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MRI Detection and Screening Related to Breast Cancer Mortality

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Abstract

Early breast cancer detection can play an important role in the outcome of cancer diagnosis. Genetic predisposition for breast cancer puts women at an increased risk of acquiring breast cancer at an earlier age and more frequently when compared to those without any predispositions. Due to the decreases in sensitivity of mammograms in pre-menopausal women with high breast density, alternative imaging such as magnetic resonance imaging (MRI) should play a more projecting role in screening younger women who carry a genetic predisposition. Clinicians need to have the knowledge to appropriately screen women with family history of breast cancer, along with ordering correct imaging studies to maximize the opportunity to discover suspected or undiagnosed breast cancer. This study will look to determine if there is a decrease in mortality with use of breast MRI. The evidence shows that though breast MRI is the highest quality screening and diagnostic tool available, more long-term studies need to be done to determine the patient outcomes.

Background

The second leading cause of cancer death among women in the United States is breast cancer (Sui, 2016). A woman who has family history of breast cancer will be at an increased risk for cancer, even if there is no mutation found in her or her family. There is evidence that the lifetime risk for breast cancer in a woman who has three or more relatives with breast cancer to be 20%-40% (Narod, 2011). There are many factors that can place a woman at higher risk of developing breast cancer: genetic mutation of the BRCA gene, family history, chest radiation at a young age, and increasing in age. Many different imaging studies can be used to identify lesions that are suspicious for breast cancer. Thus, imaging studies show the importance of screening and its value for patients who are most likely to develop breast cancer and for those whom early treatment can be more effective than later treatment in the

reduction of mortality (Elmore, 2018a). Mammography has been the foundation of screening for breast cancer (Elmore, 2018b). Ultrasonography is also commonly used a diagnostic test when follow up of an abnormality is needed from mammography detection. Ultrasound can also be used for women with dense breasts. The role of MRI is emerging, with MRI screening and mammography only targeted to high-risk women (Elmore, 2018b). There is now evidence that MRI is by far the most sensitive imaging available in young high-risk women (Bick, 2015). MRI does carry a high sensitivity for breast cancer and has led to increasing use for detection, assessment, and treatment monitoring, however appropriate indications, techniques and interpretations vary among healthcare facilities (Slanetz, 2018). It is shown that in high-risk screening, that at least 30% of breast cancers will be discovered with the use of MRI, and without MRI would have been missed. Breast MRI was introduced into clinical practice in the 1990's, and has shown to be more sensitive to detecting breast cancer. However, there is increased cost and lower specificity with breast MRI when compared to mammography. Warner et al. (2011) states "If MRI screening were to lead to reduced mortality in women with BRCA mutation, then the incidence of advanced breast cancers should be reduced in MRI-screened women compared with women at similar risk who undergo conventional surveillance" (p. 1664).

It is important to note that breast MRI has many different clinical indications; screening, diagnostic, staging or treatment and surveillance for recurrence. Screening is performed on a woman who has no previous diagnosis of invasive or in situ breast cancer, and is asymptomatic at the time of MRI. Screening is done when there is no physical or breast abnormalities in the past six months (Stout et al., 2013). A diagnostic test is done as part of the evaluation or follow-up of a symptom, or when there is a physical abnormality found by

either the patient or clinician, and/or if there is a radiologic breast abnormality, even on a MRI, in the past six months. If a woman has had a new biopsy-proven diagnosis of breast cancer in the previous six months, an MRI is done for staging or treatment. Lastly, surveillance for recurrence is a routine MRI on a woman with a positive diagnosis of an invasive or in situ cancer, and there are no new symptoms for more than six months following a surgery or treatment (Stout et al., 2013). Randomized trials of mortality will need to be done to determine the association of risk reduction with MRI screening (Patani & Mokbel, 2008). Lastly, there are contraindications to breast MRI; pregnancy, implanted devices, foreign bodies, gadolinium allergy and decreased renal function (Slanetz, 2018). Another potential barrier to MRI is the cost, as it is ten to fifteen times more expensive than mammography or ultrasound, and not always reimbursed by insurance.

The U.S. Preventive Services Task Force (USPSTF) has reviewed evidence on many screening recommendations for breast cancer. The recommendation set forth by the USPSTF is that there be a biennial screening mammography for women aged 50 to74 (Siu, 2016). The USPSTF recommends screening at age 40 when there is a parent, sibling, or child with breast cancer. It is interesting to note that the USPSTF found inadequate evidence on the benefits or harms of adjunctive screening, such as MRI, and that no information has been detected on the effects of health outcomes, including breast cancer mortality. Risk calculators, such as the National Cancer Institute's Breast Cancer Risk Assessment Tool, can be used to show predicted and actual outcomes of a woman's risk for breast cancer. From several studies, in 2007, the American Cancer Society has recommended that annual breast MRI be done for all women with a risk of 20% to 25% (Boetes, 2011).

For the patient Nicole Smith, discussed in the case study in the addendum, the importance was to determine what type of screening she would need as a healthy individual with no medical concerns for herself. However, there is strong family history of breast cancer with her mother, aunts and cousins, and a grandmother with ovarian cancer. Finding the best screening available to her is essential in decreasing her mortality if she should have some type of breast lesion.

Case Report

Patient is a 31-year-old, single, Caucasian female, with no prior medical history, arrives for an establish patient care visit. Her only past surgical history is an appendectomy in her childhood years. She has always had routine yearly physical exams. Her last Pap test was one year ago, and was negative for any findings. All of her vaccines are current and up to date. She takes a multivitamin and combination oral contraceptive pill daily. She reports an allergy to penicillin. She is an elementary teacher who lives with her boyfriend. Patient denies smoking or any illicit drug use and reports drinking one to two alcoholic drinks every other week. Patient has no concerns today about her health or medications.

Concerning family history, her mother is deceased, at the age 40 from breast cancer. Her father is alive and in good health. She has one brother who is in good health. Her maternal grandmother is deceased, and had ovarian cancer. Her maternal aunt is deceased and had breast cancer. She has a female cousin, age 30, who currently has breast cancer. She is unaware if any of her family members had genetic testing done, such as BRCA1 and BRCA2.

Upon review of systems, she denies any symptoms. Objectively, she is a pleasant 31-year-old female and appears to be in no distress. Conjunctivae and extra ocular eye movements are normal. Heart was regular rate and rhythm, normal tones, and without rubs, murmurs or gallops. Respiratory rate was with normal effort and breath sounds were clear to auscultation. She was in no respiratory distress. Abdomen was soft and without mass or tenderness. Patient was alert and oriented to person, place and time. Her skin was warm and dry and without lesions or bruising. Patient declined breast and genitourinary exam. Her mood and affect were normal.

Lab studies today include a TSH. Mammogram is recommended yearly. The GAIL model was attempted to use for breast cancer risk, but this patient is too young of age for that model. However, with her familial risk of putting her at an increased risk of developing breast cancer, it is recommended that breast MRI be done yearly. A referral has been made to a genetic counselor, due to the patient's strong family history of breast and ovarian cancer. If she goes forward with testing and is BRCA positive, it would be imperative that she have a breast MRI yearly along with her mammogram. Her birth control was changed from a combination pill to a progesterone only pill. It is recommended that the patient do monthly self-breast exams, maintain a healthy diet and exercise four to five times a week.

Literature Review

A search was completed using the University of North Dakota Harley E. French Library of Health Sciences website. The search engines CINAHL and UptoDate were used. CINAHL was the first search engine used. According to Mateo and Foreman, 2014 "CINAHL is primarily

used by nursing scientists" (p. 107). Headings within the CINAHL search engine were used to give concentration to the search. The first heading used was "breast MRI" AND "decreased mortality." This yielded three articles. CINAHL search engine was used again for further concentration of the search. The second heading used was "breast MRI" AND "mortality." This yielded thirty-two results. The English Language and Peer Reviewed limits were added, along with a date range of 2008-2018; still resulting in twenty-four articles. Of these articles, ten were reviewed in detail and found to be relevant to the clinical question. In the overall CINAHL search, "breast MRI" was tagged as the major concept. UptoDate was the next search engine utilized. Headings used were "breast MRI." This resulted in thirty articles. This narrowed the search to twelve articles. One of these articles, four were reviewed in detail and were found to focus on the intent of this study.

After many article reviews through CINAHL and UptoDate there were several articles that were found to be relevant that were referenced in other articles. These articles were then searched on the University of North Dakota Harley E. French Library website and found within the CINAHL search. Some of the MeSH terms that can be used to find access to such articles are "Breast cancer" AND "screening." Adding the free full text search limit will decrease in the number of articles found, along with the specific year of the article being searching for.

The novelty of this case is to determine if there is a decrease in mortality rates with the use of breast MRI. Different guidelines have been brought forth in the past decade giving indications for breast MRI in women who have an increased risk of developing breast cancer. According to Boetes, (2011), the first nonrandomized studies were done in the 1990s to determine the additional value of breast MRI compared to mammography in women who carried a BRCA gene or at least a 20%-25% risk of developing breast cancer. From these studies, the

American Cancer Society has recommended that annual breast MRI be done for all women with a risk of 20% to 25% (Boetes, 2011). One of the cohort studies by Boetes (2011) looked at 179 women with a risk of 15% or more, with thirteen total breast cancers detected, seven on mammogram, and full detection of all thirteen cancers on MRI, thus determining that a screening MRI in asymptomatic, high-risk women is instrumental as an important role in the detection of malignant tumors.

As with any screening tool for any form of cancer, there will always be benefits and risks. Primary benefits are a decrease in mortality. In a study done from 2012-2015, screening with mammography has shown to decrease mortality, by 20% (Elmore, 2018a). Elmore (2018a) also noted that data for reduction in mortality related to more advanced imaging is limited. However, a decrease in breast cancer as a whole, in 2012, was recognized to screening alone (Elmore, 2018a). Potential harms that can be associated with screening are over-diagnosis, false-positive results, anxiety, and unnecessary treatment. Estimated over-diagnosis is 10 percent or less to 50 percent of all women who have breast cancer diagnosis (Elmore, 2018a). False-positive results are based on many factors including age and breast density. In the United States, about 10 percent of mammography exams are false positive (Elmore, 2018a). The occurrence of false-positive studies can increase anxiety for the patient. Many studies have shown that several cancers, especially those in mammary ducts are biologically insignificant and would never be evident in the patient's lifetime (Elmore, 2018a). This leads to potential for unnecessary treatment.

Important to note that different prediction models are used for breast cancer risk. Models will vary and concentrate more on family risk, BRCA mutation genes, history of biopsies or breast density. The most widely used tool for calculating breast cancer risk is the Breast Cancer

Risk Assessment Tool, or known as the Gail Model (Elmore, 2018a). The Gail model is easy to access and use, and is intended for women who have never had diagnosis of breast cancer. Its other indication is for those who do not have a strong family history of breast cancer. Elmore (2018a) does report that the Gail model does come with limitations; no estimate of risk with BRCA gene mutations, only offers two race ethnicities, and low sensitivity results. There are other models for use for women who have family history of breast or ovarian cancer and carry the BRCA mutations: Ontario Family History Risk Assessment Tool, Manchester scoring system, Referral Screening Tool, Pedigree Assessment Tool and Family History Screen (Elmore, 2018a). These tools, along with referral to genetic counseling are supported by the USPSTF.

Stout et al. (2013) determined through their study that the greatest increase in use of breast MRI was for screening and surveillance. The screening for breast MRI should meet the guidelines of the American Cancer Society, but it has been noted that there are a decreased number of those that actually meet the guidelines. Breast MRI can have a high false-positive rate, but expanding the scope by using this in women with lower risk would assist in decreasing the positive predictor value of the test. Screening MRI can generate false positive results, and tin turn cause and increase in anxiety and cost (Kurian, Sigal & Plevritis, 2010). Although benefits are prevalent with breast MRI, through observational studies, there is no evidence of long-term mortality benefits (Stout et al., 2013).

Over the past ten years, much of the research has been focused on comparing sensitivity of mammography and MRI. To date, MRI sensitivity for breast cancer screening has by far exceeded mammography (Narod, 2011). However, Narod, (2011) noted that even though sensitivity of MRI exceeds that of mammography, it has not yet shown that this leads to a decline in mortality. Another mortality rate associated with breast MRI compares that of the gold

standard with detection, mastectomy. This is difficult to assess given that there are several factors that play; the relationship of tumor size, BRCA carriers and non-carriers. Narod (2011) summarized through studies that MRI has replaced mammography as the gold standard in screening women who are at high-risk, but cannot conclude that a decrease in mortality has been detected. Many previous model-based analyses have been done addressing the BRCA mutation gene. Kurian et al. (2010) concluded that prophylactic surgeries can improve life expectancy, and few considered current improvements in the detection of cancer with breast MRI.

Several models and calculations have shown that BRCA1 and BRCA2 mutation carriers will have an increased risk of death before age 70. This is where the importance of early detection and secondary prevention play a large role. Bick (2015) argued that there is little reliable data available concerning the effectiveness of surveillance with breast MRI in high-risk women and reducing mortality. Bick even suggests that this data may be difficult to obtain, related to ethical dilemmas of having to offer nothing to one arm of a study and full screening to another arm of a study. Such a study would also need to occur over a longer time period and follow-up of at least 10 years. Elmore (2108b) also suggests that a randomized trial to evaluate MRI screening and morality rates in women with BRCA mutations would be unlikely, as is would require a large number of participants, and some at high-risk would have to consent to be assigned a non-screening section. Studies have shown that with intensified surveillance, there is little effect in BRCA1 carriers where more advanced staging occurs (Bick, 2015). Finally, it was concluded that MRI can detect the immense majority of breast cancers at early stages, however, other risk-reducing measure have been demonstrated to be highly effective in decreasing breast cancer mortality in women who are high-risk (Bick, 2015). However, according to Elmore (2018b) reports that two studies have been done that support MRI screening for women who are

high-risk breast cancer and show a decrease in mortality, but the numbers are small and many biases are carried out through the studies; patient selection, lead time bias and differences in treatments.

A study by Houssami et al (2014) looked at the association of preoperative breast MRI and breast cancer recurrence. MRI has been utilized in practice for newly diagnosed breast cancer because it can detect additional disease. It is shown that MRI does not improve surgical outcomes of breast cancers, and may increase the chances of receiving mastectomy surgical procedure (Houssami, 2014). However, the use of MRI for detection of additional disease and giving guidance for extensive surgeries is beneficial. This has the potential of decreasing mortality, but no studies have been done to show this as of this time.

The Dutch MRI Screening Study has been found to the be only prospective study that addressed log-term survival. In this study, high risk breast cancer women were screened annually with mammography and MRI, and those who developed breast cancer continued to be followed for about 5 years (Isaacs, 2018). At six years, two groups of women with metastasis-free and overall six years survival of invasive cancer with BRCA gene was 83.9 percent and 92.7 percent respectively (Isaacs, 2018). This data looks hopeful, but still does not show a direct correlation with a decrease in mortality, as there is no control group.

Learning Points

Practitioners are responsible to know what screening, testing, imaging, and referrals should be done with the care of a patient who is at high risk of developing breast cancer. Knowing how to calculate a risk with different guidelines is easily accessible for any provider. Becoming knowledgeable on different imaging studies done for breast cancer detection will

provide patients with the best care and outcome. If breast MRI is suggested, continuing with yearly care for that patient will be best for preventive care. Having the knowledge that MRI can be done for screening and diagnostic purposes shows the scope of MRI imaging. Collaborating with gene specialists and possibly surgeons may be necessary to help reduce the risk of mortality in breast cancer patients. MRI has been shown to be better at detecting breast lesions when compared to MRI. Though it has not been shown to date that MRI will decrease mortality, in time, it is possible that further long-term studies could bring forth such information.

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