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WOMEN'S HEALTH CARE PHYSICIANS

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The Society of Gynecologic Oncology endorses this document. This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice in collaboration with committee member Catherine Witkop, MD, MPH.

Cascade Testing: Testing Women for Known Hereditary Genetic Mutations Associated With Cancer

ABSTRACT: "Cascade testing" refers to the performance of genetic counseling and testing in blood relatives of individuals who have been identified with specific genetic mutations. Testing protocols and other interventions may save lives and improve health and quality of life for these family members. Obstetrician–gynecologists should know who is eligible for cascade testing and should use all available resources to ensure that cascade testing is offered and occurs in a timely manner. Despite the clear health benefits for specific populations and individuals, obstetrician–gynecologists should be aware of the potential barriers to cascade testing and should know which options can help patients overcome those barriers. Such barriers, however, may be overcome with health care provider awareness and participation in local and state initiatives to improve implementation of cascade testing. Resources (available within federal and state agencies, professional societies, and in advocacy and community groups) are critical to the successful implementation of cascade testing. This Committee Opinion focuses specifically on cascade testing and the role of the obstetrician–gynecologist in clinical and public health efforts to increase identification of women with hereditary cancer syndromes.

Recommendations and Conclusions

The American College of Obstetricians and Gynecologists makes the following recommendations and conclusions regarding genetic cascade testing for hereditary gynecologic cancer:

- Cascade testing refers to the performance of genetic counseling and testing in blood relatives of individuals who have been identified with specific genetic mutations. Testing protocols and interventions may save lives and improve health and quality of life for these family members.
- Cascade testing has been shown to be cost effective in part because testing for specific mutations (eg, those identified in the affected relative) is less expensive than whole-gene sequencing.
- Obstetrician–gynecologists should know who is eligible for cascade testing and should use all available resources to ensure that cascade testing is offered and occurs in a timely manner.
- Obstetrician–gynecologists should be aware of the potential barriers to cascade testing and should know which options can help patients overcome those barriers.
- Obstetrician–gynecologists should understand and participate in public health efforts to increase cascade testing for hereditary gynecologic cancer.

Case Study

Your patient tells you, her obstetrician–gynecologist, that her sister recently has been treated for ovarian cancer and gives you a letter (see Box 1) with specific information about the BRCA1 *mutation identified in her sister. Your patient asks you whether she should be tested. You explain to your patient that if she is tested for* BRCA1 *and the result is positive, she can be offered enhanced screening, prophylactic surgery, or other interventions that may help prevent cancer or identify cancer at an early stage. If the test result is negative, you explain that her risk of ovarian cancer in the future returns to the baseline risk for all*

women of her age and risk factors. You discuss at length the risks and benefits of completing the test, and your patient tells you she would like to have the test completed. You order the test and ask her to schedule a follow-up visit with you when the test result is available.

Box 1. Example of a Letter Given to a Potentially Affected Family Member

Dear Family Member:

This letter is to inform you that a member of your family, _____, has tested positive for a *BRCA1* gene mutation, _____. This gene is associated with hereditary breast and ovarian cancer syndrome.

Approximately 10% of cases of breast cancer and 20% of cases ovarian cancer are due to a specific inherited genetic alteration. Having an altered gene does not mean that you definitely will develop breast or ovarian cancer, but it does increase your risk. Women with an altered *BRCA1* gene have up to an 87% lifetime risk of breast cancer and a 27–44% lifetime risk of ovarian cancer. Men with an altered gene have an increased risk of prostate cancer, breast cancer, and other types of cancer, which tend to occur at a young age. Early detection and prevention is important.

Depending on your family structure, you may have as high as a 50% chance of also having inherited this alteration in the gene. This gene is passed to males and females. Both males and females have risks of cancer if they inherit the alteration, and they can each pass the gene to their sons and daughters.

You may want to talk with your personal physician or a genetic counselor about being evaluated for your risk of having inherited this genetic mutation and your risk of developing related types of cancer. The cost of testing for this mutation ranges from $200 to $500, and most insurance companies cover the cost. I would be happy to discuss this information further with you on the telephone. You can reach me at_____.

Adapted with permission from The Cancer Genetics Department, the University of Texas Southwestern Medical Center.

Introduction

Cascade testing refers to the performance of genetic counseling and testing in blood relatives of individuals who have been identified with specific genetic mutations. Testing protocols and interventions may save lives and improve health and quality of life for these family members. This process also may be referred to as "cascade screening" because the individuals being tested are not known to have the disease. The term cascade testing will be used throughout this document for consistency. Typically, a patient for whom cascade testing may be appropriate presents with a letter from another health care provider (eg, a genetic counselor or oncologist) with information regarding a specific mutation identified in a relative. Specific genetic testing may then be offered to the patient based on the exact mutation identified in the blood relative. Cascade testing may include screening, counseling, or referral for a patient with a relative who has had a positive genetic test result. Screening, counseling, or referral for patients with a family history or diagnosis of cancer, but whose affected relatives have not undergone genetic testing, is not considered cascade testing.

Genetic testing for hereditary gynecologic cancer is expected to increase because of a corresponding increase in evidence-based guidance from multiple professional societies that recommend genetic assessment of women with certain types of gynecologic cancer or risk factors for those types of cancer. Obstetrician–gynecologists should know who is eligible for cascade testing and should use all available resources to ensure that cascade testing is offered and occurs in a timely manner. Limited access to genetic counseling services, as well as perceived and real insurance coverage issues, may prevent timely completion of cascade testing. Quality care requires current knowledge of and the ability to access available resources. This Committee Opinion will focus specifically on cascade testing and the role of the obstetrician–gynecologist in clinical and public health efforts to increase identification of women with hereditary cancer syndromes.

Background

Obstetrician–gynecologists play a critical role in identifying women with hereditary cancer syndromes, particularly those that include gynecologic cancer. Cascade testing has been shown to be cost effective in part because testing for specific mutations (eg, those identified in the affected relative) is less expensive than whole-gene sequencing (1). Increasing numbers of patients with ovarian, breast, endometrial, and colon cancer are now being identified as also having certain genetic mutations. These mutations include the well-known *BRCA1* and *BRCA2* mutations most commonly associated with hereditary breast and ovarian cancer syndrome, as well as mutations in one or more DNA mismatch repair genes (*MLH1, MSH2, MSH6, PMS2*, or *EpCAM* deletions) in Lynch syndrome, a highly penetrant, autosomal dominant condition with an increased risk of endometrial, ovarian, and colon cancer (2–4). Several other gene mutations are associated with an increased risk of additional hereditary cancer syndromes. In addition to the American College of Obstetricians and Gynecologists, other professional organizations, including the Society of Gynecologic Oncology and the American College of Medical Genetics and Genomics, have published detailed guidelines on risk assessment for gynecologic cancer predisposition (5, 6). Current information also is available from the National Comprehensive Cancer Network (http://www.nccn.org/professionals/physician_gls/f_guidelines.asp).

Clinical Considerations and Management

To initiate cascade testing, the obstetrician–gynecologist must have a letter or documentation stating that the patient's relative has a specific genetic mutation. Some obstetrician–gynecologists are fully trained and qualified to counsel patients regarding genetic issues and to order genetic testing. If an obstetrician–gynecologist or other health care provider does not have the necessary knowledge or expertise in genetics to counsel a patient appropriately, referral to a genetic counselor, medical or gynecologic oncologist, or other genetics specialist should be considered. The specifically indicated test should be ordered only after the patient has been counseled about potential outcomes and has expressly decided to be tested. After the result is obtained and posttest counseling is completed (7), testing and preventive services can be recommended to the patient, as indicated. Although the ethical issues surrounding disclosure of test results to family members is complex, tested patients generally should be informed that they have a duty to notify relatives of the familial risk. It is neither required nor appropriate for an obstetrician–gynecologist or other health care provider to contact and notify at-risk family members because sharing that information may violate the Health Insurance Portability and Accountability Act (HIPAA), or state laws, or both. For more information on counseling, see Committee Opinion No. 693, *Counseling About Genetic Testing and Communication of Genetic Test Results* (7).

Obstetrician–gynecologists should understand and participate in public health efforts to increase cascade testing for hereditary gynecologic cancer. The Centers for Disease Control and Prevention (CDC) has highlighted hereditary breast and ovarian cancer syndrome and Lynch syndrome as high priority syndromes for cascade testing (the CDC uses the term "cascade screening"). The efforts of the CDC's Office of Public Health Genomics align with other initiatives and evidence-based recommendations aimed at increasing the identification of women with hereditary cancer syndromes. The *Tier 1 Genomic Applications Toolkit for Public Health Departments* describes model approaches developed by state programs to implement public health genomics. (www.cdc.gov/genomics/implementation/toolkit/index.htm.)

Obstetrician–gynecologists should be aware of ongoing efforts in their states, including educational programs for patients, families, and health care providers; attempts to increase access to genetic counseling; bidirectional cancer registries (in which information and guidance are sent back to the institution that originally reported the data); and surveillance systems used to track Tier 1 recommendations. Policies that support increased access to and reimbursement for indicated genetic testing also have the potential to increase the use of cascade testing and, thereby, increase identification of women at risk of heritable gynecologic cancer at a population level. Additionally, enhanced access to screening allows relatives of tested patients that lack the identified mutation to avoid potentially unnecessary further enhanced screening, medications, and surgery.

Despite the clear health benefits for specific populations and individuals, obstetrician–gynecologists should be aware of the potential barriers to cascade testing and should know which options can help patients overcome those barriers. Genetic testing is not always completed for the index patient (the first patient in the family diagnosed with the cancer resulting from the specific mutation). Even if tested, the index patient may not be emotionally or physically able to process the information or present it to his or her family members. Logistical challenges (eg, if the index patient is estranged or geographically separated from family members) also may result in lack of communication with family members by the index patient. Potential solutions regarding correspondence with family members include the use of standardized tools, such as templates for patient and health care provider letters. Finally, a lack of reimbursement by Medicare, Medicaid, and third-party payers could present barriers to genetic risk assessment or follow-up management. There are additional resources, such as advocacy groups, to assist the index patients and their relatives (see For More Information). The American College of Obstetricians and Gynecologists supports coverage for appropriate counseling, genetic testing, and follow-up care.

Conclusions

Obstetrician–gynecologists should be aware of the importance of cascade testing for hereditary gynecologic cancer. There are currently many barriers to the successful completion of cascade testing. Such barriers, however, may be overcome with health care provider awareness and participation in local and state initiatives to improve implementation of cascade testing. Resources (available within federal and state agencies, professional societies, and in advocacy and community groups) are critical to the successful implementation of cascade testing.

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at https://www.acog.org/About-ACOG/ACOG-Departments/Genetics.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's website, or the content of the resource. The resources may change without notice.

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