The term "evidence-based medicine" was first coined by Sackett and colleagues[1] as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients." The key to practicing evidence-based medicine is applying the best current knowledge to decisions for individual patients. Medical knowledge is continually and rapidly expanding and it is impossible for an individual clinician to read all the medical literature. For clinicians to practice evidence-based medicine, they must have the skills to read and interpret the medical literature so that they can determine the validity, reliability, credibility and utility of individual articles. These skills are known as critical appraisal skills. Generally, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis, and economics as well as clinical knowledge.

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsors a program entitled. "Evidence-Based Reviews in Surgery (EBRS)," supported by an educational grant from Ethicon Inc and Ethicon Endo Surgery Inc. The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. During the academic year, 8 clinical articles are chosen for review and discussion. They are selected not only for their clinical relevance to general surgeons but also because they cover a spectrum of issues important to surgeons; for example, causation or risk factors for disease, natural history or prognosis of disease, how to quantify disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodologic and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS website. A listserve discussion is held where participants can discuss the monthly article. Fellows and candidates of the College can access Evidence-Based Reviews in Surgery through the American College of Surgeons website (www.facs.org). All journal articles and reviews are available electronically through the website. Currently we have a library of 40 articles and reviews which can be accessed at any time. Each October a new set of articles are available each month until May. Surgeons who participate in the current (modules) packages can receive CME credits by completing a series of MCQ. For further information about EBRS go to the ACS website or email the administrator, Marg McKenzie at mmckenzie@mtsinai.on.ca.

In addition to making the reviews available through the ACS and CAGS websites, 4 of the reviews are published in condensed versions in the *Canadian Journal of Surgery* and the other four will be published in the *Journal of the American College of Surgeons* each year.

REFERENCE

1. Evidence Based Medicine Working Group. Evidence-based medicine. JAMA 1992;268:2420–2425.

SELECTED ARTICLE

Efficacy of MRI and Mammography for Breast-Cancer Screening in Women with Familial or Genetic Predisposition

Kriege M, Brekelmans CTM, Boetes C, et al. N Engl J Med 2004;351:427–437.

Reviewed by

Steve Latosinsky, MD, Geoffrey Porter, MD, Todd Tuttle, MD, for Members of the Evidence-Based Reviews in Surgery Group.

ABSTRACT

Question: In women with a familial or genetic predisposition for breast cancer is screening with MRI more effective than mammography or usual care?

Design: Prospective cohort study

Setting: Six familial cancer centers in the Netherlands

Patients: One thousand and nine women aged 25 to 75 years with a cumulative lifetime risk of breast cancer of 15% or more owing to a familial or genetic predisposition based on a modified Clasus model were included.

Description of Test and Diagnostic Standard: Two view mammography (oblique and craniocaudal views and if necessary, compression views or magnification) and dynamic breast MRI with gadolinium containing contrast medium using a standard protocol were performed yearly. Clinical breast examination was performed every 6 months. When possible, both imaging investigations were performed on the same day or same time period between day 5 & day 15

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of the menstrual cycle. The results of both investigations, which were blinded were scored in a standardized way, according the Breast Imaging Reporting and Data Systems (BI-RADS) Classification.

Main Outcomes Measure: Sensitivity and specificity of clinical examination, mammography and MRI.

Main Results: The sensitivity of clinical breast examination, mammography and MRI for detecting invasive breast cancer was 17.9%, 33.3% and 79.5% respectively and the specificity was 98.1%, 95.0% and 89.8% respectively.

Conclusion: MRI appears to be more sensitive than mammography in detecting tumors in females with a genetic or familial predisposition to breast cancer

Commentary: Although Kriege et al,[1] address two questions in this study, the focus of this review is the comparison of mammography to MRI in detecting breast cancers in women with a familial or genetic predisposition to breast cancer.

The study screened 1909 women who had a cumulative lifetime risk of breast cancer of ≥ 15% owing to a familial or genetic predisposition according to the modified tables of Claus and colleagues. Three hundred and fifty eight females were carriers of germ-line mutations (BRCA 1 or 2 carriers). Each woman had a clinical breast examination every six months and once a year standard two-view mammography and dynamic breast MRI with gadolinium were performed. Imaging was assessed independently. Median follow-up was 2.9 years. A total of 45 study eligible cancers were detected, largely in the germline mutation carriers. The authors concluded that MRI appeared to be more sensitive than mammography in detecting tumors in women with an inherited susceptibility to breast cancer.

The importance of the study is apparent because fewer than half of breast cancers in BRCA 1 and 2 mutation carriers are detected through conventional screening mammography programs. Cancers in these mutation carriers are identified more frequently in the interval between annual mammograms. This is likely attributable, at least partially, to the less optimal operating characteristics of mammography in the dense breast tissue of younger women. Moreover, up to 50% of patients will have positive lymph nodes when screening mammography is the only tool used in mutation carriers.

Table 1.

	Likelihood ratios			
	Mammography		MRI	
BI-RADS cutoff	Positive	Negative	Positive	Negative
5 Highly suspicious	undefined	0.93	137.5	0.87
4 Suspicious	84.0	0.76	43.7	0.54
0 Need additional imaging	34.4	0.67	18.0	0.37
3 Probably benign	8.0	0.63	7.0	0.32
2 Benign	4.1	0.62	3.8	0.33
1 Negative	1.0	undefined	1.0	undefined

There are several methodologic issues worth noting in this study. The rationale for including women with a lifetime risk of ≥ 15% was never provided. What percentage of women in the overall population might meet this criterion? Generalizability of the study is favourable given that patients came from 6 different centers, more than 80% of eligible women participated and a validated tool was utilized to identify patients with a cumulative lifetime risk of at least 15%, in addition to the patients with BRCA mutations. It is likely that participating centers had considerable breast imaging expertise.

Sensitivity and specificity are the more common test characteristics used to describe a diagnostic test. Memorizing how to set up a two by two table comparing a new diagnostic test to a gold standard is a valuable exercise because once set up properly, sensitivity, specificity, and positive and negative predictive values can all be derived with ease. These test characteristics were reported in the current study for different BI-RADS classifications (see Table 1 for categories) of mammographic and MRI images. If a probably benign or higher BI-RADS lesion is further investigated, the sensitivity of mammography would be 40%, while MRI would be 71.1%. The specificity of the two modalities at this cutoff would result in twice as many false positives in women being screened with MRI. Thus, for every 10 women tested with MRI one would require further investigation. The study is somewhat biased in favour of MRI because at the prevalence (initial) screen approximately 75% of women had had a previous mammogram in the past 2 years while very few had had a MRI. This accounts for the sensitivity of mammography being relatively consistent between first and subsequent screenings at 37.5% and 42.9% respectively, while the sensi-

tivity of MRI decreased from 79.2% with the initial screen to 61.9% at subsequent screenings.

Test characteristics at each of the BI-RADS cutoffs can also be presented graphically using a receiver operating curve as was provided by the authors. The x-axis is 1-specificity and the y-axis is sensitivity. The best cutoff is that which most closely approximates the perfect test of a sensitivity and specificity of 100% and thus has the greatest area under the curve. In this study the superiority of MRI can be ascertained from the greater area under the curve compared to mammography indicating fewer false positives and false negatives.

Likelihood ratios (LR) are reported less commonly, but have been purported to be more useful because the prevalence of the target disorder is considered.[2] A positive/negative LR expresses the odds that a given level of a diagnostic test result would be more likely/less likely in a patient with (as opposed to one without) the target disorder. Positive likelihood ratios [sensitivity / (1-specificity)] and negative likelihood ratios [(1-sensitivity) / specificity] for each test can be calculated from the information provided in the study and are presented Table 1. A rough guide to the interpretation of LRs is that: a LR greater than 10 or a LR less than 0.1 generates large and often conclusive changes in the post-test chance of a diagnosis. LRs between 2 and 5 or between 0.5 and 0.2 generate small, but sometimes important, changes in the chance of a diagnosis, and a LR between 1 and 2 or between 0.5 and 1.0 alters the post-test chance of the diagnosis only to a small degree.[3] Likelihood ratios in this study are useful for determining cut-off points where further investigations are indicated rather than for comparing the two tests.

Although this study demonstrates that MRI is superior to mammography in detecting breast cancer in these select women, this study does not address whether there is improved survival with early detection. Cancers could have already metastasized or non-lethal cancers may be being diagnosed.[4] In addition, this study does not address the cost of each additional breast cancer diagnosis. If the benefit:cost ratio with MRI is not cost saving, a value judgment must be made whether it is worth pursuing in terms of other opportunities (opportunity costs). Quality of life has also not been addressed. The negative effects of screening with MRI from more false positives may be more acceptable in these women than the average population because they are carriers or have affected family members. Although it may be impossible to randomize women with a known genetic mutation to a trial of screening with or without MRI, randomized controlled trials of patients defined in this paper as at high or moderate risk are needed to answer survival, cost-effectiveness, and quality of life questions before making screening MRI a standard of care.

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The Evidence-Based Reviews in Surgery Group comprises: