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Retroperitoneal Lymph Node Dissection (RPLD) in Conjunction with Nephroureterectomy in the Treatment of Infiltrative Transitional Cell Carcinoma (TCC) of the Upper Urinary Tract: Impact on Survival

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Abstract

Objectives: To evaluate the prognostic impact of retroperitoneal lymph node dissection (RPLD) performed during nephroureterectomy on time to recurrence and survival in patients with infiltrative transitional cell carcinoma (TCC) of the upper urinary tract.

Methods: The charts of 82 patients with T2–T4 TCC of the upper tract were retrospectively reviewed. The median patient age was 67.7 yr. Seventy-nine patients underwent nephroureterectomy and three had partial nephrectomy. Forty patients (48.8%) had RPLD with removal of more than five nodes after nephroureterectomy (group 1), whereas 42 (51.2%) had nephroureterectomy only (group 2). Median follow-up was 64.7 mo. The prognostic role of RPLD, T (2 vs. 3–4), G (2 vs. 3), N (0 vs. 1–2 vs. x), age (<65 vs. >65 yr) and sex on time to recurrence and survival were evaluated.

Results: Median time to recurrence and overall survival were 51.2 and 52.5 mo, respectively, in group 1 and 18.5 and 21.2 mo in group 2. Univariate analysis demonstrated that RPLD and T and N status were significantly related both to time to recurrence ($p = 0.009$, 0.008, and 0.009, respectively) and survival ($p = 0.000006$, 0.003, and 0.003). When analyzed using the Cox proportional hazard model, RPLD and T category were the only two factors demonstrating independent significance on overall survival ($p = 0.004$ and 0.008).

Conclusions: The results indicate a possible curative role of RPLD in the treatment of patients with infiltrative TCC of the upper urinary tract. Further randomized trials are needed to confirm these results.

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1. Introduction

Transitional cell carcinoma (TCC) of the upper urinary tract is relatively uncommon accounting for 2–10% of all urothelial tumors [1]. About 30% of patients have tumors invading the musculature of the renal pelvis or the ureter and an additional 30% have an involvement of peripelvic or periureteral soft tissue, renal parenchyma, or regional lymph nodes at the time of initial diagnosis [2]. The standard treatment for infiltrative TCC of the upper urinary tract consists of nephroureterectomy with removal of a bladder cuff. The definitive role of lymphadenectomy and its extension has not been established. Some authors suggest its possible therapeutic benefit in selected patients with lymph node metastases, whereas others suggest it only for staging [1,3]. The aim of this retrospective study was to evaluate the prognostic impact of retroperitoneal lymph node dissection (RPLD) in conjunction with nephroureterectomy in patients with advanced TCC of the upper urinary tract on time to recurrence and survival.

2. Patients and methods

The charts of 83 consecutive patients with advanced TCC of the upper urinary tract treated from January 1980 to December 2002 at the Department of Urology of the Estense Institute in Modena and the B. Ramazzini Hospital in Carpi (Modena) were reviewed. Because of insufficient data, one patient was excluded from this analysis. This report includes 82 patients who were treated, fully evaluated, and regularly followed-up. The median age was 67.7 yr (range: 35–82 yr); 59 patients were men and 23 women.

2.1. *Diagnosis*

Urinary cytology, intravenous pyelography (IVP), and abdominal ultrasound (US), or computed tomography (CT) was used for diagnosis and staging. Ureteroscopy was performed in only three patients, whereas urethrocystoscopy was always done before surgery to detect any associated bladder tumors. After 1999, URO-CT was routinely adopted instead of IVP. In 48 patients (58.5%) tumors were on the right side and on the left in 34 patients (41.5%). In 47 patients (57.3%) tumors were localized in the renal pelvis or calices, in 28 cases in the ureter (34.1%), and in 7 patients (8.5%) in both. Fifteen of 82 patients (18.3%) had a concomitant tumor of the bladder detected during the initial cystoscopy. They were all non–muscle-invasive tumors. Five of 82 patients (6.1%) presented with distant metastases in the lung (3), adrenal (1), and colon (1) at the time of initial diagnosis.

2.2. *Treatment*

Seventy-nine patients underwent nephroureterectomy with the excision of a bladder cuff including the ureteral meatus, whereas three patients with tumors located in the renal pelvis and calices in a solitary kidney had a partial nephrectomy. In 40 patients (48.8%) unilateral RPLD was performed in conjunction with nephroureterectomy (group 1); in 42 patients (51.2%) nephroureterectomy alone was done (group 2). RPLD was performed in patients with an infiltrative disease or with enlarged nodes on a preoperative evaluation (CT), in case of enlarged nodes discovered perioperatively, and at the surgeon's discretion. Before 1999 limited RPLD was performed in one institution and the number of nodes removed varied from 5 to 10 (mean, 7.1); after the results of our first report [4], which showed a clear positive prognostic impact of lymphadenectomy, an extended RPLD was routinely adopted. The number of lymph nodes removed varied from 5 to 24 (mean, 11.5).

The extent of lymphadenectomy was determined by the location of the primary tumors. For renal pelvis and upper ureteral tumors the para-aortic, paracaval, or interaortocaval nodes from the hilus to the inferior mesenteric artery were removed, for the mid-ureteric cancers lymphadenectomy was carried out from the renal hilus to the bifurcation of the common iliac artery, and for the lower ureteric tumors the pelvic nodes of the ipsilateral side were removed.

Nephroureterectomy was performed through a median transperitoneal incision in 74 patients and through a flank incision in 8. In these patients RPLD was not performed. Fifteen patients with bladder tumors underwent transurethral resection (TUR) in the same surgical session.

2.3. *Follow-up*

Patients were followed every 3 mo for the first year with urinary cytology and US. Cystoscopy was suggested after 3 mo and, if negative, every 6 mo for 5 yr and then yearly for a further 5 yr. IVP/CT or URO-CT were carried out every year for 5 yr and, if negative, every 2 yr for 10 yr. Ureteroscopy was used only in case of positive cytology with negative cystoscopy or bladder mapping. The results of cytology and cystoscopy were considered important for the further decision-making during follow-up. The median length of follow-up was 64.7 mo (range: 24–288 mo).

The Union Internationale Contre le Cancer (UICC) classification [5] was used for staging. Tumors were graded as G1 = well differentiated, G2 = moderately well differentiated, and G3 = poorly differentiated.

2.4. *Statistical analysis*

Univariate analysis was used to correlate RPLD and T and N status to recurrence and survival. The Cox proportional hazard model was used to evaluate the independent significance of RPLD, T, and N in terms of overall survival.

3. Results

The intraoperative mortality, within the first 30 d after surgery, was 0.

The pathologic stage was: pT2 in 38 patients (46.3%), pT3 in 36 patients (43.9%), and pT4 in 8