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Breast Cancer Risk by the Extent and Type of Atypical Hyperplasia

Amy C. Degnim, MD,
Division of Subspecialty General Surgery, Mayo Clinic, Rochester, Minnesota

Daniel W. Visscher, MD,
Division of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota

Derek C. Radisky, PhD,
Cancer Biology, Mayo Clinic, Jacksonville, Florida

Marlene H. Frost, PhD,
Division of Medical Oncology, Mayo Clinic, Rochester, Minnesota

Robert A. Vierkant, MAS,
Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, Minnesota

Ryan D. Frank, MS,
Division of Biomedical Statistics and Informatics, Mayo Clinic, Jacksonville, Florida

Stacey J. Winham, PhD,
Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, Minnesota

Celine M. Vachon, PhD,
Division of Epidemiology, Mayo Clinic, Rochester, Minnesota

William D. Dupont, PhD, and
Department of Biostatistics, Vanderbilt University, Nashville, Tennessee

Lynn C. Hartmann, MD
Division of Medical Oncology, Mayo Clinic, Rochester, Minnesota

We have previously reported that women with atypical hyperplasia (AH) have a 4-fold–increased risk of breast cancer (BC) in comparison with the general population, and this risk is stratified by the extent of atypia, with stepwise increases in risk for women with 1, 2, and ≥3 foci of AH (relative risks of 3.2, 5.5, and 7.6, respectively).[1] Therefore, we reviewed with interest Collins et al's article entitled "Breast Cancer Risk by Extent and Type of Atypical Hyperplasia: An Update From the Nurses' Health Studies."[2] In this article, they state that a greater extent of AH did not correlate with a significant increase in BC risk. They found that in women with atypical ductal hyperplasia (ADH), the risk was no higher for ≥3 foci (odds ratio [OR], 2.7) versus 1 or 2 foci (OR, 3.5). In women with atypical lobular hyperplasia (ALH), the risk appeared higher for women with ≥3 foci (OR, 8.0) versus women with 1 or

CONFLICT OF INTEREST DISCLOSURES
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2 foci (OR, 5.2), but the difference was not statistically significant. They suggest that the varying results for the Nurses' Health Study (NHS) and the Mayo Benign Breast Disease Cohort Study may be due to the fact that the analyses presented for the Mayo cohort were not stratified by the type of AH, and they conclude that "the extent of ADH or ALH should not influence management decisions for individual patients." We applaud the authors for investigating whether the extent of AH may have differing effects on risk according to the subtype of AH. However, we respectfully disagree with their conclusion, and in this issue of *Cancer*, we report that an additional analysis of the Mayo cohort data by AH subtype shows an increase in the BC risk for both ADH and ALH.[3] For ADH, the relative risks are 2.6, 5.2, and 6.4 for 1, 2, and ≥3+ foci, respectively (*P* for trend = .006), and for ALH, the relative risks are 2.6, 3.5, and 6.8, respectively (*P* for trend =.001).

Furthermore, methodological and sample size differences between the studies may explain the differences in the findings. The NHS sample was based on incomplete procurement of biopsy materials, which was described as ">50% of those giving permission," with the most common reason being that specimens were destroyed or were no longer available. The largest subgroup of women with AH had ≥3 foci (43%); this contrasted with the Mayo study (17%). This may indicate a selection bias in the NHS sample: benign biopsy materials with a greater extent of atypia may have been retained longer at the original institutions because of the extent of the findings or because the specimens belonged to women who had later developed cancer. Finally, the NHS analysis compared ≥3 foci with all others, possibly because the sample size precluded comparisons of 1, 2, and ≥3 foci as 3 distinct levels. However, grouping together the lowest risk group (a single focus) with an intermediate-risk group (2 foci) could have masked differences across the 3 levels.

In summary, although the NHS report did not identify any statistically significant increases in risk based on the extent of AH, we believe that their statement that this is not a clinically important risk feature is not warranted, and disease extent remains an important component of BC risk assessment for women with AH.

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References

1. Hartmann LC, Degnim AC, Santen RJ, Dupont WD, Ghosh K. Atypical hyperplasia of the breast—risk assessment and management options. N Engl J Med. 2015; 372:78–89. [PubMed: 25551530]
2. Collins LC, Aroner SA, Connolly JL, Colditz GA, Schnitt SJ, Tamimi RM. Breast cancer risk by extent and type of atypical hyperplasia: an update from the Nurses' Health Studies. Cancer. 2016; 122:515–520. [PubMed: 26565738]

3. Degnim AC, Dupont WD, Radisky DC, et al. Extent of atypical hyperplasia stratifies breast cancer risk in 2 independent cohorts of women. Cancer. 2016; 122:2971–2978. [PubMed: 27352219]