Case Description: 34 y/o female patient with a strong family history of breast cancer in her mother, grandmother, aunt and cousin without BRCA proven mutation who presents for advice on the best method of screening in her and the interval for screening.

Clinical Question: Is mammogram the best screening tool for patients with a high risk of developing breast cancer?

Search: The English language literature was searched via PubMed. Search terms used were High Risk and screening and mammography and magnetic resonance imaging. This search revealed 230 articles. This paper was then chosen for further review.


Study Type: This was an open prospective, nonrandomized, multicenter study designed to prospectively compare clinical breast examination (CBE), mammography, ultrasonography, and MRI in the surveillance of women at high risk of breast cancer.

Research Question: Does routine MRI screening find more breast cancers than CBE, mammography, and ultrasonography in high risk women without increasing the number of false positives and causing unnecessary invasive procedures?

Importance/Relevance: Studies have shown that MRI provides a screening strategy with higher sensitivity compared with mammography alone but many studies did not include ultrasound, excluded women with previous breast cancer, and had large differences in sample size, number of screening events and age of enrolled women.

Methods: Patients: Asymptomatic women older than 25 who were at high risk for developing breast cancer were enrolled. High risk was defined as having the BRCA1 or BRCA2 gene, having a 1st degree relative with this gene or categorized as having a strong family history of breast or ovarian cancer with 3 or more events in 1st or 2nd degree relatives. Excluded patients were those that already had a bilateral mastectomy, pregnant or breast feeding women, those undergoing chemotherapy, those with a terminal illness or patients that had a contraindication to an MRI or gadolinium contrast.

Intervention/Comparison: Every patient underwent a clinical breast exam, mammogram, ultrasound, and MRI during the 1st 2 rounds that were 1 year apart and then after that a CBE, mammography, ultrasound, or optional MRI was planned and investigators were free to offer further surveillance then just one year intervals. In all 7 rounds were performed.

Outcomes: When suspicious lesions were palpated on CBE or were rated a BI-RADS 4 or 5 on imaging, these were followed up by an FNA or biopsy and a true positive was when the findings were pathologically proven to be invasive cancers or ductal carcinomas in situ. False positives were considered if pathology was benign. Suspicious imaging not explored with FNA or biopsy were considered false positives if they had follow-up later that showed negative result. A negative CBE or BI-RADS 1-3 on imaging were considered true negative if no cancer was detected on 1 yr follow-up. These were considered false negatives if another imaging modality made an area suspicious that was later pathologically proven or an interval cancer was discovered. These results were then used to determine sensitivities and specificities of each test.

Evidence Based Evaluation:
1. Did the experimental and control groups start out with a similar prognosis? Not really, some had a proven BRCA gene that has been showed to have a higher incidence developing breast cancer in that
individual while others just had a family member with the BRCA gene or they just had many family members with breast cancer so their risk may not have been as high.
2. Were patients randomized? No
3. Was randomization concealed? No randomization
4. Were patients analyzed in the groups to which they were randomized? They were analyzed all within one group
5. Were groups similar regarding known prognostic factors? Yes since there was only one group
6. Did the experimental and control groups retain a similar prognosis after the study started? Yes
7. Were patients, clinicians, and outcome assessors aware of group allocation? Yes
8. Was follow-up complete? No, they lost 227 patients to withdrawal or loss at follow-up.

**Results:** In all there were 52 cancers detected, 49 during screen detection and only 3 during interval detection. Of the 50 cancers that were found in patients screened with mammography, 25 were diagnosed (both film-screen and digital) and 25 were not diagnosed. This was a sensitivity of 50%. MRI was found to have a sensitivity of 93%. Of all 52 cancers detected, 16 cancers were only detected by MRI and this was equally distributed between women under 50 and women over 50. They also compared the sensitivities of combining MRI plus mammography and MRI plus ultrasonography and MRI plus mammography and ultrasonography and they did not have a significant difference from just MRI alone.

**Applying Results:** This study can easily impact patient care in those individuals who are at high risk of developing breast cancer. In the patient presented above, I would push for an annual MRI for her screening to ensure that she had the maximum chance of detecting a breast cancer early. Moreover this study also showed that MRI is superior in both younger and older patients so continuing annual MRI screening in patients at high risk for developing breast cancer past the age of 50 would still be beneficial. I would offer annual MRI screening to my high risk patients but will most likely be limited by the patient’s insurance company actually paying for the procedure.