EXCLUSION CRITERIA ENHANCES SPECIFICITY OF NMP22 & BTA STAT
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INTRODUCTION AND OBJECTIVES: In this study we analyzed the false positive results of two urinary tumor markers - NMP22 and the BTA stat tests: 1) to examine the clinical categories of the false positive results or the low positive predictive value (PPV), 2) to establish absolute and relative exclusion criteria, and 3) to re-analyze the specificity and the PPV of the NMP22 and the BTA stat tests using our exclusion criteria.

METHODS: 278 patients were enrolled as candidates at risk for bladder cancer and submitted a single voided urine sample. Each sample was divided into three aliquots. One aliquot was assayed for NMP22, second for BTA stat and the third sent for cytological examination. All the above patients subsequently had a cystoscopy done.

RESULTS: Of the 278 patients evaluated in this study, 112 presented with microscopic hematuria, 77 with gross hematuria, and 89 had chronic symptoms of urinary frequency or dysuria. Histologically confirmed bladder cancer was seen in 34 (12%) of the patients. Of these 34 cancers, NMP22 detected 28 (82.4%) cases, BTA stat 23 (67.7%), whereas cytology was positive in only 10 (29.4%) patients. In the 72 patients with elevated NMP22 values, 28 cancers were detected with 44 false positive NMP22 values, yielding a specificity of 82.0% and a PPV of 38.9%. Similarly, in the 66 patients with a positive BTA stat test, 23 cancers were detected, with 43 false positive values, yielding a specificity of 82.4% and a PPV of 34.9%. The majority (>75%) of the false positive results fell into 6 categories: 1) benign inflammatory or infectious conditions, 2) presence of renal or bladder calculi, 3) current or a recent history of a foreign body, 4) any bowel interposition segment, 5) other genitourinary cancers, and 6) an instrumented urine sample. A seventh category of “no known pathology” was included as a control. Of these six categories, two categories resulted in a 100% false positive rate: 1) history of a foreign body and 2) any bowel interposition segment. Exclusion of these two absolute categories improved the specificity and PPV of NMP22 (85.5%, 45.2%) and BTA stat (85.2%, 39.7%). If the remaining four categories were also considered as relative exclusion criteria, then the specificity and PPV improved for both NMP22 (95.6%, 87.5%) and BTA stat (91.5%, 69.7%), similar to urinary cytology.

CONCLUSIONS: Exclusion of the two absolute false positive categories increased the specificity of both NMP22 and BTA stat tests. Awareness of the other false positive categories significantly improves the specificity and PPV, enhancing the clinical utility of these urinary tumor markers.