

Should I be tested for breast cancer genes?

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News reports of medical advances in genetics are appearing in the lay press almost daily. These reports, coupled with women's fear of breast cancer, mean that more women are asking about screening for mutations in the breast cancer susceptibility genes *BRCA1* and *BRCA2*.

When to screen

Ordinarily, the *BRCA* genes produce proteins that prevent abnormal growth within cells. When certain mutations are present, however, the risk that breast and ovarian cancers will develop increases by 60% to 85% and by 10% to 26%, respectively.¹ Current estimates indicate that *BRCA* mutations affect approximately 1 in every 300 to 500 persons.¹

Although 20% to 30% of patients with breast cancer have a positive family history for the disease, genetic abnormalities account for only 5% to 10%²—and *BRCA* mutations for 2% to 3%³—of all breast cancers. Given this background, universal screening for mutations in *BRCA1* or *BRCA2* cannot be justified. The US Preventive Services Task Force (USPSTF) has confirmed this.⁴ However, the USPSTF did say there was fair evidence to support genetic testing for women whose family history suggests a mutation in *BRCA1* or *BRCA2*.⁴

A woman may be at risk for a *BRCA* mutation if she has biological family members with any of the following: breast cancer diagnosed before age 50 years; bilateral breast cancer; breast cancer in a male; recurrent breast cancer with a different tumor type; breast cancer associated with ovarian cancer; both ovarian and breast cancer; multiple cases of breast or ovarian cancer; breast or ovarian cancer in a first-degree or second-degree relative of Ashkenazi Jewish heritage.

Components of genetic counseling

There are technologic, medical, emotional, and social issues that must be explored before a woman undergoes testing. Testing, even by DNA sequencing, is not absolutely reliable. The incidence of false-positive results is approximately 13%, and false-negative results range from 12% to 15%.¹ Not all women with mutations in *BRCA1* or *BRCA2* develop cancer, and there is no way to identify which patients will. Furthermore, there are no data to indicate that testing reduces morbidity or mortality.¹ Positive results on genetic testing may lead to a

number of undesirable consequences, including additional interventions. Negative results on genetic testing can reduce a woman's anxiety. However, she can still acquire breast cancer.

Options for women with a mutation

The recommendations presented here are based on meta-analysis, data extracted from secondary analysis of studied populations, and observational studies, not on clinical trials.

Surgery Prophylactic bilateral mastectomy appears to be associated with an 85% to 100% reduction in the incidence of breast cancer.³ Prophylactic bilateral oophorectomy appears to decrease the incidence of ovarian cancer by 85% to 100% and that of breast cancer by 53% to 68%.³

Chemoprevention Tamoxifen or raloxifene decreases the risk of primary and secondary breast cancers in women with a family history of breast cancer that is estrogen-receptor-positive. However, these drugs may increase the risk of other diseases, and women interested in chemoprevention should be referred to appropriate ongoing clinical trials for treatment.⁵

Increased surveillance Evaluation must occur more frequently than annually because of the aggressive nature of carcinomas associated with *BRCA* mutations; MRI has the greatest sensitivity (approximately 77%), followed by mammography (36%), breast ultrasonography (33%), and clinical breast examination (9%), in detecting cancers in women with *BRCA* gene mutations. The combination of MRI, mammography, and ultrasonography has a sensitivity of 95%.³

Bottom line

Genetic counseling and *BRCA* gene mutation testing should be offered to all women at risk for this genetic defect. □

For information that can be photocopied and handed to patients, please see page 62.

REFERENCES

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