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Impact of Distal Ureter Management on Oncologic Outcomes Following Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma

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Abstract

Background: There is a lack of consensus regarding the optimal approach to the bladder cuff during radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC).
Objectives: To compare the oncologic outcomes following RNU using three different methods of bladder cuff management.
Design, setting, and participants: Retrospective analysis of 2681 patients treated with RNU for UTUC at 24 international institutions from 1987 to 2007.
Intervention: Three methods of bladder cuff excision were performed: transvesical, extravesical, and endoscopic.
Outcome measurements and statistical analysis: Univariable and multivariable models tested the effect of distal ureter management on intravesical recurrence, recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS).
Results and limitations: Of the 2681 patients, 1811 (67.5%) underwent the transvesical approach; 785 (29.3%), the extravesical approach; and 85 (3.2%), the endoscopic approach. There was no difference in terms of RFS, CSS, and OS among the three distal

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ureteral management approaches. Patients who underwent the endoscopic approach were at significantly higher risk of intravesical recurrence compared with those who underwent the transvesical ($p = 0.02$) or extravesical approaches ($p = 0.02$); the latter two groups did not differ from each other ($p = 0.40$). Actuarial intravesical RFS estimates at 2 and 5 yr after RNU were 69% and 58%, 69% and 51%, and 61% and 42% for the transvesical, extravesical, and endoscopic approaches, respectively. In multivariate analyses, distal ureteral management ($p = 0.01$), surgical technique (open vs laparoscopic; $p = 0.02$), previous bladder cancer ($p < 0.001$), higher tumor stage (trend; $p = 0.01$), concomitant carcinoma in situ (CIS) ($p < 0.001$), and lymph node involvement (trend; $p < 0.001$) were all associated with intravesical recurrence. Excluding patients with history of previous bladder cancer, all variables remained independent predictors of intravesical recurrence.

Conclusions: The endoscopic approach was associated with higher intravesical recurrence rates. Interestingly, concomitant CIS in the upper tract is a strong predictor of intravesical recurrence after RNU. The association of laparoscopic RNU with intravesical recurrence needs to be further investigated.

1. Introduction

Radical nephroureterectomy (RNU) with excision of the bladder cuff is the standard of care for high-risk noninvasive and invasive urothelial carcinoma of the upper tract (UTUC) [1]. The outcomes of different bladder cuff management approaches remain poorly investigated [2,3]. Recently, Li et al. [4] reported no difference in oncologic outcomes among three different approaches of the distal ureter (transvesical, extravesical, and endoscopic) in a retrospective single-center study of 301 patients. This study had a relatively small sample size and short follow-up, limiting its statistical power to assess the impact of distal ureteral management approaches on intravesical recurrence. The aim of the current study was to assess the impact of the three, different, distal ureter management approaches on intravesical recurrence-free survival, recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS) in a large, international, multicentric cohort of patients treated with RNU.

2. Materials and methods

2.1. Patients

In this institutional review board-approved study, all participating sites provided necessary institutional data-sharing agreements prior to study initiation. A total of 24 centers worldwide provided data. A computerized databank was generated for data transfer. After combining the data sets, reports were generated for each variable to identify data inconsistencies and other data integrity problems. Through regular communication with all sites, resolution of all identified anomalies was achieved before analysis. Prior to final analysis, the database was frozen and the final data set was produced for the current analysis.

From 1987 to 2007, 2681 patients underwent RNU with bladder cuff excision for UTUC. None of the patients received preoperative chemotherapy or radiotherapy, and none had previous muscle-invasive bladder cancer. Adjuvant chemotherapy was administered at the clinicians' discretion based on tumor stage and overall health status as well as patient preference.

2.2. Surgical technique

RNU was performed either open or laparoscopically, based on the surgeon's preference. The distal bladder cuff was removed either through a transvesical, extravesical, or endoscopic approach. The transvesical technique was performed via an incision in the lower quadrant or midline. It involved creating an anterior cystotomy in the bladder, confirming the contralateral ureteral orifice, and circumferentially incising the ipsilateral ureteral orifice through the full thickness of the bladder. The RNU specimen with the bladder cuff was removed en bloc and the anterior cystotomy was closed in two layers.

In the extravesical technique, the intramural portion of the ureter was completely dissected. With gentle traction on the ureter, a right-angle clamp or stapler was used to transect the distal ureter with its bladder cuff. The bladder was also closed with a two-layer suture.

In the endoscopic approach, the patient was placed in the lithotomy position and underwent cystoscopy. A resectoscope was inserted into the bladder via the urethra using sterile water for irrigation and the ipsilateral ureteral orifice was endoscopically coagulated. The bladder was kept semidistended to prevent excessive extravasations during the procedure. A hook electrode was used to incise a circumferential 10-mm cuff of bladder mucosa around the ureteral orifice. Endoscopic-guided dissection and incision deep to the level of perivesical fat and detachment of the intramural ureter were performed. After complete hemostasis, the bladder was catheterized. The patient was repositioned for RNU. The first step of RNU was to identify and ligate the ureter below the level of the tumor prior to mobilizing the kidney. After completing nephrectomy, the distal ureter, including the bladder cuff, was gently retracted and removed. The ureter was checked for complete removal by identifying the coagulated edge of the bladder cuff at the distal ureteral end.

2.3. Pathologic analysis

All surgical specimens were processed according to standard pathologic procedures at each institution [5]. Tumors were staged according to the 2002 American Joint Committee on Cancer–Union Internationale Contre le Cancer (AJCC/UICC) TNM classification [6]. Tumor grade was assessed according to the 1998 World Health Organization/International Society of Urologic Pathology consensus classification [7]. Tumor location was defined as either renal pelvic or ureteral [8,9]. Tumor multifocality was defined as the synchronous presence of two or more pathologically confirmed tumors in any location (renal pelvis or ureter) [10,11]. Lymphovascular invasion (LVI) was defined as the presence of tumor cells within an endothelium-lined space without underlying muscular walls [12].

2.4. Follow-up

Patients were followed, generally, every 3–4 mo for the first year following RNU, every 6 mo from the second through the fifth year, and annually thereafter. Follow-up consisted of a history, physical examination, routine