler et al.\textsuperscript{23} concluded that these 2 groups had no significant difference in bladder recurrence (24% vs. 24.7%), local recurrence (4% vs. 6%), or distant metastases (15.5% vs. 15.2%). Currently,
indications for open nephroureterectomy include surgeon preference and experience, prior abdominal procedures with concern for adhesions, or a patient history of severe chronic obstructive pulmonary disease.

Role of Lymph Node Dissection

The role of lymph node dissection in upper tract TCC remains unclear and controversial. Lymph node dissection has not been shown to offer any therapeutic benefit in patients with upper tract TCC. In past series, nearly all patients with node-positive disease progressed to early distant metastasis despite lymph node dissection. A retrospective analysis of patients who underwent lymphadenectomy in the setting of open nephroureterectomy showed that regional lymphadenectomy offered no survival benefit when patients were stratified by grade. In open surgery, lymph node dissection may add only little morbidity and operative time while offering a possible occasional therapeutic benefit and additional prognostic information. Regional lymph node dissection may also help identify candidates for adjuvant chemotherapy. In patients with invasive bladder cancer, cystectomy with regional lymphadenectomy remains standard care. Survival among bladder cancer patients with both node-positive and node-negative disease is directly proportional to the number of lymph nodes removed. Extrapolating this data to upper tract TCC provides additional support for regional lymph node dissection in the setting of either laparoscopic or open nephroureterectomy. Performing lymphadenectomy is consistent with sound oncologic principles, provides additional prognostic information, and carries minimal additional morbidity and surgical risk.

References