Ovarian cancer screening does not appear to reduce risk of ovarian cancer death

June 5 2011

In a clinical trial that included nearly 80,000 women, those who received ovarian cancer screening did not have a reduced risk of death from ovarian cancer compared to women who received usual care, but did have an increase in invasive medical procedures and associated harms as a result of being screened, according to a study in the June 8 issue of *JAMA*, a theme issue on cancer.

In the United States, ovarian cancer is among the 5 leading causes of cancer death in women. Most women with ovarian cancer are diagnosed with advanced stage disease, which has a 5-year survival of only 30 percent. The recognition that early detection of ovarian cancer may have the potential to improve prognosis prompted the development of randomized controlled trials to evaluate the efficacy of transvaginal ultrasound and serum cancer antigen 125 (CA-125) as screening tools to reduce ovarian cancer mortality, according to background information in the article.

Saundra S. Buys, M.D., of the University of Utah Health Sciences Center, Salt Lake City, and colleagues examined the ovarian cancer-specific mortality results from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial to evaluate the effect of screening for ovarian cancer. The randomized controlled trial included 78,216 women, ages 55 to 74 years, assigned to undergo either annual screening (n = 39,105) or usual care (n = 39,111) at 10 screening centers across the United States between November 1993 and July 2001. The intervention group was offered annual screening with CA-125 for 6

years and transvaginal ultrasound for 4 years. Participants and their health care practitioners received the screening test results and managed evaluation of abnormal results. The usual care group was not offered annual screening with CA-125 for 6 years or transvaginal ultrasound but received their usual medical care. Participants were followed up for a maximum of 13 years for cancer diagnoses and death until February 28, 2010.

Through the follow-up period, 212 ovarian cancer cases were diagnosed in the intervention group and 176 cases in the usual care group. There were 118 deaths caused by ovarian cancer in the intervention group and 100 deaths in the usual care group. Analysis of data indicated that the difference in survival between the intervention and usual care groups was not statistically significant.

"All-cause mortality (excluding deaths from ovarian, colorectal, and lung cancer) was similar in the 2 study groups; there were 2,924 deaths in the intervention group and 2,914 deaths in the usual care group. Mortality rates for the major causes of death were generally similar between the 2 study groups," the authors write.

Of 3,285 women with false-positive results, 1,080 underwent surgery (32.9 percent for oophorectomy [surgical removal of one or both ovaries]) as part of the diagnostic workup. Of these 1,080 women, 163 (15 percent) experienced a total of 222 distinct major complications, which yielded a rate of 20.6 complications per 100 surgical procedures. A total of 1,771 women in the intervention group (7.7 percent) and 1,304 in the usual care group (5.8 percent) reported oophorectomy, with women in the intervention group having a higher rate of oophorectomy than women in the usual care group.

Regarding the outcomes of this trial, the researchers suggest that although the screening tests as used in this study did not reduce

mortality, it is possible if used differently that CA-125 and transvaginal ultrasound may have the potential to be beneficial. For example, assessing the changes in CA-125 over time rather than a single CA-125 value as used in this study may allow detection of cancers at an earlier stage when cure is possible. However, there is no evidence from other clinical trials to support this approach at this time. The authors also suggest that even an optimized program of annual screening may be insufficient to detect cancers early enough to reduce mortality. "Evidence from modeling suggests that aggressive cancers progress rapidly through the early stages, limiting the ability to detect these cancers with yearly screening. In contrast, more ovarian cancers were diagnosed in the screened group than in the usual care group (212 vs. 176), suggesting that some of the additional cancers detected by screenings were not clinically important and, if left undetected, may never have caused any symptoms or affected the women during their life-limes (i.e., overdiagnosis)."

"We conclude that annual screening for ovarian cancer as performed in the PLCO trial with simultaneous CA-125 and transvaginal ultrasound does not reduce disease-specific mortality in women at average risk for ovarian cancer but does increase invasive medical procedures and associated harms," the authors write.

More information: *JAMA*. 2011;305[22]2295-2303