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Ovarian Cancer Screening

by Ann Gerhardt, MD *November 2009*

Bottom Line at the Top: Screening for ovarian cancer with the blood test CA-125 should only be done in women who have symptoms of possible cancer or who have strong risk factors for ovarian cancer. Otherwise a large number of women will have unnecessary surgery, assuming considerable risk of complications.

Ovarian cancer accounts for 3% of cancers in American women, but is the fifth leading cause of their cancer-related deaths. That's pretty scary, given that ovarian cancer eludes diagnosis and resists treatment.

Most women aren't diagnosed until they have symptoms, which means advanced, Stage III or IV, disease. The symptoms are non-specific, like abdominal or pelvic pain, urinary urgency, abdominal size or bloating, and early fullness after eating, so doctors usually think of other, more common, diagnoses first. Hence the usual, advanced-stage diagnosis, with poor outcome. Since advanced disease is rarely curable, women and doctors alike would love to have a marker that detects curable disease.

Recent ovarian cancer scares have women emailing each other with pleas to undergo CA-125 screening to make an early diagnosis. CA-125 is a blood test that, when positive, often indicates the presence of ovarian cancer. For a disease that may be curable if found when it is localized disease and is usually fatal if it is plastered all over the abdomen, this test sounds like a no-brainer. The problem is that the CA-125 test result is not very sensitive or predictive.

CA-125 is positive in 80% of women with ovarian cancer. It is also positive in 1-2% of normal women and in a significant percentage of women with other abdominal processes, such as endometriosis, fibroids, pelvic inflammatory disease, hepatitis, pregnancy, normal menstrual periods, peritonitis, abdominal surgery and other cancers.

An 80% positive rate is high, but certainly not the absolutely sensitive marker we would like. And, unfortunately, CA-125 doesn't do a good job of detecting curable cancer. Only 50% of Stage I ovarian cancers are positive for CA-125. Stage 1 cancers have a 90% cure rate, while Stage IV disease has only a 19% cure rate.

Much of the screening concept depends on the notion that any screening test will detect small, early and treatable cancers. There is also no proof that ovarian cancer starts with Stage I and evolves to higher Stages over time. There is no early lesion, like a polyp, that signals likely progression to invasive cancer. Some cancers don't seem to have a primary focus of tumor, possibly starting as a burst of small tumors throughout the abdominal cavity. So it's not clear that screening would find a curable process.

The low prevalence of ovarian cancer – a life-time risk of only 1.4% of all women and a yearly incidence of only 40 cases per 100,000 women over age 50 – requires that any screening test be sensitive enough to catch the positives and specific enough exclude the non-cancer cases. It the test misses 20% of cancers, what good is it? Or if it falsely identifies even 5% of women who don't really have disease, that's 5% more who will risk the potential complications of invasive surgery, the only way to confirm or refute the presence of ovarian cancer.

A Swedish study found elevated CA-125 levels in 175 out of 5550 women. Only six of those had ovarian cancer at surgery. Three other women, with normal levels, ultimately developed ovarian cancer. Elevated CA-125 levels were more likely to rise over time in those with cancer. So if clinical suspicion and CA-125 levels aren't particularly high, serial testing might save some women from unnecessary surgery.

Advanced age (over 55 years) increases risk, but not enough to justify screening all older women. So far screening trials of large numbers of women over age 50 have not saved women's lives. In one trial combining CA-125 testing with trans-vaginal ultrasound, 10% of women turned up positive and 3.5% ended up having surgery, but only 5.1% of those had cancer (0.002% of the original group). Most of the cancers (75%) were Stage III and IV disease. Another 0.001% of the original group who tested negative on screening ended up with ovarian cancer. So screening led to a large number of unnecessary surgeries, missed a third of cancers and didn't detect particularly treatable cancers.

Newer trials combine CA-125 testing with trans-vaginal ultrasound and other blood tests. So far combined testing detects more ovarian cancers, but the other markers are even less specific for ovarian cancer than CA-125, so they identify more people without cancer, possibly subjecting them to unnecessary surgery.

Screening is more appropriate for women with risk factors, but 90% of women with ovarian cancer have no known risk factors. Having used oral contraceptives, been pregnant or breast-fed a child reduces risk. Having the BRCA gene mutation or a family history of ovarian or breast cancer in the immediate family greatly increases risk for ovarian cancer. Extremely high risk women should consider having their ovaries and fallopian tubes removed as soon as they are done having children, rather than waste time with imperfect screening methods.