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Study Examines Diagnostic Accuracy of Pathologists Interpreting Breast Biopsies

In a study in which pathologists provided diagnostic interpretation of breast biopsy slides, overall agreement between the individual pathologists' interpretations and that of an expert consensus panel was 75 percent, with the highest level of concordance for invasive breast cancer and lower levels of concordance for ductal carcinoma in situ and atypical hyperplasia, according to a study in the March 17 issue of *JAMA*.

Approximately 1.6 million women in the United States have breast biopsies each year. The accuracy of pathologists' diagnoses is an important and inadequately studied area. Although nearly one-quarter of biopsies demonstrate invasive breast cancer, the majority are categorized by pathologists according to a diagnostic spectrum ranging from benign to pre-invasive disease. Breast lesions with atypia or ductal carcinoma in situ (DCIS; abnormal breast cells that have not spread outside the duct into the normal surrounding breast tissue) are associated with significantly higher risks of subsequent invasive carcinoma, and women with these findings may require additional surveillance, prevention, or treatment to reduce their risks. The incidence of atypical ductal hyperplasia (atypia; a benign lesion of the breast that indicates an increased risk of breast cancer) and DCIS breast lesions has increased over the past 3 decades as a result of widespread mammography screening. Misclassification of breast lesions may contribute to either overtreatment or undertreatment, according to background information in the article.

Joann G. Elmore, M.D., M.P.H., of the University of Washington, Seattle, and colleagues examined the extent of diagnostic disagreement among pathologists compared with a consensus panel reference diagnosis. The study included 115 pathologists who interpret breast biopsies in clinical practices in 8 U.S. states. Participants independently interpreted slides between November 2011 and May 2014 from test sets of 60 breast biopsies (240 total cases, 1 slide per case), including 23 cases of invasive breast cancer, 73 DCIS, 72 with atypical hyperplasia (atypia), and 72 benign cases without atypia. Participants were blinded to the interpretations of other study pathologists and the three consensus panel members, who were experienced pathologists internationally recognized for research and continuing medical education

on diagnostic breast pathology. Among the consensus panel members, unanimous agreement of their independent diagnoses was 75 percent, and concordance with the consensus-derived reference diagnoses was 90 percent.

For all the cases, the participants provided 6,900 total individual interpretations for comparison with the consensus-derived reference diagnoses. Participating pathologists agreed with the consensus panel diagnosis for 75 percent of the interpretations. The overall concordance rate for the invasive breast cancer cases was 96 percent. The participants agreed with the consensus-derived reference diagnosis on less than half of the atypia cases, with a concordance rate of 48 percent. The overall concordance rate for benign without atypia was 87 percent; for DCIS, it was 84 percent.

Although overinterpretation of DCIS as invasive carcinoma occurred in only 3 percent, overinterpretation of atypia was noted in 17 percent and overinterpretation of benign without atypia was noted in 13 percent. Underinterpretation of invasive breast cancer was noted in 4 percent, whereas underinterpretation of DCIS was noted in 13 percent and underinterpretation of atypia was noted in 35 percent.

Disagreement with the consensus-derived reference diagnosis was significantly more frequent when breast biopsies were interpreted by pathologists with lower weekly case volume, from non-academic settings, or smaller practices; and from women with dense breast tissue on mammography (vs low density), although the absolute differences in rates according to these factors were generally small.

“The variability of pathology interpretations is relevant to concerns about overdiagnosis of atypia and DCIS. When a biopsy is overinterpreted (e.g., interpreted as DCIS by a pathologist when the consensus-derived reference diagnosis is atypia), a woman may undergo unnecessary surgery, radiation, or hormonal therapy. In addition, overinterpretation of atypia in a biopsy with otherwise benign findings can result in unnecessary heightened surveillance, clinical intervention, costs, and anxiety,” the researchers write.

“Given our findings, clinicians and patients may want to obtain a formal second opinion for breast atypia prior to initiating more intensive surveillance or risk reduction using chemoprevention or surgery.”

The authors conclude that further research is needed to understand the relationship of these findings with patient management.

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Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Expertise vs Evidence in Assessment of Breast Biopsies - An Atypical Science

“An undesirable short-term outcome from the study by Elmore et al will undoubtedly be heightened anxiety among women who undergo breast biopsy and concern among their physicians about the accuracy of the pathologic diagnosis,” write Nancy E. Davidson, M.D., of the University of Pittsburgh Cancer Institute and UPMC CancerCenter, Pittsburgh, and David L. Rimm, M.D., Ph.D., of the Yale University School of Medicine, New Haven, Conn., in an accompanying editorial.

“However, this study confirms that the majority of diagnoses, especially at either end of the spectrum from benign to invasive cancer, are readily and accurately made by practicing pathologists. It also identifies areas of uncertainty that must be addressed, providing a framework for process improvement in the pathology and scientific communities, especially in the diagnosis of atypia. The study supports the value of a second opinion in cases of ambiguity. Indeed, it is axiomatic [unquestionable] that an abnormal breast biopsy is certainly a cause for concern but does not constitute a medical emergency. Extra time and care devoted to confirmation of the histologic diagnosis and a thoughtful discussion of the treatment options are imperative.”

“Importantly, breast pathology is a biological continuum from normal to invasive cancer whereas prescription of treatment requires categorization into specific diagnoses. The goal should be to match emerging biological understanding about breast carcinogenesis with opportunities for tailored treatment in an era of ever more precise, evidence-based medicine.”

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