CA125 Plus Ultrasound May Flag Early Ovarian Ca

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CHICAGO — Frequent serum CA125 testing in tandem with transvaginal sonography may be an effective screening method to detect ovarian cancer early in women at increased risk of the disease.

When serial CA125 levels were analyzed using the previously established risk of ovarian cancer algorithm (ROCA), the overall specificity was 99.7% and positive predictive value was 13% among 2,343 high-risk women. The prospective pilot study included women with a BRCA mutation, who are known to have a 20%-40% increased lifetime risk of ovarian cancer.

The results are encouraging because no proven strategy exists for this high-risk group, but larger studies are needed to validate the findings, Steven J. Skates, Ph.D., reported at the annual meeting of the American Society of Clinical Oncology.

"Serial CA125 testing essentially establishes a baseline value for each woman that personalizes the interpretation of each new CA125 result to determine if ultrasound is indicated at a particular time," Dr. Skates said in an interview. "The hope is that the serial approach will increase the sensitivity of CA125 testing without loss of specificity. The ROCA has previously shown greater positive predictive value and sensitivity than a single CA125 test in screening healthy postmenopausal women for ovarian cancer (J. Clin. Oncol. 2005;23:7919-26).

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The current study defined high-risk women as those with a BRCA1 or BRCA2 mutation or first- or second-degree relatives with a BRCA mutation or multiple breast or ovarian cancers, or women of Ashkenazi heritage and at least one first-degree or two second-degree relatives with breast or ovarian cancer. Women with a prior diagnosis of ovarian cancer were excluded.

Participants underwent CA125 testing every 3 months, and the risk of having ovarian cancer was recalculated after each test based on the CA125 profile. Women with a greater than 1% risk were referred to ultrasound, and those with a greater than 10% risk to a gynecologic oncologist.

Between July 2001 and September 2006, a total of 19,549 CA125 tests were performed, totaling 6,284 women-years of screening. The average number of CA125 tests performed was three per year. Of 628 referrals made to ultrasound, 414 were performed, resulting in 38 women (9%) undergoing study-indicated surgeries.

Nine ovarian cancers were identified during screening—three were prevalent (one early stage, two late stage) and six were incident (five early stage, one late stage), reported Dr. Skates, ROCA Screening Study Group, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston.

Three of the incident carcinomas were found on prophylactic oophorectomy in early stage. The ROCA detected two of the three remaining incident cases in early stage, and three of three prevalent cases. Positive predictive value was 5/38 or 13% and sensitivity was 5/6 or 83%. The sample size was too small to determine sensitivity for incident cases. Overall specificity was excellent for the combined strategy at 99.7%, Dr. Skates said.

The positive predictive value of ROCA was higher at 22% in the study of postmenopausal women, but is acceptable at 13% in a group of high-risk women considering prophylactic oophorectomy after childbearing, Dr. Skates said.

The researchers also evaluated other serum biomarkers, and observed that the HE4 and B7-H4 proteins seemed to confirm CA125 levels.

There was high compliance throughout the study, with 84%, 85%, 85%, and 82% of participants returning within 1 month for the first four tests.

A definitive screening study with more than 30 incident cases and possibly additional biomarkers is needed to define sensitivity for longitudinal ROCA for early-stage ovarian cancer, said Dr. Skates, who received grant support from Fujirebo Diagnostics Inc., a cosponsor of the study with the National Cancer Institute. ■