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Original article

Multi-institutional validation of the ability of preoperative hydronephrosis to predict advanced pathologic tumor stage in upper-tract urothelial carcinoma

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Abstract

Objective: The presence of hydronephrosis (HN) has been implicated as a predictor of poor outcomes for patients diagnosed with bladder cancer. Small, single institution preliminary reports suggest a similar negative relationship may exist for upper-tract urothelial carcinoma (UTUC). Herein, we attempt to validate the prognostic value of preoperative HN in a large, multi-institutional cohort of UTUC patients.

Materials and methods: Data on 469 patients with localized UTUC from 5 tertiary referral centers who underwent a radical nephroureterectomy (91%) or distal ureterectomy (9%) without neoadjuvant chemotherapy were integrated into a relational database. Preoperative HN data, including presence vs. absence and high vs. low grade, were available in 408 patients. The association of HN with pathologic features was evaluated.

Results: A total of 254 men and 154 women with a median age of 69 years (IQR 15) were analyzed. Overall, 192 patients (47%) had ≥pT2 disease, 145 (36%) had non-organ-confined (NOC) cancers (≥pT3 and/or positive lymph nodes), and 298 (73%) had high grade UTUC on final pathology. Forty-six percent of patients had tumors in the renal pelvis, 27% in the ureter, and 27% in both locations. Preoperatively, 223 patients (55%) were noted to have ipsilateral HN (39% low grade and 61% high grade). Hydronephrosis was associated with ≥pT2 stage ($P < 0.001$), NOC disease ($P < 0.001$), and high grade cancers ($P = 0.04$). On multivariate analysis adjusting for gender, age, and tumor location, HN was an independent predictor of muscle invasive (HR 7.4, $P < 0.001$), NOC (HR 5.5, $P < 0.001$), and high pathologic grade (HR 1.6, $P = 0.03$) UTUC disease.

Conclusion: The presence of preoperative HN was associated with advanced stage UTUC. This readily available imaging modality may improve preoperative risk stratification for UTUC patients thereby guiding use of endoscopic versus extirpative surgery as well as the need for neoadjuvant chemotherapy regimens.

Keywords: Computed tomography (CT); Magnetic resonance imaging (MRI); Intravenous pyelogram (IVP); Renal ultrasonography (RUS); Transitional cell carcinoma (TCC); Renal pelvis; Ureter

1. Introduction

Upper-tract urothelial carcinoma (UTUC), comprising cancers of the ureter and renal pelvis, account for 5% of all urothelial malignancies and 10% of renal tumors [1]. Rad-

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ical nephroureterectomy (RNU) with an ipsilateral bladder cuff excision is the gold standard for surgical management of these lesions. Contemporary oncologic outcomes with extirpative therapy demonstrate durable responses [2].

The ability to accurately predict UTUC pathology prior to initiating therapy may optimize perioperative management strategies and outcomes. In particular, improved identification of tumor stage may guide choice of primary therapy (RNU vs. endoscopic ablation) as well as utilization of neoadjuvant chemotherapy regimens. Specifically, while low grade, non-muscle-invasive UTUC respond favorably to endoscopic ablation, higher grade and stage lesions require RNU [3,4]. Additionally, contemporary data has suggested that neoadjuvant chemotherapy for high-risk UTUC may yield a significant rate of pathologic downstaging (41.5% reduction in tumors $\geq$ pT3) with 14% of such patients experiencing a complete remission [5]. Despite such theoretical advantages, appropriate patient selection continues to be challenging.

For patients with bladder cancer, hydronephrosis is associated with more advanced tumor stage as well as poorer oncologic outcomes [6–8]. In particular, Stimson and colleagues recently highlighted in a series of 753 patients managed by radical cystectomy that hydronephrosis was an independent predictor of extravesical (OR 2.01, $P < 0.001$) and lymph node positive (OR 1.94, $P < 0.001$) bladder cancer [8]. A similar association has been implicated for UTUC. Several studies have suggested that delayed renal excretion of contrast medium is associated with invasive ureteral carcinoma [9–11]. Proposed mechanisms have included luminal obstruction, intramural invasion, or extrinsic compression. More recently, Ng et al. highlighted that hydronephrosis on preoperative axial computed tomography (CT) was associated with features of high risk UTUC and predicted advanced pathologic stage for both renal pelvic and ureteral cancers [12]. Inherent limitations of these series, however, are relatively small case numbers as well as interpretation by a limited number of radiologists. As such, the ability to generalize conclusions may be challenging.

Therefore, in this large multi-institutional cohort of patients undergoing radical surgery for UTUC, we sought to better determine the relationship between hydronephrosis on preoperative imaging and final pathologic disease characteristics.

2. Patients and methods

2.1. Study population

Institutional review board (IRB) approval was obtained at all participating institutions. The charts of 469 patients with clinically localized UTUC who underwent a RNU or distal ureterectomy at 5 U.S. medical centers between September 1997 and August 2008 were retrospectively reviewed. RNU was performed by an open or laparoscopic approach with management of the distal ureter at the surgeon's discretion. All distal ureterectomies were performed via an open approach. Patients who received neoadjuvant chemotherapy and those with prior or concurrent bladder cancer were excluded to minimize the potentially confounding impact on imaging and pathologic data. Preoperative data on ipsilateral hydronephrosis was available for 408 patients (87%) who formed the cohort for analysis.

2.2. Ipsilateral hydronephrosis

Assessment of hydronephrosis was determined from radiographic reports of upper-tract imaging including CT +/− intravenous contrast, magnetic resonance imaging (MRI) +/− intravenous contrast, intravenous pyelography (IVP), or renal ultrasonography (RUS). For classification of the degree of hydronephrosis, renal units reported as having mild or moderate (or grades I or II) dilation were categorized as low grade, while severe (or grade III) dilation was classified as high grade hydronephrosis. One author (J.D.R.) blinded to the radiology reports or final classification used in study analysis then reviewed 80 of the 408 films (20%) to assess concordance with outcomes derived from radiology reports. Within this re-reviewed cohort, there was a 98% concordance for assessing presence or absence of hydronephrosis, and an 89% concordance for classification of high vs. low grade hydronephrosis. Of note, we observed that grade of hydronephrosis was not associated with differences in final pathologic stage of tumors (Results section). Therefore, to avoid small subgroups and heterogeneity with respect to grading of HN, we elected only to evaluate presence or absence of HN on multivariate analysis.

Only imaging studies performed within 6 weeks of RNU or distal ureterectomy were included for evaluation. Patients who had either nephrostomy tube drainage or a ureteral stent inserted for HN were included in the study cohort provided their imaging study prior to drainage occurred within 6 weeks of definitive surgery. For renal pelvic lesions, the presence of hydrocalyx was included in the cohort of patients considered to have HN. Hydrocalyx was defined as any degree of dilation within a focal calyx with our without the presence of obvious obstruction at the draining infundibulum. For ureteral tumors, any degree of dilation in any component of the ureter or associated renal unit was classified as hydronephrosis.

2.3. Final pathology specimens

All specimens were histologically confirmed to be urothelial carcinoma. Tumor classification was assessed according to the 2002 American Joint Committee on Cancer–Union International Contre le Cancer (AJCC-UICC) Tumor-Node-Metastasis (TNM) classification. Tumor grading was assessed according to the 2004 WHO/ISUP (International Society of Urologic Pathology) consensus classification.