HYDRONEPHROSIS AS A PROGNOSTIC INDICATOR IN BLADDER CANCER PATIENTS

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ABSTRACT

Purpose: Pathological stage is the standard measure of prognosis in patients who have undergone radical cystectomy for bladder cancer. Despite the development of new imaging techniques, clinical staging for bladder cancer continues to be inaccurate. We investigated whether the presence of unilateral or bilateral upper tract obstruction could accurately predict advanced cancer stage (extravesical extension, stage greater than p3b or N+).

Materials and Methods: A retrospective study of 415 patients diagnosed with transitional cell carcinoma of the bladder who were treated with radical cystectomy between 1983 and 1993 was conducted. All patients were followed for survival. The criteria for analysis included hydronephrosis status (no obstruction, unilateral, bilateral) as well as pathological stage of the tumor.

Results: Of 415 patients 72% presented with no, 22.7% unilateral and 5.3% bilateral obstruction. Our results showed a significant correlation between hydronephrosis and advanced cancer stage (p <0.0001), and decreased patient survival (p <0.0001). More than 90% of patients with bilateral obstruction had disease with extravesical extension. Of the patients with unilateral obstruction a third had disease confined to the bladder with a significant proportion confined to the bladder mucosa.

Conclusions: The presence of unilateral or bilateral hydronephrosis is a clinical datum that is already available to help accurately stage bladder tumors. The presence of bilateral obstruction is an ominous sign, while a significant proportion of patients presenting with unilateral obstruction have disease confined to the bladder.

KEY WORDS: neoplasm staging; carcinoma, transitional cell; bladder neoplasms; prognosis; hydronephrosis

Transitional cell carcinoma of the bladder is the second most common malignancy in the genitourinary tract.[1] Pathological stage has been accepted as the gold standard to predict the survival of patients with bladder cancer.[2-4] Other factors shown to be prognostic indicators by univariate analysis include clinical tumor stage, patient age, irritative voiding symptoms, histological grade, history of definitive radiation therapy, tumor location, tumor size, lymphatic or vascular invasion, direct tumor spread and tumor growth pattern.[1,4,5] Studies have also indicated aneuploidy by deoxyribonucleic acid flow cytometry and abnormal nuclear morphometry as prognostic factors.[5] Recently research on the molecular level has implicated p53 and p21 gene mutations in bladder cancer and as markers for prognosis.[6] Historically, hydronephrosis has been believed to be indicative of deeply invasive tumor.[7] The accuracy of this finding in predicting advanced stage disease is unclear. We further investigate the association among hydronephrosis, bladder cancer stage and survival.

MATERIALS AND METHODS

A retrospective review of 415 patients with transitional cell carcinoma of the bladder who underwent radical cystectomy and urinary diversion at our medical center between 1983 and 1993 was performed. Patient and followup information was entered into a database for analysis. Hydronephrosis status was determined by excretory urogram (IVP) at the initial evaluation. The diagnosis of transitional cell carcinoma was made by cystoscopy and transurethral resection of the tumor. Patients referred to the medical center were diagnosed by review of the original pathological slides. Preoperative

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screening included physical examination, chest radiograph, complete blood count, blood urea nitrogen, creatinine, electrolyte analysis and IVP. Furthermore, patients were usually evaluated by bone scan and computerized tomography (CT). The pathological stage of the tumor was determined from the radical cystectomy specimens. Patients were seen 3 weeks, 4 months and 1 year after cystectomy. A small percentage of patients with advanced pathological stages p3 and p4 or N+ disease also received adjuvant chemotherapy. All patients were followed annually for 5 years and subsequently biannually.

We examined the relationship between hydronephrosis and cancer stage, and probability of overall survival and survival stratified by stage. Survival was calculated from date of cystectomy to date of death or last followup. Patients were classified into 3 tumor stage groups of disease confined to the bladder and negative lymph nodes (p0-p3a, N−), extravesical disease and negative lymph nodes (p3b-p4 N−) and positive lymph nodes (N+). Contingency tables and Pearson's chi-square test were used to determine associations between cancer stage and hydronephrosis. We used Kaplan-Meier plots to estimate survival,[8] Greenwood's formula[9] to estimate the standard errors (SE) in the Kaplan-Meier curves, and the log rank test[9] to evaluate the relationship between obstructive urography and patient survival.

RESULTS

A total of 332 men and 83 women diagnosed with transitional cell carcinoma underwent radical cystectomy between 1983 and 1993. Of the patients 380 had invasive transitional cell carcinoma and 35 had carcinoma in situ. Pathological stage was determined postoperatively (table 1 and fig. 1).

TABLE 1. *Distribution of patients by cancer stage*

Stage	No. Pts.		
	No Obstruction	Unilat. Hydronephrosis	Bilat. Hydronephrosis
p0	1	0	0
PIS	37	5	0
Pa	14	4	0
P1	70	7	2
P2	38	5	0
P3a	36	18	0
P3b	67	31	9
P4a	33	20	11
P4b	3	4	0
Totals (%)	299 (72.0)	94 (22.7)	22 (5.3)

Median patient age was 65 years (range 31 to 90). Median followup was 7 years (range 7.2 months to 14 years). Preoperative IVP revealed unilateral and bilateral hydronephrosis in 94 (22.7%) and 22 (5.3%) patients, respectively. The remaining 299 patients (72.0%) had no evidence of ureteral obstruction (table 1).

Log rank analysis of the Kaplan-Meier survival curves indicated an overall mean 5-year survival of 56.8 ± 2.5%. When the same analysis was performed but stratifying by hydronephrosis status, a significant difference in survival between patients with no obstruction and those with unilateral and bilateral hydronephrosis was observed (p <0.0001) (fig. 2). The 5-year survival was 62.6% for patients with no obstruction, and 44.7% for those with unilateral and 30.7% for those with bilateral obstruction (table 2).

Further criteria were established to determine if there was a correlation between the presence of hydronephrosis and pathological stage. Cases were subsequently stratified into 3 categories of p0-p3a, N− for intravesical tumors, p3b-p4, N− for transmural/extravesical tumors and N+ for tumors metastasized to regional nodes (table 3). Chi-square analysis indicated a statistically significant association between hydronephrosis and increasing cancer stage (p <0.0001). Of the patients presenting with bilateral obstruction 54.6% had

metastatic and 36.4% had p3b-p4, N− disease and, thus, 91.0% had advanced disease. Of the patients presenting with unilateral obstruction 34.0% had metastatic and 33.0% had p3b-p4, N− disease and, thus, two-thirds had advanced disease. Of the patients presenting with no obstruction 20.3% had stage p3b-p4, N− and 23% had metastatic disease and, thus, 43.3% had advanced disease.

Kaplan-Meier survival curves were prepared by tumor stage subgroups and stratified by hydronephrosis status. Log rank analysis of these curves showed no statistically significant difference in survival within each stratum and based on obstruction (fig. 3 and table 4). The 5-year survival data indicated, as expected, that there was a significant difference in overall survival based on stage. Of the patients 27% received preoperative or postoperative chemotherapy as part of treatment (24% with no obstruction, and 36% with unilateral and 36% with bilateral hydronephrosis). There was no statistically significant difference in the survival of these patients when stratified by pathological stage.

DISCUSSION

It has been widely reported that cancer stage is the best prognostic indicator for survival of patients who have undergone radical cystectomy for bladder cancer.[1–3,10,11] Despite the development of new imaging techniques, clinical staging for bladder cancer continues to be inaccurate. Skinner et al reported that in more than 50% of patients clinical stage diagnosis was inconsistent with the pathological stage of the tumor.[12] Treatment regimens that include preoperative (neoadjuvant) chemotherapy or bladder salvage regimens have been difficult to assess because of the limitations of clinical staging. We investigated whether the presence of unilateral or bilateral upper tract obstruction could accurately predict advanced cancer stage (extravesical extension, stage p3b or N+).

Historically, it was believed that any obstruction detected on IVP was a poor prognostic indicator for patients diagnosed with bladder cancer.[7] Previous studies have shown that there is muscle invasion in 70 to 90% and metastasis in 55% of patients
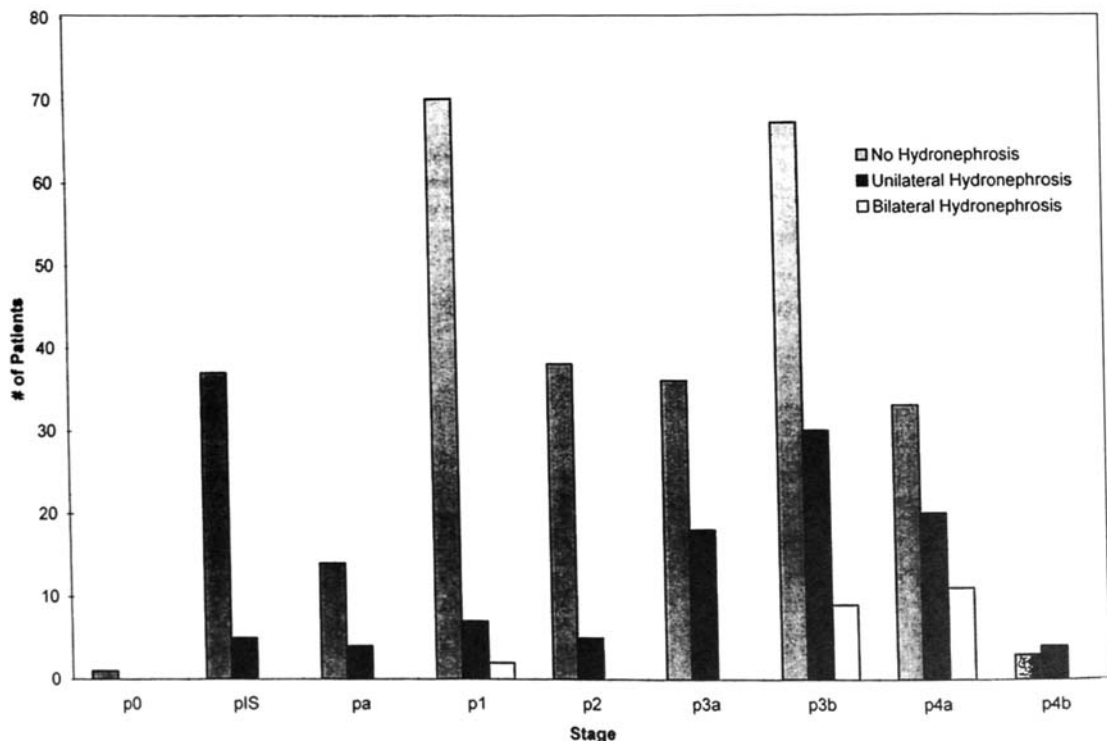

FIG. 1. Patient distribution by cancer stage