

Prevention Is Key in *BRCA*-Related Cancers

Written by Emma Hitt Nichols, PhD

Although *BRCA1* and *BRCA2* mutations are not common, their presence confers a high risk of developing breast or ovarian cancer. Noah D. Kauff, MD, of Memorial Sloan-Kettering Cancer Center, New York, New York, USA, presented current preventative measures for breast and gynecologic cancers as a result of *BRCA1* and *BRCA2* mutations.

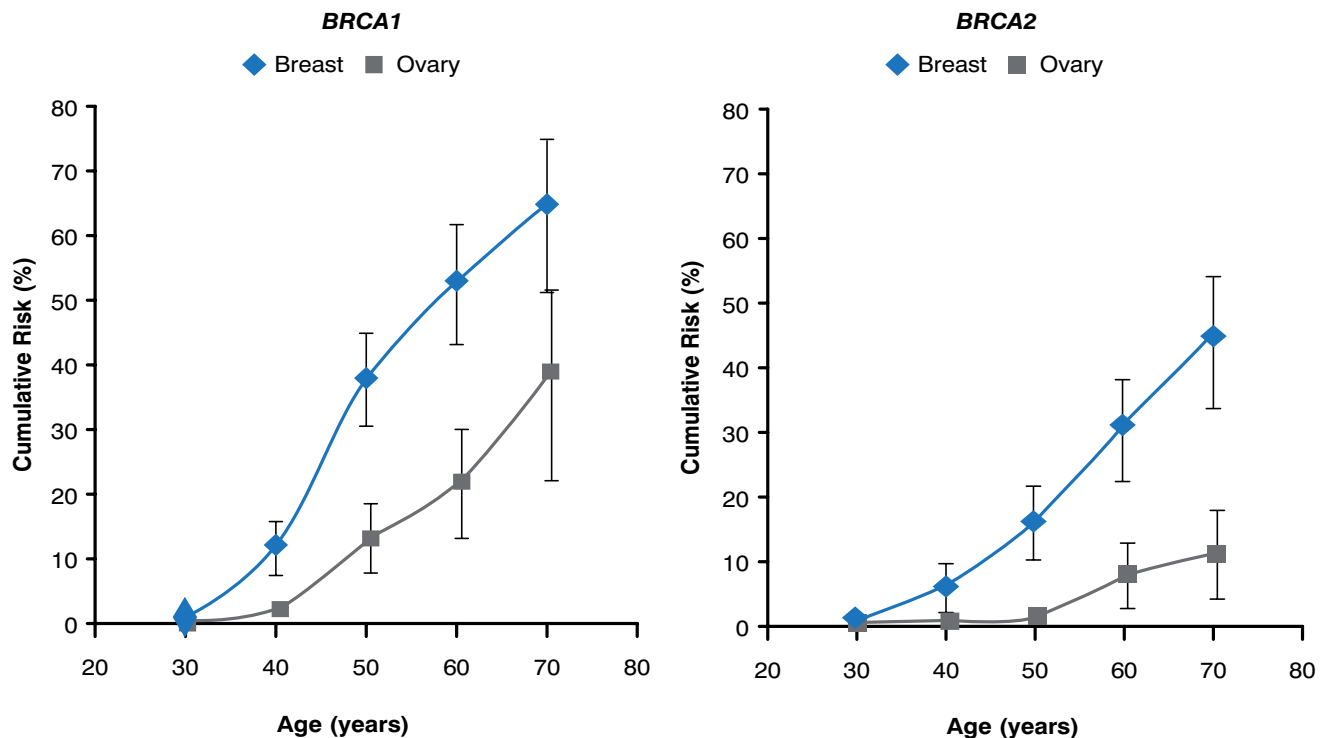
Breast, uterine, and ovarian cancers are among the top 5 most common cancers in women. Up to 10% of these are associated with a single gene mutation. A common cancer susceptibility syndrome is hereditary breast and ovarian cancer, in which the *BRCA1* or *BRCA2* gene is mutated. Patients with *BRCA1* mutations have up to a 25% risk of estrogen receptor (ER)-positive breast cancer and up to a 46% risk of ovarian cancer, whereas patients with *BRCA2* mutations have up to a 79% risk of ER-positive cancer and up to a 27% risk of

ovarian cancer (Figure 1) [Antoniou A et al. *Am J Hum Genet* 2003; King MC et al. *Science* 2003].

Patients with confirmed *BRCA* mutations should undergo intensive surveillance, receive chemoprevention, and/or undergo risk-reducing surgery to prevent breast and ovarian cancer. Mammography is estimated to have a 42% to 56% sensitivity in patients with *BRCA* mutations, with the ability to detect lymph node metastases in 25% to 56% of patients [Brekelman et al. *J Clin Oncol* 2005; Scheuer L et al. *J Clin Oncol* 2002]. However, magnetic resonance imaging (MRI) has been demonstrated to have greater sensitivity than mammography for the detection of breast cancer (Table 1) [Leach MO et al. *Lancet* 2005]. In addition, MRI is more sensitive at detecting breast cancer in earlier stages when compared to mammography [Warner E et al. *J Clin Oncol* 2011].

Chemoprevention with tamoxifen can be offered to women with a 5-year projected risk of breast cancer of 1.66%; however, there is no overall health or survival benefit [Visanathan K et al. *J Clin Oncol* 2013]. In patients with *BRCA* mutations, use of oral contraceptives and increased duration of use are associated with a decreased

Figure 1. Cumulative Risk Estimates for Patients With *BRCA* Mutations



Reproduced from Antoniou A et al. Average risks of breast and ovarian cancer associated with *BRCA1* or *BRCA2* mutations detected in case series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet* 2003;72(5):1117-1130. With permission from Elsevier.



■ OTHER NEWS

Table 1. Enhanced Sensitivity for Breast Cancer Detection With Magnetic Resonance Imaging

	Dutch MRISC Study (Kriege et al. 2004)	Toronto, Canada (Warner et al. 2004)	MARIBS (Leach MO et al. 2005)
No. of women	1909	236	649
No. of <i>BRCA1</i> and <i>BRCA2</i> carriers	354	236	120
MRI sensitivity (95% CI)	71.1%	77.3%	77%
MRI specificity	89.8%	95.4%	81%
Mammogram sensitivity	40%	36.4%	40%
Mammogram specificity	95%	99.8%	93%

MRI=magnetic resonance imaging.
Adapted from Leach MO et al. *Lancet* 2005.

risk of ovarian cancer [Moorman PG et al. *J Clin Oncol* 2013; Cibula D et al. *Expert Rev AntiCancer Ther* 2011].

Risk-reducing surgery results in a clear decrease in the risk of developing breast or ovarian cancer when compared with surveillance alone [Domchek SM et al. *JAMA* 2010; Kauff ND et al. *N Engl J Med* 2002; Rebbeck TR et al. *N Engl J Med* 2002]. Interestingly, Dr. Kauff highlighted that, when carrying out risk-reducing surgery, it is essential to isolate the ovarian blood supply and to ligate it distal to its insertion into the ovary in order to reduce the risk of primary peritoneal cancer in the event that an ovarian remnant remains. In addition, there is a question as to whether a concomitant hysterectomy should be performed with risk-reducing salpingo-oophorectomy (RRSO). Advantages of this approach include ensuring the removal of the entire fallopian tube and eliminating the risk of uterine cancer, whereas the disadvantages include a higher risk of complications and increased operating time and cost.

Patients with *BRCA* mutations who wish to have children have several fertility preservation options, including natural conception with limited breast feeding and continued surveillance, embryo/oocyte cryopreservation for future *in vitro* fertilization followed by RRSO, and risk-reducing mastectomy with RRSO in the mid-40s.

Dr. Kauff concluded by highlighting the challenges of identifying individuals at risk of breast and gynecologic cancers, and he stated that he was hopeful that advances in chemoprevention may one day render risk-reducing surgery obsolete.

The editors would like to thank the many members of the 2014 American Congress of Obstetricians and Gynecologists presenting faculty who generously gave their time to ensure the accuracy and quality of the articles in this publication.

