Genetic Testing Indicated for All Patients with Pancreatic Cancer

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Recent studies by Ambry Genetics and other investigators have demonstrated a high prevalence of hereditary pancreatic cancer, highlighting the importance of multigene panel testing (MGPT) for all patients diagnosed with pancreatic cancer.

Why This Matters to You

Due to these recent studies, NCCN® guidelines now recommend BRCA1/2 testing for patients with a personal and/or family history of pancreatic cancer diagnosed at any age1. These studies also suggest that MGPT should be considered to identify more patients with hereditary pancreatic cancer.

Prospective Study of Germline Genetic Testing for Pancreatic Cancer*

Key Study Findings²

- In the first multi-center, prospective study of its kind, 298 consecutive, unselected patients with pancreatic ductal adenocarcinoma (PDAC) underwent MGPT for 32 genes.

- 41/298 (14%) patients were identified to have a mutation in a cancer susceptibility gene.

- 29/41 (70.7%) mutations were considered clinically actionable. (Figure 1)

- Using then current guideline-based testing, 52% of mutations in known PDAC genes would have been missed.

* Ambry Genetics study

Figure 1. Breakdown of Clinically-Actionable Positive Results

1 ATM
1 BARD1
1 TP53
1 PMS2
1 PALB2
1 MSH6
1 CDKN2A

4 BRCA2
4 BRCA1
5 CHEK2
Multigene Hereditary Cancer Panels Reveal High-Risk Pancreatic Cancer Susceptibility Genes*

**KEY STUDY FINDINGS**

1. A case-control study of 1,652 patients with pancreatic cancer undergoing MGPT estimated the risk of pancreatic cancer associated with mutations in cancer susceptibility genes.

2. 20.73% of patients were found to have a germline mutation.

3. ATM, BRCA2, CDKN2A, MSH2, MSH6, PALB2, TP53 were associated with high risk (OR >5) of pancreatic cancer.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Odds Ratio (OR)</th>
<th>95% CI</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>ATM</td>
<td>8.96</td>
<td>6.12-12.98</td>
<td>&lt; .001</td>
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<tr>
<td>BRCA1</td>
<td>2.95</td>
<td>1.49-5.60</td>
<td>.002</td>
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<tr>
<td>BRCA2</td>
<td>9.07</td>
<td>6.33-12.98</td>
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<td>CDKN2A</td>
<td>35.97</td>
<td>14.68-85.93</td>
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<td>CHEK2</td>
<td>2.08</td>
<td>1.15-3.67</td>
<td>.02</td>
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<td>MSH2</td>
<td>7.10</td>
<td>1.04-37.16</td>
<td>.047</td>
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<tr>
<td>MSH6</td>
<td>7.79</td>
<td>3.85-15.16</td>
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<td>PALB2</td>
<td>14.82</td>
<td>8.12-26.22</td>
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<tr>
<td>TP53</td>
<td>7.15</td>
<td>2.78-18.13</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**KEY FINDINGS FROM OTHER SUPPORTING STUDIES**

1. Case-control study of 3,030 pancreatic cancer patients undergoing germline MGPT found significant associations between pancreatic cancer and mutations in ATM, BRCA1, BRCA2, CDKN2A, MLH1, and TP53.

2. Study of 289 unselected PDAC patients undergoing germline and somatic MGPT found that 9.7% of patients had a mutation.

**POINTS FOR YOUR PRACTICE**

1. Roughly 5-20% of pancreatic cancer patients have a mutation in a cancer susceptibility gene, and identification of these patients is critical for appropriate medical management, including determining clinical trial eligibility.

2. NCCN guidelines now indicate that BRCA1/2 testing should be considered for all patients with pancreatic cancer.

3. Patients with pancreatic cancer are at-risk for clinically actionable mutations in genes beyond BRCA1/2, therefore, MGPT may be an appropriate option for identifying cancer susceptibility.

* Ambry Genetics study

**REFERENCES**


