Validation of a second-generation multivariate index assay for malignancy risk of adnexal masses

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Overview

To improve on OVA1's prediction of benign masses, the serum biomarker panel was modified keeping 3 original biomarkers (cancer antigen-125 [CA-125], transferrin and apoprotein A-1) and adding two new markers (follicle-stimulating hormone [FSH] and human epididymis protein 4 [HE4]). Risk was calculated on a scale of 0 to 10 using a re-designed proprietary algorithm and a single cutoff of 5 to separate high-risk from low risk.

The re-designed test was validated using stored serum of all evaluable subjects from a previously published "intended-use" OVA1 trial (OVA500 trial; N=493) with observed cancer prevalence of 18.7% (92/493).

Inclusion criteria:

1. *Women age 18 years*
2. *Signed informed consent*
3. *Agreeable to phlebotomy*
4. *Documented pelvic mass planned for surgery within 3 months of imaging*
5. *Non-Gynecologic Oncologist as enrolling contact*

Four risk assessment modalities (Overa, OVA1, CA-125, and modified ACOG guidelines) were compared with sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) as primary clinical endpoints.

Key Results

- Specificity (69%) and PPV (40%) were significantly improved over OVA1, with 62 more benign masses accurately classified as low-risk
- Like OVA1, Overa showed higher sensitivity and NPV (91% and 97%, respectively) than CA-125 (76%, 95%) or modified ACOG guidelines (83%, 95%)
- Overa sensitivity was higher than CA-125 or mod-ACOG for epithelial (95%), non-epithelial (80%), borderline (75%) and early-stage (89%) cancers, like OVA1

Conclusion

The second-generation test, Overa, significantly improved the efficiency of assessing benign masses without sacrificing high sensitivity and NPV, which are essential for the effectiveness of identifying malignant disease.

Comparison of Four Risk Assessment Modalities

Performance	Overa	OVA1	CA-125	Modified ACOG
Sensitivity	91%	94%	76%	83%
Specificity	69%	54%	94%	81%
Postive Predictive Value	40%	31%	75%	50%
Negative Predictive Value	97%	97%	95%	95%

Sensitivity	Overa	OVA1	CA-125	Modified ACOG
Epithelial ovarian ca	95%	95%	85%	92%
Non-epithelial ovarian ca	80%	80%	40%	60%
Early stage ovarian ca	89%	91%	69%	80%

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