Evidence-Based Diagnostic Accuracy Measurement in Urine Cytology: Comparison of Pre- and Post-Paris System Performance Using Likelihood Ratios

Myles N 1,2, Kanber Y 1, Caglar D 1, Auger M 1, Brimo F 1
1 McGill University, Montreal QC, Canada 2 The University Of British Columbia, Vancouver BC, Canada

OBJECTIVES
Modern cytopathology classification systems recently become more evidence-based and introduced risk of malignancy (ROM) as a measure of test performance. While ROM represents post-test probability (synonym: positive predictive value), it changes with prevalence (synonym: pre-test probability) of malignancies in various practices, making it difficult to compare across different clinical settings. Here we propose a practical solution available from Evidence-Based Medicine to solve this problem.

The Likelihood Ratios (LRs) are fixed metrics of diagnostic test, independent of prevalence in various practices and should be used in multi-level reporting systems. LRs represent a ratio of % true to % false results against definitive outcome (i.e. biopsy) per each level of diagnostic test result. They indicate how many times true test result is more or less likely than the false test result. LRs are broadly used in clinical medicine and provide a realistic measure of intrinsically imperfect, yet valuable diagnostic information.

We aimed
a. to apply LRs to cytopathology practice using urine cytology
b. to compare diagnostic accuracy of pre- and post-Paris systems.

MATERIAL AND METHOD
We determined LRs for pre-Paris (institution-based sequential 188 cases) and post-Paris (167 cases) with void urine cytology cases with known histologic outcomes (yes/no High Grade Urethelial Carcinoma). The observers were blinded of the histologic outcomes (ref #1). Catmaker open source software (Oxford University, UK available at www.cebm.net) was used for all calculations and data visualization. We used formulae:

Test Category                  Pre-Paris (LR)                  Post-Paris (LR)
Benign                         0.3 [95%CI 0.2-0.5]       0.2 [95%CI 0.1-0.36]
AUS                            0.5 [95%CI 0.3-0.8]       0.9 [95%CI 0.6-1.6]
Suspicious for HGUC           5.2 [95%CI 2.1-13.2]     3.1 [95% CI 1.04-9]
HGUC                           10 [95%CI 3.7-27]        7 [95%CI 3.2-18.5]

Interpretation:
LR = 1 Non-discriminatory result (indeterminate)
LR >1 to 10 Moderately discriminatory positive test (may rule in cancer)
LR >10 Highly discriminatory positive test (rule in cancer)
LR 0.1-0.99 Moderately discriminatory result (may rule out cancer)
LR < 0.1 Highly discriminatory (almost definitively rules out cancer)

RESULTS

Pre- vs-post-Paris systems: comparable diagnostic accuracy

TEST             Urine cytology  TARGET DISORDER                 Malignancy

<table>
<thead>
<tr>
<th>Present</th>
<th>Absent</th>
<th>Number</th>
<th>Proportion</th>
<th>Number</th>
<th>Proportion</th>
<th>Likelihood Ratio (95% CI)</th>
<th>Post-test Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative for malignancy</td>
<td>14</td>
<td>0.18</td>
<td>50</td>
<td>0.24</td>
<td>0.20 (0.13 to 0.30)</td>
<td>3.0%</td>
<td></td>
</tr>
<tr>
<td>None of unknown significance (AUS)</td>
<td>10</td>
<td>0.13</td>
<td>50</td>
<td>0.27</td>
<td>0.20 (0.13 to 0.30)</td>
<td>3.0%</td>
<td></td>
</tr>
<tr>
<td>Suspicious for high grade urothelial Carcinoma</td>
<td>22</td>
<td>0.26</td>
<td>50</td>
<td>0.22</td>
<td>2.22 (0.86 to 6.29)</td>
<td>81%</td>
<td></td>
</tr>
<tr>
<td>High Grade Urethelial Carcinomas</td>
<td>34</td>
<td>0.41</td>
<td>50</td>
<td>0.41</td>
<td>2.22 (0.86 to 6.29)</td>
<td>81%</td>
<td></td>
</tr>
</tbody>
</table>

Pre-test probability: 4% | 95%CI 0.1-0.5 | 95% CI 0.5 to 0.95 | Pre-test Odds: 0.24

Examples of how to use LRs to determine post urine cytology test probability of bladder malignancy in individual patients
a. Benign scenario
Low 5% pre-test risk of cancer decreased to less than 1% after negative urine cytology test result with LR 0.2

b. High risk scenario
High 50% pre-test risk of cancer increases to 95% and higher after HGUC urine cytology result with LR 10.

c. Indeterminate scenario
High 50% pre-test risk of cancer does not change after AUS urine cytology test result with LR 0.9. The 95%CI 0.6-1.6 includes point of indifference = 1, thus the result is truly indeterminate and requires other investigations.

CONCLUSIONS
This is, to our knowledge, the first report on the applicability of LRs in cytopathology practice. In our setting, the main impact of the Paris system was the improvement of the clinical significance of the AUC category, while all other categories show similar moderate diagnostic accuracy performance.

The LRs could be used as a performance measure across different settings, adding more precise and reproducible numeric information on diagnostic test accuracy and provides with an estimate of ROM in various clinical scenarios or settings.

REFERENCES

Nothing To Disclose – The authors of this presentation have indicated that they have no conflicts of interest that relate to the content of this research.