MRI Bests Mammography for At-Risk Women

BY MARY ANN MOON

FROM THE JOURNAL OF CLINICAL ONCOLOGY

MRI remains strongly superior to mammography over the long term in screening women who are at increased risk of developing breast cancer, according to one study.

The advantage in sensitivity was highly significant for BRCA1 mutation carriers, but not for those who carried BRCA2 mutations and were more likely to present with ductal carcinoma in situ (DCIS).

Previous research showed that in the short term, MRI was approximately twice as sensitive as mammography in detecting breast cancer among women susceptible to the disease, and most guidelines now recommend MRI screening in those who carry BRCA1 or BRCA2 mutations. However, there is no consensus on the screening protocol for other risk groups, few studies have assessed BRCA1 carriers separately from BRCA2 carriers, and until now no studies have evaluated longer-term screening results, said Dr. Adriana J. Rijnsburger of Erasmus University Medical Center, Rotterdam, the Netherlands, and her associates.

To address these issues, the investigators enlarged and extended the Dutch MRI Screening Study (MRISC) and report their findings after following 2,157 women at six cancer or academic centers for 5 years.

The study subjects, aged 25-75 years at enrollment, had never had breast cancer but were at increased risk because they carried either the BRCA1 or BRCA2 mutation (raising their cumulative lifetime risk of developing breast cancer to 50%-85%), had a high-risk family history (raising their cumulative lifetime risk of developing breast cancer to 30%-50%), or had a moderate-risk family history (raising their cumulative lifetime risk of developing breast cancer to 15%-30%). They underwent biannual clinical breast examination and annual mammography and MRI.

During 5 years of follow-up, 97 breast cancers developed in 94 women, including 78 (80%) invasive tumors and 19 (20%) cases of DCIS.

Sensitivity at detecting breast cancer was 71% with MRI, significantly greater than the 41% sensitivity of mammography. When only invasive breast cancers were considered, MRI sensitivity increased to 78%, while mammography's sensitivity decreased to 36%. When the analysis was restricted only to women who carried genetic mutations, the sensitivity of MRI (67%) was "strikingly" higher than that of mammography (25%) for BRCA1 carriers. In contrast, MRI sensitivity (69%) was only slightly higher than mammography's sensitivity (62%) in BRCA2 carriers.

This difference can be explained, at least in part, by the higher proportion of DCIS in BRCA2 than in BRCA1 carriers; mammography was much more sensitive in detecting DCIS (69%) than in detecting invasive tumors (36%).

The specificity of the two screening methods was not significantly different.

Overall, 43% of breast cancers were detected by MRI only. This included 46% of the cancers in BRCA1 carriers, 31% in BRCA2 carriers, 41% in women with a high-risk family history, and 47% in the women with a moderate-risk family history, Dr. Rijnsburger and her colleagues said (J. Clin. Oncol. 2010; doi:10.1200/JCO.2009.27.2294).

These findings "support the recommendation of the American Cancer Society to use annual MRI screening not only for BRCA1/2 mutation carriers, but for all women with an approximately 20%-25% or greater cumulative lifetime risk of breast cancer due to a familial predisposition," they noted.

Five women, all BRCA1/2 mutation carriers, developed distant metastases, and four of them died during follow-up. Two of the women who died had had a favorable tumor stage at diagnosis. This finding underscores the need for clinicians to avoid guaranteeing that all breast cancer deaths can be prevented by early detection via screening, the researchers said.

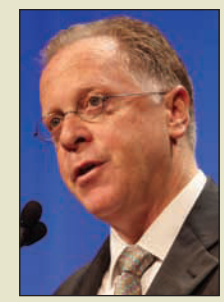
BRCA1-associated tumors "behaved completely differently" from BRCA2-associated tumors. They developed at a younger patient age, were not detected as well on mammography, were more likely to develop during the interval between screenings, were more likely to be invasive, and were larger at diagnosis. This indicates that the current screening schedule for BRCA1 carriers may need to be modified, perhaps by increasing MRI screening to twice rather than once yearly, they said.

This study was supported by the Dutch government and the Cancer Genomics Center in the Netherlands. The investigators reported having no financial conflicts of interest. ■

VIEW ON THE NEWS

Findings May Alter Routine Practice

"The investigators have conducted the largest such trial of MRI screening in high-risk individuals, and their new report that MRI screening appears to be preferentially useful in BRCA1 mutation carriers as compared to BRCA2 has potentially practice-changing implications," said Dr. Andrew D. Seidman.



"The favorable overall survival in all high-risk groups reported suggests that careful MRI screening is not only superior to mammography alone, but may be an attractive alternative to risk-reducing prophylactic mastectomy for some women."

ANDREW D. SEIDMAN, M.D., *is on the American Society of Clinical Oncology communications committee and is an oncologist at Memorial Sloan-Kettering Cancer Center, New York. These comments were taken from an ASCO press statement accompanying the online report of Dr. Rijnsburger's study.*

Important Adjunct

MRI *from page 1*

mammography is an imperfect tool for detection, Dr. DeMartini said. This is critical in women with a personal history of treated breast cancer because they are at elevated risk for a second cancer, and finding second cancers early increases their chance of survival. "Annual screening with MRI may be important in this group."

Disadvantages of MRI include the use of intravenous contrast material, the potential for false positives, and increased cost. DeMartini said that the typical cost of breast MRI is between $1,000 and $2,000. The American Cancer Society's most recent guidelines issued in 2007 recommend annual screening MRI in addition to mammography for women in two high-risk groups: those with genetic mutation such as the *BRCA* gene or first-degree relatives with the gene and those with greater than or equal to 20%-25% lifetime risk, based on family history. The guidelines concluded that there was insufficient evidence to recommend for or against breast MRI in patients with only a personal history of the disease but no genetic or family risk.

"And thus it's been quite challenging as you can imagine for women and their physicians to know whether these breast cancer survivors should be having breast MRI once a year with their mammograms," she said.

This study was designed to compare the diagnostic performance of screening breast MRI in women with a personal history of treated breast cancer alone, to that in women with a genetic or family history of breast cancer.

A retrospective review of the University of Washington's electronic medical database identified all women who underwent a first screening breast MRI for a clinical indication and had either a personal history or genetic or family history of breast cancer during the period January 2004 – June 2009. Each patient contributed their first screening breast MRI to the study. For each examination, the highest level final breast imaging-reporting and data system (BI-RADS) assessment was used. Cancer status was followed for 365 days following index breast MRI and was considered positive if there was a diagnosis of invasive carcinoma or ductal carcinoma in situ.

Measures of diagnostic performance that were calculated included the recall rate, or number of women recalled for additional testing; the positive predictive value for malignancy at biopsy; the cancer yield, or percent found to be malignant among those screened; and the sensitivity and specificity.

Of the 1,026 women who underwent a first screening breast MRI in the study interval, 973 were screened for personal history and/or genetic or family history. These made up the study population. Of these, 646 (66%) were screened for personal history alone, and the remaining 327 (34%) were screened for genetic or family history. Women who fell into both categories were classified as genetic or family history.

In the 973 women, 27 malignancies were found, said Dr. DeMartini. "Twenty-five of them were found with breast MRI," she said. The other two were not found with breast MRI and were false negatives; both occurred in the personal history group. Of the 25 malignancies, MRI detected 20 in the personal history group and 5 in the genetic family group, she said.

In diagnostic performance, the recall rate – the percentage recalled for additional testing – was 9.3% (60 of 646) in the personal history group, significantly lower than the 15.0% (49 of 327) in the genetic or family history group.

The positive predictive value of biopsy – the percentage found to be malignant – in the personal history group was 35.7% (20 of 56), significantly higher than in the genetic and family history group (12.2%, or 5 of 41). The cancer yield – the fraction of all women screened who were found to have a malignancy – was 3.1% (20 of 646) in the personal history group, or more than twice the 1.5% (5 of 327) found in the genetic and family history group (P =.14). The sensitivity was 90.9% (20 of 22) in the personal history group (which had two false negatives not found with breast MRI) vs. 100% (5 of 5) in the genetic and family history group. Specificity was 93.6% (584 of 624) in the personal history group, higher than the genetic and family history group's 86.3% (278 of 322).

The date of original cancer was available for 18 of the 20 malignancies detected by MRI, and 11 of the 18 were detected greater than 5 years after the original cancer.

"The diagnostic performance of screening breast MRI was similar to or higher overall in women with personal history alone compared to those with a genetic or family history," said Dr. DeMartini. "Women with a personal history of breast cancer had a lower recall rate, higher positive predictive value, higher cancer yield (although not statistically significant) and higher specificity."

Screening breast MRI may therefore be an important adjunct to mammography in women with a personal history of breast cancer, she said, and should be a step in the direction of evidence-based, personalized surveillance of women who are breast cancer survivors. ■