Clinical performance of a multivariate index assay for detecting early-stage ovarian cancer


Overview
1,016 prospective patient cases, which included 86 early-stage ovarian cancers, were evaluated with preoperative biomarkers, clinical assessment of ovarian cancer risk, and modified ACOG guidelines. For all early-stage ovarian malignancies, OVA1 combined with clinical assessment had significantly higher sensitivity compared to clinical assessment alone, CA-125, and modified ACOG guidelines. The performance was consistent across menopausal status.

Clinical assessment: a clinical prediction of malignancy based on physical examination and imaging, per the study inclusion criteria, and CA-125, if used.

CA-125: Cancer antigen marker values cutoff in accordance with ACOG referral criteria of 200 U/mL (premenopausal) or 35 U/mL (postmenopausal)

Modified (Dearking) ACOG guidelines:
Premenopausal women who meet one the following criteria:
CA-125 >67 U/mL, Ascites, or Evidence of abdominal or distant metastasis.

Postmenopausal women who meet one the following criteria:
CA-125 >35 U/mL, Nodular or fixed pelvic mass, Ascites, or Evidence of abdominal or distant metastasis.

Key Results
- OVA1 with clinical assessment had 95% sensitivity to early-stage malignancy, which was statistically superior to clinical assessment alone (69%), CA-125 (63%), and modified ACOG guidelines (77%)
- Adding OVA1 to clinical assessment reduced the percent of early-stage malignancy missed from 31% to 5% and in turn, increased the NPV (confidence a negative result is truly negative)
- There was no case of early-stage malignancy correctly identified by CA-125 or modified ACOG guidelines but missed by OVA1
- Performance across all cancer cases:

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<thead>
<tr>
<th></th>
<th>Clinical assessment</th>
<th>OVA1 + clinical assessment</th>
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</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75%</td>
<td>95%</td>
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<tr>
<td>Specificity</td>
<td>86%</td>
<td>44%</td>
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<tr>
<td>PPV</td>
<td>65%</td>
<td>36%</td>
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<tr>
<td>NPV</td>
<td>91%</td>
<td>97%</td>
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</tbody>
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Conclusion
This large, prospectively enrolled, multi-institutional study demonstrated that use of OVA1 detected more early-stage malignancy than the current standard of care.

Comparative Sensitivity By Cancer Stage

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<thead>
<tr>
<th></th>
<th>Stage I</th>
<th>Stage II</th>
<th>Early Stage</th>
<th>Late stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVA1 + clinical assessment</td>
<td>93%</td>
<td>93%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>OVA1</td>
<td>89%</td>
<td>100%</td>
<td>92%</td>
<td>99%</td>
</tr>
<tr>
<td>Modified ACOG</td>
<td>69%</td>
<td>96%</td>
<td>77%</td>
<td>98%</td>
</tr>
<tr>
<td>Clinical assessment</td>
<td>64%</td>
<td>80%</td>
<td>69%</td>
<td>91%</td>
</tr>
<tr>
<td>CA-125</td>
<td>57%</td>
<td>76%</td>
<td>63%</td>
<td>95%</td>
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