Number 2

Effective Health Care

Effectiveness of Noninvasive Diagnostic Tests for Breast Abnormalities

Executive Summary

Background

Breast cancer is the second most common malignancy in women. The American Cancer Society estimated that in the United States in 2005, 212,930 women would be newly diagnosed as having breast cancer and there would be 40,870 deaths due to this disease. Because early breast cancer is asymptomatic, the only way to detect it is through screening. Mammography is a widely accepted method for breast cancer screening. As a screening test, mammography is used to rule out cancer by missing very few cases of cancer—i.e., by having a low false negative rate. As a result, most women who have an abnormal mammogram do not have cancer.

Because an abnormal screening mammogram requires a diagnostic test to confirm whether cancer is present, many women who do not have cancer will undergo diagnostic tests. Typically, suspicious lesions are evaluated with tissue biopsy, either by excision or by needle sampling. If a noninvasive diagnostic test were available that could accurately exclude malignancy, many women with an abnormal mammogram who do not have cancer could avoid biopsy. However, such a test must be sufficiently accurate not to miss cancer in those women who have it. Positron emission tomography (PET)

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions for treating health problems. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

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scanning, scintimammography, magnetic resonance imaging (MRI), and ultrasonography (US) have been proposed for this purpose, yet the accuracy of these noninvasive diagnostic technologies in excluding breast cancer in women at average risk remains unclear.

An ideal diagnostic test to evaluate breast abnormalities found by mammography or breast examination would distinguish women who need to have a biopsy from those who can safely avoid one. A woman who has a negative test result should be very confident that she does not have breast cancer before deciding to forgo a biopsy. To help patients, policymakers, and clinicians determine whether these noninvasive tests are sufficiently accurate to be appropriate for evaluation of women with an abnormal mammogram or exam finding, this report summarizes available data on the performance of these tests in the evaluation of women presenting with breast abnormalities that suggest the possibility of breast cancer. The report addresses the following questions:

1. What are the sensitivity and specificity of the tests for diagnosis of breast cancer in women presenting with an abnormal mammogram or a palpable breast abnormality?
2. For women with relevant demographic risk factors (e.g., age, family history) and clinical risk factors (e.g., Breast Imaging Reporting and Data System [BIRADS] status or morphologic characteristics of the lesion), what are the positive and negative predictive values of the above diagnostic tests?
3. Are there other factors that affect the accuracy or acceptability of the tests considered in Questions 1 and 2?

Conclusions

- A total of 81 studies met inclusion criteria to evaluate the accuracy of MRI, PET, scintimammography, or US for the diagnosis of breast cancer in women. The findings of accuracy for these tests, summarized as sensitivity, specificity, and negative likelihood ratios, are summarized in Table A. Although all of the technologies evaluated could reduce the need for biopsy in women with an abnormal mammogram who do not have cancer, each would miss some cancers.
- To place the tests' accuracy information into perspective, an average woman in the United States who has an abnormal mammogram requiring a biopsy for evaluation has approximately a 20-percent risk of cancer. For women at this average level of risk of cancer after an abnormal mammogram, based upon the tests' negative likelihood ratios:
  - For every 1,000 women who had a negative PET scan, about 924 women would have avoided an unnecessary biopsy, but 76 women would have missed cancers.
  - For every 1,000 women who had a negative scintimammogram, about 907 women would have avoided an unnecessary biopsy, but 93 women would have missed cancers. (These numbers are for nonpalpable lesions only; numbers could not be calculated for all lesions.)
  - For every 1,000 women who had a negative MRI, about 962 women would have avoided an unnecessary biopsy, but 38 women would have missed cancers.
  - For every 1,000 women who had a negative US, about 950 women would have avoided an unnecessary biopsy, but 50 women would have missed cancers.
- An individual woman's risk of breast cancer in the face of a suspicious finding on mammogram or clinical examination may vary widely from the average; the woman and her health care provider should discuss the extent of cancer risk. In general, the higher a woman's risk of cancer is before undergoing a noninvasive test, the higher is the risk that she has cancer even if the test is negative.
- If a less than 2-percent risk of having breast cancer with a negative diagnostic test is considered an acceptable level of risk for a diagnostic test to reliably preclude biopsy, none of these tests was sufficiently accurate to replace biopsy for women at average risk of breast cancer.
- Based on results for only nonpalpable lesions (usually detected by mammography), data were

Table A. Summary of Major Findings on Noninvasive Diagnostic Tests for Breast Abnormalities

Category	Test characteristic	PET scanning	Scinti-mammography	MRI	Ultrasound
Suspicious lesions in general	Sensitivity	82.2%	NC	92.5%	86.1%
	Specificity	78.3%	NC	72.4%	66.4%
	Negative likelihood ratio	0.33	NC	0.16	0.21
	Negative predictive value at 20% prevalence	92.4%	NC	96.2%	95.0%
	Stability of estimates	Low	Unexplained heterogeneity	Moderate	Moderate
Nonpalpable lesions	Sensitivity	NC	68.7%	NC	NC
	Specificity	NC	84.8%	NC	NC
	Negative likelihood ratio	NC	0.41	NC	NC
	Negative predictive value at 20% prevalence	NC	90.7%	NC	NC
	Stability of estimates	Insufficient evidence	Moderate	Insufficient evidence	Insufficient evidence
Palpable lesions	Sensitivity	NC	NC	NC	NC
	Specificity	NC	NC	NC	NC
	Negative likelihood ratio	NC	NC	NC	NC
	Negative predictive value at 20% prevalence	NC	NC	NC	NC
	Stability of estimates	Insufficient evidence	Insufficient evidence	Insufficient evidence	Unexplained heterogeneity

Abbreviations: PET = positron emission tomography. MRI = magnetic resonance imaging. NC= not calculated.

Notes: Sensitivity is the probability that a test is positive in those with the disease. Specificity is the probability that a test is negative in those without the disease. In this table, sensitivity is the mean threshold sensitivity reported in the included studies. The sensitivity threshold is the degree of abnormality that prompts a recommendation for biopsy. The corresponding specificity was determined using the Summary Receiver Operating Characteristic (SROC) curve. The SROC curve (in which the true positive rate is given on the y-axis and the false positive rate on the x-axis) depicts the relationship between sensitivity and specificity, illustrating that a change in the sensitivity threshold of a test inevitably affects the specificity of the test. Negative likelihood ratio is the ratio of the probability of a negative test in women with cancer to the probability of a negative test in women without cancer; based on the risk of having the disease prior to the test, it is used to calculate the risk of having the disease despite a negative test result. The negative likelihood ratios in this table were calculated using fixed-effects meta-analytic pooling. The negative likelihood ratio that can be calculated from the sensitivity and specificity reported in the table differs slightly from the summary negative likelihood ratio obtained by meta-analytic pooling; however, these values are not statistically different. Negative predictive value is the probability of not having cancer in women with a negative test result. Negative predictive value was calculated using the summary negative likelihood ratio.

insufficient to estimate the accuracy of PET scanning, MRI, or ultrasound. Scintimammography was not sufficiently accurate to avoid biopsy in women at average risk as judged by the acceptability standard of less than a 2-percent risk of breast cancer with a negative diagnostic test.

- Based on results for only palpable lesions, data were insufficient to estimate the accuracy of PET scanning, MRI, ultrasound, and scintimammography.
- The evidence supporting our conclusions permits us to be moderately confident that publication of future studies will not overturn our findings. Flaws in the evidence base include incomplete reporting of study design and patient characteristics, and insufficient numbers of studies reporting data for particular subgroups of patients; these flaws are responsible for ranking our confidence in our overall conclusion as moderate rather than strong.

Remaining Issues

- There was insufficient evidence to estimate how accurate these tests are in women whose mammogram indicates a lesion that probably is benign. Because these noninvasive tests are most likely to be used to evaluate such women, this is a major shortcoming of the current literature.
- A limitation of the available studies is the extremely high prevalence of breast cancer in the patients enrolled in them. This limitation reduces confidence that the results apply to all women who have suspicious mammograms.
- Analyses of benefits and harms using data from studies that enroll women more representative of the population of women who have suspicious mammograms would directly address the question of whether women benefit overall from being evaluated by noninvasive imaging methods.

Full Report

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