Prognostic Factors in Patients With Non-Muscle-Invasive Bladder Cancer Treated With Bacillus Calmette-Guerin: Multivariate Analysis of Data From Four Randomized CUETO Trials


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Objectives: To evaluate the prognostic factors of recurrence and progression after intravesical adjuvant bacillus Calmette-Guerin (BCG) immunotherapy in patients with non-muscle-invasive bladder tumors. Methods: From February 1990 to May 1999, the Spanish Club Urologico Espanol de Tratamiento Oncologico (CUETO) group has performed four randomized phase 3 studies comparing different intravesical treatments in patients with noninvasive bladder cancer. Data from 1062 evaluable patients treated only with BCG were analyzed. Most patients received BCG once weekly for 6 consecutive weeks and a short-term BCG maintenance (once every 2 wk 6 times more). Associated tumor in situ (TIS) was found in 7.5% (n=80) of cases. There were 22.1% (n=235) patients with T1G3 tumors, 22.9% of whom (n=54) were associated with TIS. Stepwise multivariate Cox regression models with stratification by study and dose were used to assess the independent effect of predictive factors and hazard ratios (HRs) were estimated from the Cox model. Results: Multivariate analysis demonstrated that female gender (HR=1.71) compared to male gender, recurrent tumors (HR=1.9) compared to primary tumors, multiplicity, and presence of associated TIS (HR=1.54) increased the risk of recurrence. Recurrent tumors (HR=1.62) compared to primary tumors, high-grade tumors (HR=5.64) compared to G1 tumors, T1 tumors (HR=2.15) compared to Ta tumors, and recurrence at 3-mo cystoscopy (HR=4.6) increased the risk of progression. Conclusion: Significant independent predictors for recurrence were female gender, history of recurrence, multiplicity, and presence of associated TIS. Age, history of recurrence, high grade, T1 stage, and recurrence at first cystoscopy were independent predictors of progression by multivariate Cox analysis.

Editorial Comment: Prognostic factors from more than 1,000 patients treated with BCG in 4 randomized trials from Spain confirm previous observations—recurrent tumors, T1 tumors and a positive 3-month cystoscopy are predictive of muscle invasive disease. A re-staging transurethral resection of bladder tumor was not a specific part of the protocols, so some of the early recurrences were probably due to incomplete initial resection.

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Bladder Cancer Detection With CT Urography in an Academic Medical Center

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Purpose: To evaluate the performance characteristics of computed tomographic (CT) urography for the detection of bladder cancer in patients at risk for the disease. Materials and Methods: Institutional review board approval was obtained for this retrospective HIPAA-compliant review of medical records of 2600 consecutive patients undergoing CT urography. Of these, 838 CT urograms in 779 patients (449 men, mean age of 62 years, range of 27–92 years; 330 women, mean age of 56 years, range of 18–86 years) evaluated for hematuria or a history of urothelial cancer, who had undergone cystoscopy within 6 months of the CT urogram, were included in the study. Clinical reports of CT
urograms containing a bladder lesion interpreted as suspicious for malignancy were classified as positive. All others were classified as negative. Cystoscopy reports were classified as positive if a lesion underwent biopsy or was resected or negative if no lesion was detected. Performance characteristics for both CT urography and cystoscopy were determined by using pathologic findings or clinical follow-up as the reference standard. Ninety-five percent confidence intervals were estimated for each test characteristic. Results: The overall sensitivity, specificity, accuracy, positive predictive value, and negative predictive value (NPV) for bladder cancer detection were 79% (117 of 149), 94% (649 of 689), 91% (766 of 838), 75% (117 of 157), and 95% (649 of 681) for CT urography and 95% (142 of 149), 92% (634 of 689), 93% (776 of 838), 72% (142 of 197), and 99% (634 of 641) for cystoscopy. The NPV of CT urography was higher in patients evaluated for hematuria alone (98%, 589 of 603). However, the accuracy of CT urography was considerably lower in patients with a prior urothelial malignancy (78%, 123 of 158). Conclusion: CT urography is an accurate noninvasive test for detecting bladder cancer in patients at risk for the disease. The high NPV of CT urography in patients with hematuria may obviate cystoscopy in selected patients.

Editorial Comment: This retrospective study involves patients who have undergone CT urography (CTU) studies during a 5-year period as well as cystoscopy within 6 months of the CTU. Patients who underwent cystectomy were excluded from study. Nine additional patients were excluded due to technically inadequate CTU or cystoscopy. This study included 779 patients with 838 CTUs.

CT urography has been proved beneficial for upper tract imaging and is effective for renal mass imaging as well. Patients with hematuria usually undergo upper tract imaging (often CTU) and then cystoscopy for complete evaluation of the urothelium. If the performance of CT urography in detecting bladder tumors is good and well established, CT urography alone may provide adequate information, and cystoscopy, an invasive procedure, may be avoided in some patient populations.

In this study CT urography performed well. The overall negative predictive values were 95% and 99% for CTU and cystoscopy, respectively. Patients were separated by study indication into CTU for hematuria or a history of urothelial malignancy. Patients with hematuria had NPVs of 98% for CTU and 100% for cystoscopy. For patients with a history of urothelial malignancy the NPV for CTU vs cystoscopy was 77% vs 93%. Patients with a history of transitional cell carcinoma are at significantly increased risk for multifocal disease with the bladder being the most common site, and so these results are not surprising. In this particular study 51% of the patients with a history of transitional cell carcinoma had a bladder malignancy.

Cystoscopy is more sensitive than CT urography and provides an opportunity not only to identify a bladder mass, but also to biopsy it. However, in the patient population with a history of hematuria and no history of uroepithelial malignancy negative CT urography has a large NPV and may obviate the need for cystoscopy, especially in patient populations with a low risk (young women).

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