UTILITY OF NMP22 BLADDERCHEK POINT-OF-CARE ASSAY IN EVALUATION OF HEMATURIA: A MULTICENTER STUDY

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Author Disclosure
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Introduction

• Early diagnosis of bladder cancer saves lives
• Hematuria is the most common early sign of bladder cancer
• AUA guidelines for work up of hematuria for patients at risk include cystoscopy and urine cytology
Nuclear Matrix Protein and Transitional Cells of the Urinary Tract

- Nuclear matrix proteins (NMP) make up the structural framework of the nucleus and coordinate its functions.

- NMP are cell type specific.

- NMP22 protein is specific for transitional cells in the urinary tract.
Nuclear Matrix Protein in Normal and Malignant Transitional Cells

- Upon cell death NMP22 is released into the urine.
- Malignant transitional cells contain up to 80 times higher concentration of NMP22 protein than normal cells.
- Urine level of NMP22 protein $\geq 10$ U / ml is associated with a high probability of TCC.
- Unlike cytological examination, detection of NMP22 is not dependent on recovery of intact cells.
Objectives

1. Investigate the utility of NMP22 “BladderChek” point-of-care test, as an adjunct to cystoscopy in detection of bladder cancer among patients with hematuria.

2. Investigate the efficacy of NMP22 “BladderChek” point-of-care test, compared with voided urine cytology, as an adjunct to cystoscopy, in the detection of bladder cancer among patients with hematuria.
Methods

Study Design and Execution

- Prospective, multi institutional study: 23 facilities in 10 states; Academic, private practice and VA.
- From September 2001 to May 2002, 1,331 patients scheduled for cystoscopy due to increased risk of bladder cancer. Of these, 1220 (91.3%) presented with hematuria and are the focus of this presentation.
- All patients provided a voided urine sample for analysis of NMP22 protein and cytology prior to diagnostic cystoscopy.
Methods

Study Design and Execution

• Cytology was performed in-house or at a reference laboratory according to standard procedure of the participating clinic.
• Urologists were blinded to results of NMP22 test and cytology while performing and reporting the result of cystoscopy.
• TCC was diagnosed based on pathology report of excised tissue.
Methods

BladderChek Point-of-Care Device

Created to identify urinary NMP22 levels $\geq 10$ U / ml.

- Can be performed by non-physician staff members (CLIA waived).
- Requires 4 drops of freshly voided urine.
- Results available in 30 minutes.
- Built-in quality control.
The Device

- Control area
- Test area
- Urine flow
- Well for urine

Fixed anti “capture antibodies”

Fixed anti “NMP22 capture antibody complex” antibody

Free to migrate Capture antibodies for NMP22
Results
Tested Population with Hematuria
TCC Dx in 75 out of 1220, 6.1%

TCC 75* / 1,220 (6.1%)
*2 Tx patients not included in total
Results

Sensitivity of BladderChek Vs. Cytology in Detection of Bladder Cancer

![Bar graph showing sensitivity of NMP22 and cytology in detection of bladder cancer](image-url)
Comparison Between **BladderChek** and **Cytology** in the Detection of Bladder Cancer Among Patients With Hematuria

<table>
<thead>
<tr>
<th></th>
<th>Muscle Invasive Cancers</th>
<th>Invasive Cancer T1+</th>
<th>Superficial Cancers &lt;T1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NMP22</strong></td>
<td>90.0% (9/10)</td>
<td>62.2% (23/37)</td>
<td>52.6% (20/38)</td>
</tr>
<tr>
<td><strong>BladderChek</strong> (75)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cytology</strong></td>
<td>22.2% (2/9)</td>
<td>19.4% (7/36)</td>
<td>13.9% (5/36)</td>
</tr>
</tbody>
</table>

*Report of malignant or dysplastic cells considered positive

*2 patients had Tx, not included here
Cystoscopy Combined With NMP22 Vs. Cystoscopy Alone

<table>
<thead>
<tr>
<th>Detection Method</th>
<th>Muscle Invasive Cancer Detected</th>
<th>All Cancer Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystoscopy COMBINED with NMP22 BladderChek</td>
<td>90.0% (9/10)*</td>
<td>93.3% (70/75)</td>
</tr>
<tr>
<td>Initial Cystoscopy Alone</td>
<td>60% (6/10)</td>
<td>88.0% (66/75)</td>
</tr>
</tbody>
</table>

*Cancers positive by NMP22 test but not seen by cystoscopy: Cis(1), Ureteral(1), Bladder(2)

**NMP22 Test also positive for 2 TCC’s of the renal pelvis
# NMP22 BladderChek and Cytology Specificity (FP)

<table>
<thead>
<tr>
<th></th>
<th>NMP22</th>
<th>Urine Cytology</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Cancer</td>
<td>85.7%</td>
<td>99.1%</td>
</tr>
<tr>
<td></td>
<td>(977/1140)</td>
<td>(1094/1104)</td>
</tr>
<tr>
<td>No GU Disease</td>
<td>93.5%</td>
<td>99.4%</td>
</tr>
<tr>
<td></td>
<td>(474/507)</td>
<td>(486/489)</td>
</tr>
<tr>
<td>Negative Predictive Value (FN)</td>
<td>96.8%</td>
<td>94.8%</td>
</tr>
<tr>
<td></td>
<td>(977/1009)</td>
<td>(1094/1154)</td>
</tr>
</tbody>
</table>
Positive NMP22 BladderChek Among Patients Diagnosed With Non Malignant GU Disease

% Positive

- NED
- BPH
- Cystitis
- Calculi

%
Efficacy of NMP22 Vs Cytology In Workup of Hematuria

• NMP22 test is over 3x more sensitive than voided cytology (57.3% vs. 16.7%, p <0.001)

• NMP22 test plus cystoscopy is significantly more sensitive than cystoscopy alone (93.3% vs. 88.0%, p = 0.046)
Conclusions

NMP22 BladderChek Utility

- Test can be performed in doctor’s office with available clinical staff.

- Results in 30 minutes.

- Consistent with AUA guidelines recommending use of a urine test to back up cystoscopy.

- Half the cost of voided cytology.
Collaborating Investigators

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