OVA1™ Ovarian Tumor Triage Test

Search Strategy
Searches of MEDLINE and EMBASE were performed on July 8, 2010, using the search terms OVA1 AND (Vermillion OR Quest); transthyretin AND apolipoprotein A1 AND β2-microglobulin AND transferrin AND CA-125 AND ovarian cancer; OVA1. Limits used were English language, human, and published since January 1, 1996.

Description of Search Results
The first two search strategies yielded no citations, and the third search strategy yielded three citations. Only one citation related directly to the OVA1 test (Quest Diagnostics Inc.), but it was a descriptive paper of the process used to validate the test and did not present any actual data. As such, there is currently insufficient evidence to evaluate this test.

Regulatory Agency Information
Food and Drug Administration (FDA) Status: The FDA awarded premarket approval for the OVA1 test as a class II device to the test developer Vermillion Inc. on September 11, 2009. The test is approved for women older than age 18 with an ovarian adnexal mass for which surgery is planned, and who are not yet referred to gynecologic oncologists, as an aid to further assess the likelihood that malignancy is present when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not approved as a screening or stand-alone diagnostic test.

Decision Summary: http://www.accessdata.fda.gov/cdrh_docs/reviews/K081754.pdf

Conclusions
There is insufficient published evidence to perform a Genetic Test Evaluation (GTE) health technology assessment of the OVA1 test; therefore, it cannot be recommended for adoption or use at this time. The main evidence deficiencies for the OVA1 test are insufficient data on analytical validity, clinical validity, and clinical utility.

Other Relevant Information
Approximately 5% to 10% of American women will have surgery in their lifetime due to a suspected ovarian malignancy. The vast majority (80% to 90%) of these growths is benign, but no reliable test exists to accurately discriminate between benign and malignant tumors preoperatively. Current care methods for predicting the probability of ovarian cancer in women with a confirmed pelvic mass include assessing for known demographic and genetic risk factors, testing for CA-125 II and other possible serum markers, physical examinations, and transvaginal ultrasonography. Sometimes, other imaging modalities are employed, such as color doppler ultrasound and computed tomography. Age is the major independent risk factor for ovarian cancer in the general population. Incidence of disease rises dramatically after onset of menopause. Genetic alterations in the breast cancer susceptibility 1 (BRCA1) and 2 (BRCA2) genes are associated with an increased lifetime risk for development of ovarian cancer. OVA1 is a blood test that measures serum levels of five proteins (transthyretin, apolipoprotein A1, beta-2-microglobulin, transferrin, and the CA-125 II cancer antigen) believed to be markers of ovarian cancer, and uses a proprietary algorithm (OvaCalc) to combine results into a single score (ranging from 0.0 to 10.0) indicating low- or high-risk malignancy. Cutoff values for low- and high-risk stratification are currently set at 5.0 for premenopausal women and at 4.4 for postmenopausal women. The test is designed for adjuvant use and is not intended to be interpreted independently from findings of current care methods to assess risk of malignancy prior to surgery in women with a confirmed pelvic mass. No published studies exist for OVA1; study results have been published in abstract form only. The OVA-002 validity study used preoperative blood samples from 239 premenopausal and 285 postmenopausal women who underwent surgery for a suspicious pelvic mass. Blood samples were tested for the five protein markers included in the OVA1 panel using...
commercially available immunoassay systems. The OvaCalc software combined results from the five assays to produce a malignancy risk index score ranging from 0.0 to 10.0 for each blood sample. The software then stratified women into low- or high-risk malignancy categories by applying index cutoff values for premenopausal and postmenopausal women (5.0 and 4.4, respectively) as determined by previous research. Test results were compared with pathology results, which were available for all 524 patients. Benign ovarian conditions were diagnosed in 363 women, epithelial ovarian cancer was diagnosed in 96 women, and a borderline diagnosis of low malignant potential was determined for 28 women. Among the remaining 37 women, other primary ovarian malignancies were found in 9, and non-primary ovarian malignancies were diagnosed in 28. Investigators reported 92.5% sensitivity, 43.0% specificity, 41.9% positive predictive value, and 92.9% negative predictive value for the OvaCalc algorithm performance among the total study population. Performance characteristics varied between pre- and postmenopausal patient subgroups, but specificity and positive predictive values remained low in both subgroups. Negative predictive value was higher in premenopausal patients compared with postmenopausal patient populations (94.4% and 90.2%, respectively), and sensitivity was lower (86.7% and 94.8%, respectively). Among the 96 patients diagnosed with epithelial ovarian cancer, OvaCalc designated all but 1 as high-risk. This reflects the test’s high sensitivity. Not reported is how many women with benign ovarian conditions were incorrectly categorized as at high risk for malignancy, but this number is presumed to be considerable given the test’s low specificity.

There is currently insufficient published evidence to conclude that OVA1 enhances current care preoperative assessment of pelvic masses for risk of malignancy, improves referral to appropriate specialties for performing the initial surgery, or reduces the number of second surgeries performed in women who undergo surgery for a suspicious pelvic mass. There is also no evidence that the OVA1 improves patient survival. Further research is needed and study results must be published before the clinical benefits of this test can be evaluated.

Manufacturer Sites:

Quest Diagnostics Inc. (Madison, NJ)

Centers for Medicare & Medicaid Services (CMS):

There is no CMS National Coverage Determination (NCD) for the OVA1 test. In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Payer Coverage Policies:

Aetna: Aetna considers the OVA1 test to be experimental and investigational. http://www.aetna.com/cpb/medical/data/300_399/0352.html

CIGNA: CIGNA does not cover the OVA1 test because it is considered experimental, investigational, or unproven. http://www.cigna.com/customer_care/healthcare_professional/coverage_positions/medical/mm_0172_coveragepositioncriteria_tumor_markers_for_diagnosis_mgmt_cancer.pdf

Humana: Humana members may not be eligible for coverage of the OVA1 test because it is considered experimental, investigational, or not medically necessary. http://apps.humana.com/tad/tad_new/home.aspx

Regence Group: A coverage policy for analysis of proteomic patterns in serum to identify cancer was identified on the Regence Group website, but the OVA1 test is not specifically mentioned as being covered or not covered. http://blue.regence.com/trgmedpol/lab/lab41.html

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UnitedHealthcare (UHC): No coverage policy specifically related to the OVA1 test was identified on the UHC website. http://www.unitedhealthcareonline.com

Online Articles:

Online Mendelian Inheritance in Man (OMIM)
• Transthyretin; TTR (*176300): http://www.ncbi.nlm.nih.gov/omim/176300
• Transferrin; TF (+190000): http://www.ncbi.nlm.nih.gov/omim/190000

Original Search Date: July 8, 2010

Search Results with Abstracts
Databases: MEDLINE; EMBASE
Search terms: OVA1 AND (Vermillion OR Quest); transthyretin AND apolipoprotein A1 AND β2-microglobulin AND transferrin AND CA-125 AND ovarian cancer; OVA1
Search limits: English language; human; published since January 1, 1996
Search yield: 0; 0; 3 citations
Retrieved: 0 abstracts (0 citations in all)