COMMITTEE OPINION

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Committee on Genetics

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Personalized Genomic Testing for Disease Risk

ABSTRACT: Advances in genetic technologies have led to the identification of hundreds of single nucleotide polymorphisms (SNPs) that are associated with a variety of complex diseases, including cancer, diabetes, cardiovascular disease, and Alzheimer disease. Although personalized genomic tests that provide information regarding the risk of development of multiple diseases may be important tools in the near future, their use is not recommended outside of a clinical trial until these tests are validated as clinically useful in appropriately designed prospective studies. Testing for single-gene disorders should be approached in accordance with accepted guidelines that address the evaluation and management of these specific diseases.

Since the completion of the sequencing of the human genome in 2001, advances in genetic technologies have led to the identification of hundreds of single nucleotide polymorphisms (SNPs) that are associated with a variety of complex diseases, including cancer, diabetes, cardiovascular disease, and Alzheimer disease. Single nucleotide polymorphisms are sequence variations of DNA that occur when a single nucleotide in the genome sequence differs between individuals. Although a few disease-associated SNPs have been associated with a relatively large (greater than a threefold to fivefold) increase in the risk of disease, most SNPs are associated with relatively small (less than twofold) changes in the underlying disease risk. Furthermore, very few SNP disease associations have undergone rigorous prospective validation of clinical utility. Regardless, a number of companies and other entities now offer personalized genomic profile testing that involves the use of panels of SNPs to provide individual risk assessment for a variety of diseases. Some of these entities offer genomic profile testing through general practice physicians in consultation with genetic counselors. Others state that the results of this testing are for informational (nonmedical) purposes only and offer testing directly to consumers.

Given that the number and availability of these tests is almost certain to increase in the near future, the Committee on Genetics of the American College of Obstetricians and Gynecologists (the College) believes that several issues related to the use of personalized genomic tests for disease risk assessment should be addressed.

Despite the proliferation of individuals and groups offering genomic testing for disease-associated SNPs and the steadily increasing number of diseases and conditions for which testing is performed, there remains a paucity of evidence that more than a few of these SNPs, either alone, in panels, or in combination with other clinical information, provide meaningful data regarding the risk of inherited disease (1). Although many disease-associated SNPs included in genomic risk profiles have been identified in the setting of whole-genome association studies that analyze specimens from thousands of participants, few have been validated in prospective studies as being clinically useful (1). Given the predominantly retrospective nature of the studies used to identify disease-associated SNPs, many of the emerging genetic technologies used to identify such SNPs may ultimately have the power to transform the practice of medicine. However, the College’s Committee on Genetics believes that the use of these technologies should be viewed as investigational at this time. Until research is performed to assess prospectively the validity and utility of incorporating disease-associated SNPs into specific risk prediction models, the use of SNPs outside of a research protocol is not recommended.

In addition to identifying disease-associated SNPs, some genomic tests now include tests for genetic changes associated with an individual’s carrier status or risk of specific mendelian (single-gene) diseases, such as cystic fibrosis, spinal muscular atrophy, and hereditary breast and ovarian cancer. However, genetic tests for many of these diseases have specific limitations and frequently
require careful interpretation. Challenges that can arise include the need to determine the residual risk of being a carrier when the screening does not identify a particular mutation and the need to assess the risk of developing a particular disease despite a negative genetic test result. Given these potential issues, genetic testing for mendelian diseases should be approached in accordance with accepted guidelines, such as those provided by the College (www.acog.org) and the American College of Medical Genetics (www.acmg.net). When a patient presents results of a genomic test that putatively assesses the risk of specific diseases, this patient should be referred to an appropriate medical professional who is skilled in risk assessment for the diseases of interest and interpretation of genetic testing results along with the individual’s relevant medical and family history.

Another area of concern is the offering of personalized genomic tests for disease risk assessment directly to consumers. This practice raises the same fundamental issues and considerations related to direct-to-consumer marketing of genetic testing. The College’s Committee Opinion No. 409, which specifically addresses this topic, states that direct-to-consumer marketing of genetic testing raises issues of “limited knowledge among patients and health care providers of available genetic tests, difficulty in interpretation of genetic testing results, lack of federal oversight of companies offering genetic testing, and issues of privacy and confidentiality” (2). Therefore, the College’s Committee on Genetics reaffirms the conclusion stated in the Committee Opinion: “Until all of these considerations are addressed, direct and home genetic testing should be discouraged because of the potential harm of a misinterpreted or inaccurate result” (2).

Recommendations
The College’s Committee on Genetics presents the following recommendations regarding personalized genomic testing for disease risk:

- Although personalized genomic tests that provide information regarding the risk of development of multiple diseases may be important tools in the near future, their use is not recommended outside of a clinical trial until these tests are validated as clinically useful in appropriately designed prospective studies.

- When a patient presents results of a genomic test that putatively assesses the risk of specific diseases, this patient should be referred to an appropriate medical professional who is skilled in risk assessment for the diseases of interest and interpretation of genetic testing results along with the individual’s relevant medical and family history.

- Testing for single-gene disorders should be approached in accordance with accepted guidelines that address the evaluation and management of these specific diseases.

Resource

References