Original Study

Surgical Outcomes of Lobular Neoplasia Diagnosed in Core Biopsy: Prospective Study of 316 Cases

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Abstract

The purpose of the study was to identify a subset of patients who might be able to avoid surgical excision of lobular neoplasia (LN) diagnosed in core biopsies (CB). A diagnosis of classic LN including classic lobular carcinoma-in-situ and atypical lobular hyperplasia on CB targeting calcifications does not necessitate subsequent surgery when careful imaging/pathology correlation is used.

Background: Management recommendations for lobular neoplasia (LN) including lobular carcinoma-in-situ (LCIS) and atypical lobular hyperplasia (ALH) diagnosed in core biopsies (CB) are controversial. Our aim was to prospectively identify a subset of patients who do not require subsequent surgical excision (SE). **Patients and Methods:** All patients diagnosed with LN on CB were enrolled and referred for SE. Cases with coexistent ductal carcinoma-in-situ or invasive carcinoma were excluded. Cases with coexistent ductal atypia (LN-DA) and LCIS variants (LN-V) were separated from pure classic LN (LN-C). Dedicated breast pathologists and radiologists reviewed cases with careful imaging/pathology correlation. **Results:** Of 13,772 total percutaneous breast CB procedures, 302 of 370 patients diagnosed with LN underwent SE. Upgrade to carcinoma was present in 3.5% (8/228) LN-C, 26.7% LN-V (4/15), and 28.3% LN-DA (15/53). Calcifications were the imaging target for 180 (79%) of 228 LN-C cases; 7 were associated with upgrade (3.9%). Upgrades were rare for mass lesions (1/32) and magnetic resonance imaging–targeted lesions (0/14). Upgrades were similar for ALH and LCIS (3.4% vs. 4.5%). During postsurgical follow-up (mean, 34.5 months), 6.5% LN-C patients developed carcinoma in either breast. **Conclusion:** Although LN with nonclassic morphology or with associated ductal atypia requires SE, this can be avoided in LN-C diagnosed on CB targeting calcifications when careful imaging/pathology correlation is applied. Until larger numbers are studied, excising LN-C diagnosed as masses or magnetic resonance imaging–detected lesions may be prudent. Regardless of their selection for surgical management, LN patients need close surveillance in view of their long-term risk of breast cancer.

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Introduction

Lobular neoplasia (LN), including atypical lobular hyperplasia (ALH) and lobular carcinoma-in-situ (LCIS), encompasses a variety of lesions requiring different management approaches. The association of classic LN with significant long-term bilateral risk of subsequent breast carcinoma of either or both ductal and lobular types has been established.[1-6] Classic LN (LN-C) has traditionally been categorized as a marker of increased risk and nonobligate precursor with minimal potential of direct progression to invasive carcinoma. On the other hand, variants of LN, such as pleomorphic LCIS and LCIS with necrosis, may be more aggressive and similar to high-grade ductal carcinoma-in-situ (DCIS) in its capacity to progress to invasive carcinoma. The LN variants are frequently associated with invasive lobular carcinoma (ILC); when LN variants are diagnosed on core biopsies (CB), ILC is identified in the same area in 25% to 30% of subsequent surgical excision (SE).[7-10] Because of

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a lack of extensive follow-up, current National Comprehensive Cancer Network guidelines recommend treating these lesions more like DCIS than LCIS.[11]

LN-C is typically found in image-guided CB as an incidental finding and rarely presents with associated targeted calcifications or as an ultrasound-identified mass lesion.[12] In theory, the upgrade rate, defined as finding invasive carcinoma or DCIS on excision following a diagnosis of LN-C on radiologically concordant CB, should be infrequent and limited to rare, small, low-grade malignancies following the concept of low-grade breast neoplasia family.[13-15] Hypothetically, the expected upgrade rates of patients with LN-C should be similar to that of diagnosing breast cancer in a random group of women, such as those with Breast Imaging Reporting and Data System (BI-RADS) category 3 imaging assessment. As shown in previous studies, these "probably benign" lesions routinely managed by follow-up imaging are associated with an up to 2% rate of cancer diagnosis when sampled by biopsy.[16,17] Various reports in the literature have shown a much higher rate of identifying cancer in the SE after a CB diagnosis of LN-C.[18,19] However, many of these studies are retrospective, without thorough pathologic review of diagnostic slides and correlation with radiologic findings.

In our health care system, approximately 60 women per year are diagnosed with LN-C as the highest grade lesion on CB. The purpose of our study was to prospectively evaluate all LN cases diagnosed on CB, using careful pathologic and radiographic correlation, to determine if there is a subset of patients who can safely avoid SE.

Materials and Methods

This study was approved by the Allina Health institutional review board. We prospectively included all patients with a new diagnosis of LN identified on image-guided CB performed at 1 of 3 Allina-affiliated breast centers in the Minneapolis/St Paul, Minnesota, metropolitan area from June 2008 to December 2012. Patients with associated DCIS or invasive carcinoma in the same CB were excluded. All patients with LN on CB were referred for SE. This standard policy was established by the Allina Breast Committee based on existing guidelines. Abstracted patient information included personal history of breast carcinoma (previous, synchronous, or subsequent) and family history (mother, sister, or daughter) of breast cancer.

Imaging

Three breast centers with dedicated breast radiologists participated in the study. All patients with LN found in image-guided CB during the study period were identified. Suspicious abnormalities were classified as BI-RADS category 4 (suspicious lesion, recommend biopsy) or category 5 (highly suggestive of malignancy). Stereotactic biopsies were performed for evaluation of calcifications, sonographically occult masses, and asymmetries using prone stereotactic tables. A specimen radiograph confirmed the presence of targeted calcifications in the samples, and this image was sent to pathology for correlation with the microscopic evaluation of calcifications. Magnetic resonance imaging (MRI)-guided biopsies were performed for mammographically and sonographically occult abnormalities seen as MRI enhancement. Stereotactic and MRI-guided biopsies were performed using an 8- or 9-gauge vacuum-assisted biopsy probe (ATEC/Eviva Biopsy System [Suros Surgical Systems, Indianapolis, IN] or Mammotome Breast Biopsy System [Ethicon Endosurgery, Cincinnati, OH]). Ultrasound biopsies were performed for suspicious masses using a 14-gauge automated biopsy instrument (majority of cases) or an 18-gauge semiautomated biopsy instrument (Pro-Mag 2.2 [Manan Medical Products, Northbrook, IL], Achieve [Carefusion, Waukegan, IL], Max-Core [Bard Peripheral Vascular, Tempe, AZ], or Temno Evolution [Carefusion, Waukegan, IL]). A radiographic clip was used to mark the biopsy sites for the image-guided CB.

Images were reviewed and CB were performed by dedicated breast radiologists. Radiologic–pathologic correlation was performed by a breast radiologist when the pathology results became available, usually the working day after the biopsy procedure, and an addendum was dictated to the biopsy report indicating the pathologic findings and concordance/discordance. Concordance was established on the basis of previously published criteria.[20] Discordant cases included those with (1) calcifications inadequately sampled as documented by comparison with the specimen radiograph, (2) lesions radiographically suspicious for malignancy (BI-RADS 4) in which the histologic findings did not account for the imaging pattern, and (3) lesions highly suggestive of malignancy (BI-RADS 5) that were sampled with benign results. The breast radiologist and breast pathologist routinely discussed complicated cases to determine concordance. Additional central radiology review was performed in selected cases for study purposes.

Pathology

One pathology group with centralized specialty sign-out, using uniform diagnostic criteria, participated in the study. All breast CB were reviewed in real time by 2 pathologists (at least one of whom was a dedicated breast pathologist and an investigator on this study). All breast biopsy samples were processed centrally within our institution. The histologic findings were correlated with the radiology information including all pertinent imaging features of the targeted lesion or lesions in real time before issuing pathology diagnoses. For stereotactic CB performed for calcifications, the amount and nature of calcifications in microscopic slides were compared to the calcifications in the accompanying specimen radiograph. On the basis of this review, the pathologist determined if the histologic findings adequately correlated with the calcifications present on the specimen radiograph or if additional tissue levels or imaging of tissue blocks were needed. If the pathologic findings failed to correlate with the imaging findings, discordant findings were discussed with the radiologist and documented in the pathology report.

LN cases were classified as either ALH or LCIS.[1,21] LN was further classified as classic type (LN-C) or variant LCIS (LN-V), which included pleomorphic LCIS or necrotic LCIS.[10,22-24] Cases with ductal type atypia present in the same CB as LN were analyzed separately from pure LN cases. Ductal atypia included atypical ductal hyperplasia (ADH) and flat epithelial atypia. When necessary, E-cadherin immunohistochemical stain was performed for definitive classification of ductal versus lobular phenotype. Patients ultimately underwent SE of the area with LN, and all tissue from excisional biopsy specimens was submitted for microscopic review. Upgrade was defined as the incidence of invasive carcinoma or