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Original article

Distal ureterectomy is a safe surgical option in patients with urothelial carcinoma of the distal ureter

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Abstract

Objectives: We evaluated cancer-specific survival (CSS) and recurrence-free survival (RFS) rates of open distal ureterectomy (DU) compared with radical nephroureterectomy (RNU) for urothelial carcinoma of the distal ureter.

Methods and materials: We retrospectively considered patients with urothelial carcinoma of the distal ureter who underwent DU or RNU at our department. Survival analysis and Cox regression models compared CSS and RNU after DU and RNU. RFS was evaluated separately for bladder and upper tract. Covariates were age, gender, symptoms at diagnosis, pathologic stage and grade, associated carcinoma in situ, surgical margins, lympho-vascular invasion, multifocality, necrosis, and previous or concomitant bladder cancer.

Results: Forty-nine and 42 patients underwent DU and RNU, respectively. Median patients' follow-up was 51.5 months (range 4–290 mo). Two patients (4%) in the DU group were diagnosed with a recurrence in the ipsilateral upper tract after 63 and 45 months, respectively. Both patients underwent nephroureterectomy and are still alive in strict follow-up for non–muscle invasive bladder recurrence. Contralateral upper tract recurrence was observed in 1 and 3 patients in the RNU and DU group, respectively. At 5 years, CSS and RFS (upper tract) rates were 77% and 91% for DU and 78% and 96% for RNU, respectively. On univariable and multivariable analyses the type of surgery did not influence CSS and RFS ($P = 0.92$ and $P = 0.94$).

Conclusions: DU is a safe surgical option in patients with urothelial carcinoma of the distal ureter and does not compromise oncologic outcomes compared with RNU.

Keywords: Urothelial carcinoma; Upper urinary tract; Ureter; Survival; Recurrence; Ureterectomy

1. Introduction

Radical nephroureterectomy (RNU) with bladder cuff removal represents the standard treatment for upper urinary tract urothelial cell carcinomas (UUT-UCCs) [1,2]. Segmental ureterectomy (SU) represents a surgical option in selected cases preserving the ipsilateral kidney and providing adequate pathologic specimens for definitive histologic analysis [3]. It can be considered in imperative cases (renal insufficiency and solitary functional kidney) or in elective cases [4,5]. The choice of approach depends on technical constraints and the anatomic location of the tumor. Segmental resection of the mid and proximal ureter is associated with a failure rate greater than that for the distal pelvic ureter [3,6]. The National Comprehensive Cancer Network guidelines support SU as elective treatment for distal ureteral lesions [7]. Despite these recommendations limited data are available on the safety and cancer control rates of SU.

In this study, we describe the outcomes of distal ureterectomy (DU) in comparison with RNU in patients with UCC of the distal ureter.

2. Methods and materials

Patients diagnosed with UUT-UCCs were retrospectively reviewed. Only patients with a lesion of the distal ureter (defined as below the level of the iliac vessels) were included. Lesions previously treated endoscopically were excluded from this study to avoid possible confounding effects on oncologic outcomes. No patient underwent

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neoadjuvant systemic chemotherapy. Diagnostic procedures were mainly based on imaging (intravenous urography, computed tomographic [CT] urography or magnetic resonance urography, and retrograde pyelography). Preoperative ureteroscopy with biopsy was only performed in case of inconclusive imaging results. No patient had a stent in place at the time of surgery. DU was indicated in imperative (solitary kidney, chronic renal insufficiency, and impaired renal function or parenchymal rarification of the contralateral kidney or American Society of Anesthesiologists score 4) or elective cases (DU was also routinely offered to patients after detailed information). The indication for RNU or elective DU was mainly based on the surgeon's discretion (based on imaging regarding probability of successful ureteral implantation or bladder capacity or both) and on informed consent. RNU was routinely performed by double open access procedure with excision of a bladder cuff. DU was performed through a Gibson incision and the distal ureter was dissected beyond the bifurcation of the iliac vessels. Direct contact with the tumor was avoided through proximal ligation of the ureter and a wide cuff of bladder was resected. Ureteral reimplantation using the psoas-hitch technique was performed. Frozen sections of the proximal ureteral margin were done in all patients. In case of intraoperative positive margins, the proximal ureter was re-resected until frozen sections were negative. Intraoperative ureterorenoscopy was not performed. In case of DU lymphadenectomy, it was not routinely performed except in cases of clinical evidence of disease or surgeon's decision due to lack of evidence during the considered period. Pathologic features of the UUT-UCC including pT classification (uniformly adapted to TNM 2009) and grade (World Health Organization 1973) were recorded and associated with outcome [8,9]. A central pathologic review was not performed. The surveillance regimen of the patients was the same for RNU and DU based on cystoscopy, urinary cytology, and CT-urography for at least 5 years [2,10]. In DU patients, ureteroscopy was only indicated in case of suspicious urinary cytology, suspicious CT imaging and history of carcinoma in situ. All complications within the follow-up were recorded, defined, and graded according to Dindo et al.'s modification to the Clavien system [11].

Only patients without evidence of nodal or distant metastases in the preoperative imaging were included in our analysis. Deaths from UUT-UCCs were coded as cancer-specific events. All other deaths were considered other cause mortality. Median time of follow-up was calculated with time to last follow-up or death.

3. Statistical analysis

Patients were grouped by type of surgery: DU vs. RNU. Clinical and pathologic characteristics were compared by Fisher exact test and Wilcoxon test. Overall survival (OS) and cancer-specific survival (CSS) were estimated using the Kaplan-Meier method and the log-rank test. Recurrence-free survival (RFS) was assessed separately for the UUT and bladder. Subsequently, the effect of the type of surgery (DU vs. RNU) on OS, CSS, and RFS was analyzed using univariable and multivariable Cox regression models.

Covariates consisted of age, type of surgery, gender, symptoms at diagnosis, pT classification, grade, concomitant carcinoma in situ, lympho-vascular invasion, multifocality, tumor necrosis, and presence of bladder cancer preoperatively. P values <0.05 were considered statistically significant.

4. Results

Ninety-one patients with UUT-UCCs of the distal ureter were identified and operated in our institution between January 1984 and March 2011. RNU and DU were performed in 42 and 49 patients, respectively. Fifty-four patients were males, 37 females, median age was 72 years (range 48–87 y). Clinical and pathologic characteristics of the patients distinguished by type of surgery are shown in Table 1. With respect to Fisher exact test there were no statistically significant differences regarding most of the variables, except symptoms at diagnosis ($P = 0.012$) and the presence of previous bladder cancer ($P = 0.017$). None of the patients had a history of muscle-invasive bladder cancer before UUT-UUC surgery.

Overall, in 6 patients no tumor tissue was present in the specimen (pT0). These patients had undergone a prior transurethral resection of the bladder (TURBT) for non–muscle invasive urothelial carcinoma at the ureteral orifice with clinical suspicion of residual tumor tissue in the intramural ureter.

Twelve patients (7 DU and 5 RNU) had positive surgical margins at the final pathology at the distal margin intraluminally. These patients had prior TURBT of bladder tumors located around the orifice and continuously extending into the distal ureter. Thus, the positive margins corresponded with the intraluminal margin of the prior TURBT. Out of these 12 patients, 4 developed a bladder recurrence at the follow-up. The proximal margin was free in all cases. Lymphadenectomy was performed in only 1 patient undergoing RNU by muscle-invasive UUT-UCC of the distal ureter and suspicious nodes in the preoperative imaging. The final pathology was pT2G2V0L0N0. Three patients presented Clavien grade IIIb postoperative complications in the DU group, in particular there were 1 local hematoma, 1 wound dehiscence and 1 urinoma requiring surgical intervention postoperatively. In the RNU group, 2 complications were registered (Clavien grade 1 and grade 2).

Overall mean follow-up time was 51.5 months (range 4–290 mo). Survival and recurrence rate in association with type of surgery are reported in Table 2.

Two patients (4%) in the DU group were diagnosed with a recurrence in the ipsilateral upper tract after 63 and 45 months, respectively. Both patients underwent nephroureterectomy and are still alive in strict follow-up for non–muscle invasive