Drug & Device Development

Multimarker assay detects early ovarian cancer

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By Victoria Stern

NEW YORK (Reuters Health) - A new highly sensitive and specific test may help doctors detect early-stage epithelial ovarian cancer in postmenopausal women, according to a new study published online April 1st in the Journal of Clinical Oncology.

"The investigators have done good work here," Dr. Martee Hensley told Reuters Health. "Most early cancer screens are plagued by false positives, but this test seems to perform better than a single blood test." Dr. Hensley, from Memorial Sloan-Kettering Cancer Center in New York, wrote an editorial that was published with the report.

At present, no screening techniques are recommended for early detection of ovarian cancer in the general population. Senior author Dr. Anna E. Lokshin, from the University of Pittsburgh, and colleagues note in their paper that because the prevalence of ovarian cancer is low (approximately 0.03%), a screening strategy should have greater than 75% sensitivity and 99.6% specificity for early-stage ovarian cancer.

To develop their assay, the investigators used serum samples from hospital blood banks. The total study population consisted of 2,031 healthy postmenopausal women, 456 patients with early- and late-stage ovarian cancer, as well as patients with benign pelvic disease or breast, lung, and colorectal cancers.

The authors screened 96 candidate biomarkers with multiplex xMAP bead-based immunoassays, and analyzed them using a Metropolis algorithm with Monte Carlo simulation to identify an optimal biomarker panel that could discriminate women with early-stage cancer from healthy controls. This initial training set including sera from 139 patients with early-stage ovarian cancer, 149 patients with late-stage ovarian cancer, and 1,102 healthy women.

The authors reported that, from the pool of 96 candidate serum biomarkers, four markers (CA125, HE4, CEA, and VCAM-1) showed the best diagnostic power: The four-biomarker assay detected early-stage ovarian cancer with 86% sensitivity and 98% specificity.

The same 86% sensitivity and 98% specificity was found when the investigators applied the four-biomarker panel to an independent validation set of serum samples, using sera from 44 patients with early-stage ovarian cancer, 124 patients with late-stage ovarian cancer, and 929 healthy women. This panel was selective for ovarian cancer; it had sensitivity of 36% for lung cancer, 33% for benign pelvic disease, 6% for breast cancer, and 0% for colorectal cancer.

The authors conclude that a "panel of CA-125, HE4, CEA, and VCAM-1, after additional validation, could serve as an initial stage in a screening strategy for epithelial ovarian cancer." They add that the CA-125, HE4, CEA, and VCAM-1 panel could be improved by adding other biomarkers to increase sensitivity and specificity.

In her editorial accompanying the study, Dr. Hensley commented that for the four-biomarker assay to become a standard for screening postmenopausal women for early-stage ovarian cancer, "the next step needs to be a giant one: a prospective, randomized trial for postmenopausal normal-risk women, comparing four-biomarker assay screening, followed by transvaginal sonogram for women with an abnormal assay compared with no screening."

But, Dr. Hensley added in the interview, "even with an assay that helps find early-stage cancer, it doesn't mean you have an assay that saves lives. You may just find very early stage cancers that would never become relevant."

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