Mastectomy or Breast-Conserving Therapy for BRCA1/2 Variant Carriers

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Wan et al have retrospectively reviewed 8396 patients with stage I or II breast cancer, 491 with a known BRCA1 (OMIM 113705) or BRCA2 (OMIM 600185) variant, and compared the survival rate among patients undergoing breast-conserving therapy (BCT) with the survival rate among patients undergoing mastectomy, for variant carriers vs noncarriers. From NSABP B-06, EORTC 10801, and other studies, we know that BCT with radiotherapy offers overall survival similar to mastectomy.2,3 Recently, studies have shown that BCT with radiotherapy may be associated with improved survival compared with mastectomy.4 What about survival after BCT among women with a BRCA1/2 germline variant? These women are at increased risk of developing a second primary breast cancer in the same or contralateral breast.5 Wan et al found that, after 7.5 years of follow-up, BRCA1/2 variant carriers treated with BCT had no better survival than those treated with mastectomy (overall survival: hazard ratio [HR] for BRCA1, 0.61 [95% CI, 0.18-2.12]; \( P = .44 \); HR for BRCA2, 0.72 [95% CI, 0.26-1.96]; \( P = .52 \)) or mastectomy (overall survival: HR for BRCA1, 0.77 [95% CI, 0.27-2.21]; \( P = .63 \); HR for BRCA2, 0.62 [95% CI, 0.22-1.73]; \( P = .37 \)). They concluded that BRCA1/2 variant carriers treated with BCT have a survival comparable to those treated with mastectomy. To our knowledge, this is one of the largest studies to date on this topic.

The surgical treatment of patients with a genetic germline variant is complicated. In the study by Wan et al,1 conducted in China, patients and their physicians were unaware of their BRCA1/2 variant status. This is not the case in the United States, where most multidisciplinary clinics try to test patients with a suspicious family history of breast and/or ovarian cancer or women who meet National Comprehensive Cancer Network guidelines prior to undergoing surgery. Patients then are armed with the information about the implications that their genetic variant status has on subsequent risk of developing a second cancer in the future. This information can be used by patients who tend to choose bilateral mastectomy.6 However, the information provided by Wan and colleagues1 may help inform patients with BRCA1/2 variants that BCT offers survival comparable to mastectomy.

The other important issue in surgical decision-making for BRCA1/2 carriers is the contralateral breast. Patients with these variants have an increased risk of developing contralateral breast cancer, and mastectomy serves as a strong means to reduce that risk. Wan et al found that the rates of contralateral breast cancer were higher among BRCA1/2 carriers than among noncarriers. They concluded that the increased risk of contralateral breast cancer may outweigh the benefits of breast conservation. This factor is at the heart of the conversation with BRCA1/2 variant carriers. If a patient decides to undergo BCT for their cancer, we would still have to closely screen patients, with mammograms alternating with breast magnetic resonance imaging every 6 months to catch cancer at an early stage, whereas if a patient decides to undergo bilateral mastectomy, this intense screening, which can become emotionally and financially draining for patients, is not needed.

This study by Wan et al1 is a large retrospective study examining outcomes and survival among BRCA1/2 carriers addressing surgical approach and survival. The study adds much to our knowledge about treatment regimens for patients. However, surgical choice is a complex decision-making process that the patient and the physician are best to approach in a collaborative way, involving much thought and conversation.
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REFERENCES


