Women with certain type of ovarian cancer and BRCA gene mutation have improved survival at 5 years

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Among women with invasive epithelial ovarian cancer, patients having a germline (gene change in a reproductive cell that could be passed to offspring) mutation in the BRCA1 or BRCA2 genes was associated with improved 5-year overall survival, with BRCA2 carriers having the best prognosis, according to a study in the January 25 issue of *JAMA*.

"Germline mutations in the tumor suppressor genes BRCA1 and BRCA2 are the strongest known genetic risk factors for both breast and epithelial ovarian cancer (EOC) and are found in 6 percent to 15 percent of women with EOC," according to background information in the article. "The relative prognosis of BRCA1/2 carriers and noncarriers is unclear."

Kelly L. Bolton, Ph.D., of the National Cancer Institute, Bethesda, Md., and colleagues conducted a study to provide evidence of the relative effect of germline BRCA1 and BRCA2 mutations on prognosis for women with epithelial ovarian cancer. The study consisted of a pooled analysis of 26 observational studies on the survival of women with ovarian cancer, which included data from 1,213 EOC cases with pathogenic germline mutations in BRCA1 (n = 909) or BRCA2 (n = 304) and from 2,666 noncarriers recruited and followed up at variable times between 1987 and 2010. During the 5 years following EOC diagnosis, 1,766 deaths occurred.

The researchers found that 5-year overall survival was 36 percent for

noncarriers of the gene mutations, 44 percent for BRCA1 carriers, and 52 percent for BRCA2 carriers. In a model only adjusted for study site and year of diagnosis, BRCA1 carriers had a more favorable survival than noncarriers, which improved slightly after additional adjustment for stage, grade, histology, and age at diagnosis. BRCA2 carriers had a greater survival advantage compared with noncarriers, particularly after adjusting for other prognostic factors.

The survival advantage for BRCA1 and BRCA2 carriers compared with noncarriers was present but less marked among women who reported a family history of ovarian, breast cancer, or both.

"Our study results have potentially important implications for the clinical management of patients with EOC. Most immediately, our findings can be used by health care professionals for patient counseling regarding expected survival. BRCA1 and BRCA2 carriers with EOC respond better than noncarriers to platinum-based chemotherapies and have improved survival despite the fact that the disease is generally diagnosed at a later stage and higher grade. If patients could be stratified based on their BRCA status, their treatment could be tailored to reflect this, with noncarriers targeted for more aggressive treatments. Our data provide further support that there may be different functional mechanisms involved in the etiology of different subtypes of EOCs and, therefore, different therapeutic targets based on germline and somatic [changes to the genetics of a multicellular organism which are not passed on to its offspring through the germline] genetic variation," the researchers write.

"... given the important prognostic information provided by BRCAl and BRCA2 status and the potential for personalized treatment in carriers, the routine testing of women presenting with high-grade serous EOC may now be warranted."

David M. Hyman, M.D., and David R. Spriggs, M.D., of Memorial Sloan-

Kettering Cancer Center and Weill Cornell Medical College, New York, write in an accompanying editorial that the data from this study have important implications for the future of ovarian cancer research and treatment.

"Phase 3 studies that do not stratify by BRCA mutation status or account for this factor in a preplanned statistical analysis risk possible confounding because approximately 15 percent of unselected patients with serous ovarian cancer will carry germline BRCAl/2 mutations. Moreover, other studies have found differences in chemotherapy responsiveness and progression-free survival between sporadic BRCAl -and BRCA2-associated ovarian cancers. Germline BRCA testing needs to be consistently incorporated into both the routine management and future phase 3 trials of ovarian cancer."

More information: *JAMA*. 2012;307[4]:382-390.
JAMA. 2012;307[4]:408-410.