Ann Surg Oncol
DOI 10.1245/s10434-012-2255-0

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

Managing Patients at High Risk for Hereditary Breast Cancer: A Guide for the Practicing Physician

James C. Cusack Jr., MD and Kevin S. Hughes, MD

Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Breast cancer is a major public health problem worldwide and affects as many as one in seven women in Western countries. Of the 5–10% of breast cancers that follow a Mendelian inheritance pattern, 30% of these are due to *BRCA1* or *BRCA2* germ-line mutations. The principal objective of breast cancer risk assessment is to identify the carriers of the *BRCA* gene mutation, ideally before they develop breast cancer. When combined, familial and hereditary breast cancer comprise over 25% of breast cancers; fortunately the skills required to perform the initial breast cancer risk assessment are as basic as taking a thorough family history and conducting a complete physical examination. Determining the actual risk of an individual patient can be perceived as time-consuming and cumbersome, and is therefore often omitted in the busy clinic setting. The challenges for care providers who are responsible for assessing breast cancer risk can be ascribed in part to the lack of standardized tools for managing extensive family histories and calculating risk, the reluctance to utilize web-based risk assessment instruments, and the requirement in some cases of information systems (IS) support to operate these web-based instruments. As a result, the primary role of care providers and surgeons is often reduced to the rudimentary identification of patients who may be at high risk for developing hereditary breast cancer, followed by the referral of those patients for genetic counseling and possible DNA testing.

Most importantly, the care providers' role in identifying patients who may be at risk is the first step in the risk assessment process. For the surgical oncologist accurate assessment and management of breast cancer risk are critical components of the initial clinical evaluation that may lead to potentially life-saving interventions. To assess and manage breast cancer risk well, the surgical oncologist must understand the uses and limitations of risk assessment tools, clearly communicate the results of the risk assessment to patients and relatives, and effectively incorporate the results into a long-term management strategy that is acceptable to the patient.

We strongly believe that it is critical to identify carriers of *BRCA1* and *BRCA2* mutations before they develop cancer in order to prevent cancer or to find it at an earlier more treatable stage. Multiple guidelines exist as to who is eligible for testing and the reader is referred to those guidelines for more complete information [1–4]. Risk factors for hereditary breast cancer obtained from a family history include: (1) relatives with breast or ovarian cancer diagnosed at a young age (under age 45); (2) multiple primary cancers in a single individual (bilateral breast or breast plus ovarian cancer); (3) early onset of breast cancer (diagnosed before age 50) and (4) family history of male breast cancer. Patients with any one of these risk factors should be considered for genetic counseling and genetic

Acknowledgment: This educational review series, "Risk Assessment and Genetic Testing for Hereditary Breast Cancer," is supported by an educational grant from Myriad Genetics.

Annals of Surgical Oncology educational reviews represent the journal's commitment to the peer review and publication of high quality research necessary to define the safety, toxicity, or effectiveness of potential therapeutic agents compared with conventional alternatives.

This Educational Review Series may include information regarding the use of medications that may be outside the approved labeling for these products. Physicians should consult the current prescribing information for these products. Authors of *Annals of Surgical Oncology* educational reviews are provided at the time of article solicitation with this statement regarding off-label pharmaceutical information and research.

J. C. Cusack Jr., MD
e-mail: jcusack@partners.org

Published online: 13 March 2012

testing. Additional examples of patients who should be further evaluated for hereditary breast cancer include those with two primary breast cancers, a relative diagnosed with any of the following—breast cancer at an early age, ovarian cancer, or male breast cancer. In addition, any patient with a family history of a *BRCA* mutation should be considered for further evaluation. In Jewish individuals, the threshold for further testing should be lower. Testing may be performed in the office or referrals can be made to a genetics specialist.

In this issue of *Annals of Surgical Oncology,* a series of review articles have been solicited that focus on the assessment and management of hereditary breast cancer risk. In the first article, the authors describe the wide range of implications that follow the identification of an inherited DNA mutation associated with breast cancer [5]. In addition to the obvious higher risk of developing breast and other types of malignancy such as ovarian cancer in carriers of these mutations, there is also the increased risk of developing cancer in other related carriers. The diagnosis of hereditary breast cancer not only confers the need for increased screening and prevention strategies but also informs treatment decisions such as chemotherapy selection. Without an appreciation of the relatively high incidence of hereditary breast cancer and effective strategies for assessing the risk of developing hereditary cancer, unidentified carriers of these diseases will not benefit. In the second article, the authors review different models and Web-based tools that have been developed and made available to care providers to assess individual patient risk for developing hereditary breast cancer [6]. The ultimate objective of risk assessment is to identify those individuals who may benefit from genetic counseling and DNA testing. In the third article, the author addresses the surgical management options for *BRCA* gene mutation carriers as well as the treatment options for those *BRCA* gene mutation carriers diagnosed with breast cancer [7].

In summary, it is our hope that you will find this series of articles to be a useful resource for the management of patients at risk for hereditary breast cancer and a practical guide to some of the information systems available for assessing at-risk patients.

Author disclosures: Dr. Hughes gives educational lectures for Myriad Genetics, and is one of the originators of HughesRiskApps, a freeware software package that evaluates risk and may eventually generate modest revenues. Dr. Cusack has nothing to disclose.

REFERENCES

1. Robson ME, Storm CD, Weitzel J, Wollins DS, Offit K. American Society of Clinical Oncology policy statement update: genetic and genomic testing for cancer susceptibility. *J Clin Oncol*. 2010; 29:893–901.
2. The American Society of Breast Surgeons. Position statement on BRCA genetic testing for patients with and without breast cancer. 2006. https://www.breastsurgeons.org/statements/PDF_Statements/BRCA_Testing.pdf. Accessed February 27, 2012.
3. Lancaster JM, Powell CB, Kauff ND, Cass I, Chen L-M, Lu KH, Mutch DG, Berchuck A, Karlan BY, Herzog TJ. Society of Gynecologic Oncologists Education Committee statement on risk assessment for inherited gynecologic cancer predispositions. *Gyn Oncol*. 2007;107:159–62.
4. Klimberg VS, Galandiuk S, Singletary ES, Cohen A, Sener S, Talamonti MS, Witt TR, Niederhuber JE, Edwards MJ. Society of Surgical Oncology: statement on genetic testing for cancer susceptibility. *Ann Surg Oncol*. 1999;6:507–9.
5. Lynch HT, Snyder C, Lynch J. Hereditary breast cancer: practical pursuit for clinical translation. *Ann Surg Oncol.* 2012. doi: 10.1245/s10434-012-2256-z.
6. Drohan B, Roche CA, Cusack JC, Hughes KS. Hereditary breast and ovarian cancer and other hereditary syndromes: using technology to identify carriers. *Ann Surg Oncol.* 2012. doi:10.1245/s10434-012-2257-y.
7. Euhus D. Managing the breast in patients who test positive for hereditary breast cancer. *Ann Surg Oncol.* 2012. doi:10.1245/s10434-012-2258-x.