Early Diagnosis of Pulmonary Nodules: biomarker performance in patients with solitary or multiple nodules in the PANOPTIC study

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Introduction

Patients can present with a solitary pulmonary nodule, but, often they present with multiple nodules (with a specific nodule of concern) to the pulmonologist. Recently, a proteomic-based integrated classifier which uses clinical risk factors along with protein abundance from a patient’s blood sample has been shown to perform well as a predictor of the likelihood that a patient has a benign nodule. The large prospective trial (PANOPTIC) done for clinical validation, provided an opportunity to assess the test performance in patients with solitary and multiple nodules.

Methods (continued)

Chest CT scan results were reported for solitary and multiple nodules and nodule sizes. A single nodule of concern was an inclusion criteria. Multiple nodules were admissible. Statistical analysis used Fisher’s Exact test and p<0.05 was considered significant.

Results for PANOPTIC

• Total patients eligible for analyses were 392, of which 178 were in the integrated classifier intended use cohort (pCA≤50%)
• The cancer prevalence for the intended use group was 16%, mean nodule number of 3.2 (range 1-2.45) with a p-value of 0.002
• Test accuracy: sensitivity 97%, specificity 44%, PPV 25%, NPV 98%
• Clinical utility calculations were: 40% reduction in invasive procedures, 1.91) was statistically higher than solitary nodule patients (62.68 +/- 2.45) with a p-value of 0.002 (Table 1).
• Otherwise, there were no statistically significant differences in terms of gender, smoking status, nodule size or cancer prevalence.

Cancer Status by Nodule Number (N=392)

Table 1, Solitary and Multiple Nodule Results (n=178)

<table>
<thead>
<tr>
<th>Patients</th>
<th>178</th>
<th>101</th>
<th>77</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>59.52 +/- 1.55</td>
<td>67.68 +/- 1.91</td>
<td>62.68 +/- 2.45</td>
</tr>
<tr>
<td>Female</td>
<td>62.68 +/- 1.91</td>
<td>52 (51%)</td>
<td>43 (56%)</td>
</tr>
<tr>
<td>Lung Nodule</td>
<td>13.95 +/- 1.55</td>
<td>13.72 +/- 0.96</td>
<td>14.26 +/- 1.24</td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>29 (16%)</td>
<td>16 (16%)</td>
<td>13 (17%)</td>
</tr>
<tr>
<td>Benign</td>
<td>149 (84%)</td>
<td>85 (84%)</td>
<td>64 (83%)</td>
</tr>
<tr>
<td>Test Performance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>97%</td>
<td>100%</td>
<td>92%</td>
</tr>
<tr>
<td>Specificity</td>
<td>44%</td>
<td>47%</td>
<td>39%</td>
</tr>
<tr>
<td>NPV</td>
<td>98%</td>
<td>100%</td>
<td>96%</td>
</tr>
</tbody>
</table>

Methods

The prospective PANOPTIC trial was performed at 33 North American sites to validate the clinical performance of BDX-XL2 (formerly Xpresys Lung version 2; Biodesix Inc., Boulder, CO). PANOPTIC trial criteria included:
– New incidentally-found nodule 8-30 mm without workup
– Prospective collection and retrospective evaluation
– Cancer diagnosis by histo-pathology
– Benign diagnosis by histo-pathology, resolution or stability

The integrated classifier is a blood test, designed to evaluate a new nodule of concern that combines two protein analytes with 5 clinical/imaging factors to provide a result with a high negative predictive value.

The integrated classifier is in it’s second version with discovery and clinical validation published (Ref 1, 2).

Result for Solitary and Multiple Nodules (n=178)

• Nodules were solitary in 77 (43%) patients and 101 (57%) were recorded as having multiple nodules
• Mean nodule number of 3.2 (range 1-10).
• The average age of patients with multiple nodules (67.69 +/- 1.91) was statistically higher than solitary nodule patients (62.68 +/- 2.45) with a p-value of 0.002 (Table 1).
• Otherwise, there were no statistically significant differences in terms of gender, smoking status, nodule size or cancer prevalence.

Similarly, the integrated classifier performance showed no statistically significant difference between the multiple and solitary nodule patients (Table 1).

The average age of patients with multiple nodules (67.69 +/− 1.91) was statistically higher than solitary nodule patients (62.68 +/- 2.45) with a p-value of 0.002 (Table 1).

Unless otherwise noted, all p-values were calculated with Fisher’s Exact test and p<0.05 was considered significant.

References


Conclusion

Analysis of PANOPTIC study data does not show any difference in classifier performance between patients with multiple nodules compared to solitary nodules.