Creighton University Medical Center

Early Detection Research Network

EDRN High Risk Registry

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Serum CA-125 in Relation to Adnexal Dysplasia and Cancer in Women at Hereditary High Risk of Ovarian Cancer

Ovarian cancer is the fourth most common cause of death in women in Western countries. Currently there is no screening instrument available to effectively detect ovarian cancer at an early stage in the general population. Women at hereditary high risk are advised to undergo screening or prophylactic surgery. Gynecologic screening involves transvaginal ultrasonography (TVU) and testing for the level of CA-125 in their blood serum. However, the value of these screening tools has not been proven. Screening aims at early detection; CA-125 is not always high at early stage ovarian cancer, and is sometimes high in non-cancerous conditions.

An article published in the April 2007 issue of *The Journal of Clinical Oncology* reports that CA-125 level predicts ovarian cancer in women at hereditary high risk for adnexal (ovaries and fallopian tubes) cancer. Both the level of CA-125 at the time of testing and changes in the level from one screening visit to the next can aid in predicting ovarian cancer.

This study was designed to see if CA-125 levels in women at hereditary high risk of ovarian cancer follow patterns similar to those in women not at such high risk. Serum CA-125 was analyzed prior to adnexal surgery to determine whether a higher CA-125 level meant that a woman was more likely to have cancer and/or dysplasia (pre-cancerous cells) in her ovarian or tubal tissue.

The study group included 388 women who had never had ovarian cancer, but who were at high hereditary risk for breast/ovarian cancer either because they had been found to have a *BRCA1* or *BRCA2* mutation or because they had at least two relatives with breast and/or ovarian cancer. They were compared to 370 healthy female volunteers, who were matched by age to the members of the study group.

Prophylactic bilateral salpingo-oophorectomy (removal of both ovaries and fallopian tubes in order to prevent cancer in a woman who is at high risk but who, as yet, has had no symptoms of cancer) was performed on 89 women; 9 women underwent diagnostic surgery because they had exhibited possible symptoms of ovarian or adnexal cancer. In the prophylactic surgery group, 23 women had ovarian or fallopian tube dysplasia, with 3 of those 23 women having both. Three other women had ovarian or fallopian tube cancers. Nine women at hereditary risk underwent adnexal surgery because of an elevated CA-125 level and/or an abnormal TVU. Five of these women had invasive ovarian cancer, one had a borderline ovarian tumor, one had a benign ovarian tumor, one had fallopian tubal dysplasia, and one had no abnormalities.

A higher level of CA-125 was found in the 5 women with ovarian cancer detected at gynecologic screening followed by diagnostic surgery than in the 3 women whose adnexal malignancies were diagnosed during prophylactic surgery. In the group of women who underwent prophylactic surgery, the absolute value of CA-125 was a significant predictor for the presence of dysplasia in the adnexal tissue.

The difference in CA-125 levels between two consecutive visits had a higher predictive value for ovarian cancer than did the actual value of a single measurement. In this study, women with an increase of CA-125 over time were more often diagnosed with ovarian cancer.

In conclusion, CA-125 levels do not behave differently in women at hereditary risk compared with women not at increased risk, and are subject to the same changes caused by age and menopause. Both the actual level of serum CA-125 and the change in the levels from one screening visit to the next can aid in predicting ovarian cancer. However, even with yearly screening visits, ovarian cancer is often diagnosed at an advanced stage, with a consequent high death rate. An upward trend in CA-125, measured every 3 months and plotted on a curve in the patient's clinical chart, may contribute to an earlier diagnosis of adnexal cancer. Even though the exact relationship between dysplasia and the development of ovarian and fallopian tube cancer is not yet well defined, prediction of dysplasia leading to prophylactic surgery could be of importance for the prevention of ovarian cancer. Remarkably, for the presence of dysplasia, the absolute value of CA-125 is the best predictor and should therefore be taken into account as an additional factor when considering prophylactic bilateral salpingo-oophorectomy, regardless of age, menopause status, or mutation status.

Update On EDRN Grant Projects

Two new EDRN projects were introduced to eligible Registry members in 2006. New Registry members are being invited to participate in these studies upon completion of enrollment.

One project is called the Longitudinal Serum Biorepository. All High Risk Registry members are invited to participate in this biorepository. Participation involves having a serum and plasma blood sample drawn each year and shipped to Creighton University for processing and storage. If pre-cancerous or cancerous lesions should develop in a participant, any previously drawn serum/plasma samples will be invaluable to researchers in their search for early cancer detection signals in the blood.

Another project involves carriers of gene mutations that put them at risk for Hereditary Nonpolyposis Colon Cancers (HNPCC). The purpose of this study is to determine if colon adenomas or cancers can be detected by tests of stool or serum. Blood and stool samples will be collected from consenting individuals who are scheduled for a colonoscopic exam.

Eligible Registry members should have received information regarding these studies. If you have not received study enrollment materials for one or both of the above projects and believe that you should have, please contact Mary Benedetto, High Risk Registry Coordinator at (402) 280-3189, (800) 648-8133, extension 3189 or mbenedet@creighton.edu.

Registry Recruitment Update

The High Risk Registry began mailing Early Detection Research Network (EDRN) and Registry information to potential participants in March of 2001. Within the first 6 ½ years, 1,989 information packets were sent and responses were received from 536 individuals interested in participating in the Registry. Short update questionnaires are forwarded to all Registry members at one year intervals from their Registry enrollment date.

The following centers are currently distributing Registry recruitment materials:
Aegis Women's Healthcare (Bloomington, IN)
Alexian Brothers Hospital Network (Chicago, IL)
Allegheny General Hospital (Pittsburgh, PA)
Children's Medical Center (Dayton, OH)
FAP Support Group (Atlantic City, NJ)
Geisinger Medical Center (Danville, PA)
GeneWISE (Slingerlands, NY)
Harvey Institute for Human Genetics (Greater Baltimore Medical Center)
Holy Cross Hospital (Fort Lauderdale, FL)
Indiana University Northwest (Gary, IN)
Inland Northwest Genetics Clinic (Spokane, WA)
Main Line Health System – Lankenau Hospital (Wynnewood, PA)
Markey Cancer Center (Lexington, KY)
Michigan State University (East Lansing, MI)
Minnesota Colorectal Cancer Initiative (St. Paul, MN)
Northeast Health Genetic Services (Green Island, NY)
Norton Healthcare Hereditary Cancer Institute (Louisville, KY)
Oakwood Hospital and Medical Center (Dearborn, MI)
Providence Alaska Medical Center (Anchorage, AK)
Providence Health System (Portland, OR)
St. John's Hospital (Maplewood, MN)
St. Vincent's Family Life Center (Indianapolis, IN)
St. Vincent's Hospital (Green Bay, WI)
Tulane Human Genetics Program (New Orleans, LA)
Unity Hospital (Fridley, MN)
University of Arkansas for Medical Sciences (Little Rock, AR)
University of Florida Shands Cancer Center (Gainesville, FL)
University of Rochester Medical Center (Rochester, NY)
Vanderbilt University Medical Center (Nashville, TN)
Vermont Regional Genetics Center (Burlington, VT)
Waukesha Memorial Hospital (Waukesha, WI)
Wellmont Holston Valley Medical Center (Kingsport, TN)
Wright State University (Dayton, OH)

Myriad Genetic Laboratories, Inc. supports the EDRN High Risk Registry by inserting the Registry brochure in their packet of information for patients who test positive for deleterious mutations in genes associated with hereditary cancers.

Your participation in the High Risk Registry is greatly appreciated. This unprecedented endeavor in cancer research provides a promising opportunity to improve medical practice in relation to cancer prevention. If you have any questions or concerns, please contact Mary Benedetto, High Risk Registry Coordinator at (402) 280-3189, (800) 648-8133 extension 3189 or mbenedet@creighton.edu.

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Was this newsletter forwarded to you? Do you have a move coming up in the near future? Please keep the EDRN High Risk Registry informed of your current mailing address. You may call or e-mail us with your address update or complete and mail the address update form. Also if there have been recent changes in your medical history, please call the Registry at one of the numbers listed below.

(402) 280-3189 OR (800) 648-8133, extension 3189 mbenedet@creighton.edu

Name _____

Address_____

City, State, Zip_____

Telephone (Day) _____

Telephone (Evening) _____

Mail completed forms to: Creighton University Medical Center
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