

Magnetic resonance imaging was more sensitive than mammography for detecting breast cancer in high-risk women

Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med*. 2004;351:427-37.

QUESTION

In women with a familial or genetic predisposition to breast cancer, what is the diagnostic accuracy of magnetic resonance imaging (MRI) compared with mammography for screening?

METHODS

Design: Blinded comparison of MRI and mammography for detecting breast cancer.

Setting: 6 familial cancer clinics in the Netherlands.

Patients: 1909 women who were 25 to 70 years of age (mean age 40 y) and had a cumulative lifetime risk for breast cancer $\geq 15\%$ because of familial or genetic predisposition. Women < 25 years of age could be tested if they had a family history of breast cancer diagnosed before 30 years of age. Exclusion criteria were symptoms suggestive of breast cancer or personal history of breast cancer. 358 of the women were confirmed carriers of BRCA1, BRCA 2, PTEN, or TP53 genetic mutations.

Description of tests: Mammography and a dynamic breast MRI with gadolinium-containing contrast medium were done annually. When one of the tests was scored as “probably benign” or “need additional imaging evaluation,” further investigation was done by ultrasonography (with or without fine-needle aspiration) or by repeating mammography or MRI. When one of the examinations was scored as “suspicious abnormality” or “highly suggestive of malignancy,” a cytologic or histologic evaluation of a biopsy specimen was done.

Diagnostic standard: Asymptomatic breast cancer confirmed by biopsy during follow-up of an abnormal mammogram or MRI, or symptomatic breast cancer diagnosed during the period between screenings. [Histologic examinations were blinded to MRI and mammography results.]*

Outcomes: Sensitivity and specificity for detecting breast cancer.

MAIN RESULTS

50 women had breast cancer during follow-up. The Table summarizes the results. The

Diagnostic performance of magnetic resonance imaging (MRI) and mammography for detecting breast cancer in high-risk women*

Test	Sensitivity (95% CI)	Specificity	+LR	-LR
Mammography	40% (33 to 49)	95%†	8.0	0.63
MRI	71% (65 to 73)	90%†	7.1	0.32

*Diagnostic terms defined in Glossary; LRs and CI calculated from data in article.

†Proportions not reported for calculating CI.

area under the receiver-operating characteristic curve was higher for MRI than for mammography (0.827 vs 0.686; mean difference 0.141, 95% CI 0.020 to 0.262).

CONCLUSION

In women with a genetic or familial predisposition to breast cancer, magnetic resonance imaging was more sensitive than mammography for detecting breast cancer.

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*Information provided by author.

COMMENTARY

Although mammography is effective for screening older women in the general population, it has limited sensitivity, especially in younger women with dense breasts who are a key target of high-risk screening (e.g., BRCA1/2 carriers). Sensitivities range from 62% among women with extremely dense breasts to 88% among women with almost entirely fatty breasts (1). Several studies have shown the superior sensitivity of breast MRI to mammography in different settings, including the screening of high-risk women (2). A December 2003 technology assessment supported by managed care groups concluded that adequate evidence existed to support routine use of MRI for screening women who had or were thought to have a BRCA mutation (3).

The well-designed and appropriately analyzed study by Kriege and colleagues substantially supports this conclusion and goes further by showing a clinically and statistically significant stage shift in the cases of cancer identified. MRI substantially outperformed mammography in sensitivity and showed specificity similar to mammography in general screening of older women (1). Given the limited alternatives to MRI and mammography screening for very high-risk women (prophylactic mastectomy and chemoprevention), waiting for a randomized trial to prove mortality reduction before implementing selective MRI screening is unethical.

Currently, MRI for breast cancer screening should be done only at centers with adequate interest, expertise, and volume to assure high quality and replication of the test performance characteristics in published studies. For the time being, screening with MRI should also probably be limited to women with BRCA1 and BRCA2 or clear evidence of similarly very high genetic risk because such women are at high risk at a young age, when mammography alone is clearly ineffective. The ideal approach may be to combine annual MRI with mammography using a follow-up protocol similar to that of Kriege and colleagues, which impressively limited false-positive results and invasive follow-up procedures.

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References

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