Putting the "Great Mammography Debate" to Rest

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Abstract

There is a heated debate in this country about the risks and benefits associated with screening mammography. Proponents on both sides of the debate feel equally as strongly for or against annual breast cancer screening. Despite one's opinions regarding the utility of screening mammography, it is difficult to deny that the rates of false-positive exams, the rates of overdiagnosis, and the cost of annual screening are too high. We can do better. It is time to stop devoting energy to arguing about data from studies performed decades ago and start working toward gathering new evidence. In late 2015, we will initiate the WISDOM study to investigate the safety and effectiveness of a personalized breast cancer screening model. This model will use a comprehensive risk assessment process to determine individualized screening regimens for women in the interventional arm. The data collected in this study will better inform the screening debate and will allow us to shed more light and less heat on the issue.

Key words: breast cancer, screening, mammography

There is a great debate in this country about the risks and benefits of screening mammography. On one side of the debate are those in favor of the one-size-fits-all model of performing annual mammograms starting at the age of 40 for women who are not known to be at greatly elevated risk of developing breast cancer. The radiology community argues that this model reduces the rates of interval cancers, aids early detection, and should not be changed. On the other side of the debate are those who support the United States Preventive Services Task Force (USPSTF) recommendations to screen women biennially starting at age 50, and to screen women in their 40s based on personal preferences regarding the potential benefits and harms of screening.[1] Specialists on this side of the debate believe that annual screening results in unacceptably high rates of false-positive recalls, overdiagnosis, and overtreatment.

Recently, the USPSTF published a draft update to the 2009 breast cancer screening recommendations, and the debate has once again intensified. The solution to this problem is not to continue the debate with repetitious reviews of studies that were performed more than 30 years ago, but to focus ahead on how to make breast cancer screening safer and more effective. The time has come to put the debate to rest by conducting a modern-era screening trial.

Before focusing on the future, let us first take a moment to review the current state of breast cancer screening in the United States. The majority of providers in this country continue to recommend annual screening starting at age 40.[2] Proponents of annual screening mammography cite a resulting relative reduction in breast cancer mortality of 21%, which is based on data from randomized screening trials performed in the 1970s and 1980s.[3] However, this estimated benefit comes with significant drawbacks. After 10 years of annual screening, over one-half of women screened will receive a false-positive recall, and 7% to 9% will undergo a benign biopsy.[4,5] False-positive recalls and benign biopsies can cause long-lasting psychological distress that can negatively impact a woman's willingness to undergo screening for breast cancer in the future. Additionally, false-positive recalls and overdiagnosis cost the United States an estimated $4 billion per year,[6] and screening in aggregate is estimated to cost between $8 and 10 billion per year.[7] This estimate is based on a screening mammogram costing between $135 and $195. If the cost of mammography increases, the overall cost of breast cancer screening increases proportionally. As a country and as healthcare professionals, we can and should do better.

Breast cancer screening should harness the advances that have been made in breast cancer risk assessment and our understanding of breast cancer tumor biology. Screening should be more effective at finding relevant and consequential cancers, and should result in fewer benign biopsies. Screening should also be better integrated with prevention. Lastly, screening should be more cost-effective. A personalized screening model could potentially achieve all of these goals.

The aim of a personalized screening model would be to focus resources on those women who are most likely to benefit. The foundation of the model would be a comprehensive risk assessment that would take into consideration a woman's classical risk factors for breast cancer, such as her personal and family history of breast disease. This comprehensive risk assessment would also include an evaluation of breast density and germline genetic testing. These risk factors would then be placed into a breast cancer risk model that would estimate the

woman's 5-year risk of developing breast cancer, and personalized screening recommendations would be made according to this risk. Women at high risk of developing breast cancer would be screened more frequently, and women at low risk would be screened less frequently. This risk estimation could also be used to make recommendations regarding chemoprevention, thereby integrating screening and prevention, which is the real key to reducing mortality from breast cancer.

This model has the potential to optimize the benefits of mammography in the context of modern systemic therapy while minimizing harms. Using a similar risk model in 3 independent study populations, it has been shown that 50% of cancers occur in women with the top 20% predicted risk.[8] This model is also practical because these risk factors are easy to assess, and it is estimated to be more cost-effective than annual screening, despite the use of genetic testing, which has decreased in cost significantly since the Supreme Court ruling in June 2013 that stated that the human genome could not be patented.

Personalized screening may be the way forward, but this can only be determined in the setting of a randomized controlled trial. In the fall of 2015, a randomized controlled trial comparing personalized breast cancer screening with annual screening will be initiated within the Athena Breast Health Network that spans the University of California and the Sanford Health system in the Midwest. This study will be called the WISDOM study (Women Informed to Screen Depending on Measures of Risk). We have received a large grant from the Patient-Centered Outcomes Research Institute to perform this trial, and are also working with payers and self-insured employers, such as Blue Shield of California and UC Health, to create a Coverage with Evidence Development policy that will cover the medical costs of the trial. Using surrogate endpoints and long-term follow-up, we aim to determine whether personalized screening is as effective, less morbid, more preferred by women, and enables prevention more as compared with annual screening. Our hope is that this trial will provide us with the information we need in order to determine the safest and most effective way to screen women for breast cancer. Then, and only then, will we be able to put "The Great Mammography Debate" to rest.

As we move toward a more biology-based approach to the treatment of diseases, our approach to screening for and preventing those diseases should follow suit. The opportunity before us is to learn who is at risk for which type of breast cancer, and to optimize our screening and prevention strategies for each individual according to her personal risk. Over the last 20 years, many advances have been made in our understanding of the risk factors that contribute to a woman's risk of developing breast cancer. The time has come for us to harness this knowledge and apply it in an evidence-generating fashion to shed more light and less heat on the screening controversy.

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