



Factors associated with disease upgrading in patients with papillary breast lesion in core-needle biopsy

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Background: Traditionally, surgical excision is recommended for benign papillary lesions in core-needle biopsy (CNB) because of their malignant potency. The aim of this study was to identify factors associated with disease upgrading to malignancy in patients with benign papillary lesions in CNB.

Methods: A total of 179 female patients were evaluated retrospectively who were diagnosed as having a benign papillary lesion in CNB and underwent a subsequent surgical excision between January 2007 and December 2016. Ultrasonography-guided CNB was performed using a 14-gauge needle gun method.

Results: The rate of upgrade to malignancy was 10.6% (7.6% in papillary lesions without atypia *vs.* 33.3% in papillary lesions with atypia; $P=0.001$). The univariable analysis revealed that older age at diagnosis (≥ 50 years old), menopause, lesion size on ultrasonography, palpability, multifocality, and atypia in CNB were associated with upgrading. The multivariable analysis revealed that age ≥ 50 years (OR, 4.6; 95% CI, 1.5–14.1; $P=0.008$), lesion size of ≥ 2 cm (OR, 6.4; 95% CI, 1.9–21.1; $P=0.002$), and atypia in CNB (OR, 5.1; 95% CI, 1.5–18.2; $P=0.011$) were significantly associated with upgrading to malignancy.

Conclusions: Upgrading to malignancy in patients with benign papillary lesions in CNB was associated with age ≥ 50 years, lesion size ≥ 2 cm, and atypia in CNB.

Keywords: Breast papillary lesion; core-needle biopsy (CNB); management

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Introduction

Breast papillary lesion is defined as a proliferative lesion characterized architecturally by the presence of finger-like projections composed of a stromal core overlain by a layer of epithelial cells (1). Breast papillary lesions are known to have various clinical presentations and a broad pathological spectrum (2). Papillary lesions may present with nipple

discharge or as a palpable mass, or as an asymptomatic lesion detected in imaging study. The incidence of papillary lesion in core-needle biopsy (CNB) specimens of the breast is up to 6% according to previous reports (3–5).

Traditionally, breast papillary lesions are regarded as lesions that require surgical excision because of their malignant potency. The reported upgrading rates from benign papillary lesions diagnosed using CNB to

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malignancy diagnosed after a subsequent surgical excision ranged from 0% to 29% (6). However, whether all papillary lesions require surgical excision for appropriate management is controversial.

The aims of this study were to identify factors associated with upgrading to malignancy in patients with benign papillary lesions in CNB, and to avoid unnecessary overtreatment.

We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/gs-20-310>).

Methods

Medical records of patients were reviewed retrospectively who were diagnosed as having benign papillary lesions in CNB and underwent a subsequent surgical excision between January 2007 and December 2016 at Inha University Hospital and Cheil General Hospital & Women's Healthcare Center. Surgical excision was recommended to all the patients with benign papillary lesion in CNB. One hundred and seventy-nine patients underwent a subsequent surgical excision among who were diagnosed as having benign papillary lesions in CNB and these 179 patients were included in this study. Patients who had concurrent ductal carcinoma in situ (DCIS) or invasive carcinoma in the ipsilateral breast were excluded.

CNB was performed using the 14-gauge needle gun method with ultrasonography guidance. At least four or five core biopsies were done by lesions. Pathologic evaluation was performed by 3 board-certified pathologists who had received breast subspecialty training. Hematoxylin and eosin-stained slides and if needed, additional immunohistochemical stained slides for cytokeratin 5/6, myoepithelial cell markers, and/or estrogen receptor were evaluated.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review boards of Inha University Hospital (approval number: INHAUH 2017-10-016) and waived the requirement for informed consent.

The following data were analyzed: age, menopause, symptoms (palpability and nipple discharge), sonographic findings (size, multifocality, and location), pathological result from CNB, and final pathological result after surgical excision.

Upgrading was defined as the identification of DCIS or invasive carcinoma after surgical excision. On

ultrasonography, a lesion located within 2 cm from the nipple was defined as a central location, and any location further away from the nipple was defined as a peripheral location.

Statistical analyses were performed using IBM SPSS Statistics Version 19.0 for Windows (IBM Corp., Armonk, NY, USA). To identify the factors associated with upgrading, multiple regression analysis was performed. A P value of <0.05 was considered statistically significant. The results were presented as odds ratios (ORs) with their 95% confidence intervals (CIs).

Results

The mean age of the 179 patients was 44.6 years (range, 14–77 years). Among the 179 patients, 43 (24.0%) were aged ≥ 50 years and 42 (23.5%) were postmenopausal women. Of the patients, 56 (31.3%) presented with a palpable mass, 29 (16.2%) presented with nipple discharge, 28 (15.6%) had a lesion of ≥ 2 cm on ultrasonography, 34 (19.0%) had multifocal lesions, 54 (30.2%) had a centrally located lesion on ultrasonography, and 21 patients (11.7%) had an atypical papillary lesion in CNB (*Table 1*).

In the 179 patients, the upgrade rate to malignancy was 10.6% (7.6% in papillary lesions without atypia *vs.* 33.3% in papillary lesions with atypia; $P=0.001$). Concordance rate for atypia between CNB and surgical specimen was 14.3%. The univariable analysis revealed that age at diagnosis (<50 *vs.* ≥ 50 years; $P=0.004$), menopause ($P=0.013$), lesion size on ultrasonography (<2 *vs.* ≥ 2 cm; $P<0.001$), palpability ($P=0.011$), multifocality ($P=0.043$), and atypia in CNB ($P=0.001$) were associated with upgrading. The number of variables that had a P value of <0.1 in the univariable analysis was six and these were many for multiple regression analysis. Considering the characteristics of the variables, we excluded menopause and palpability from the variables for multiple regression analysis, because there is intrinsic association between menopause and age, and so between palpability and lesion size. The multivariable analysis revealed that age at diagnosis ≥ 50 years (OR, 4.6; 95% CI, 1.5–14.1; $P=0.008$), lesion size of ≥ 2 cm (OR, 6.4; 95% CI, 1.9–21.1; $P=0.002$), and atypia in CNB (OR, 5.1; 95% CI, 1.5–18.2; $P=0.011$) were significantly associated with upgrading to malignancy (*Table 2*).

Discussion

The previously reported upgrading rates from benign

Table 1 Patient clinicopathological features (N=179)

Variables	No. of patients (%)
Age (years)	
Mean \pm SD	44.6 \pm 10.2
Range	14–77
<50	136 (76.0)
\geq 50	43 (24.0)
Menopause	
Pre	137 (76.5)
Post	42 (23.5)
Size (on ultrasonography)	
<2 cm	151 (84.4)
\geq 2 cm	28 (15.6)
Palpability	
No	123 (68.7)
Yes	56 (31.3)
Nipple discharge	
No	150 (83.8)
Yes	29 (16.2)
Multifocality	
No	145 (81.0)
Yes	34 (19.0)
Location	
Central	54 (30.2)
Peripheral	125 (69.8)
Atypia (on CNB)	
No	158 (88.3)
Yes	21 (11.7)

CNB, core-needle biopsy.

papillary lesions diagnosed using CNB to malignancy diagnosed after a subsequent surgical excision ranged from 0% to 29% (6). The Upgrade rate in our study was 10.6%. *Table 3* shows the results of several previously published studies. These upgrading rates for papillary lesions were high enough to deserve attention. Thus, the proper management of benign papillary lesions is controversial.

In our study, age \geq 50 years, lesion size of \geq 2 cm, and atypia in CNB were significantly associated with upgrading to malignancy. The upgrade rate of atypical papillary

lesions in this study was significantly high at 33.3%. In many previous studies, the upgrade rates of benign papillary lesions with atypia were also significantly high, so the need for surgical excision of atypical papillary lesions in CNB was generally accepted (12). However, proper management of benign papillary lesions without atypia diagnosed in CNB is still controversial.

Some authors believe that benign papillary lesions without atypia can be managed safely with clinical and radiological follow-up if the radiological and pathological findings are concordant. However, others recommend excision for these patients to rule out any hidden malignancy. The potential heterogeneity in the distribution of atypia or carcinoma, if present, within a papillary lesion can disrupt accurate diagnosis (6).

In this study, 106 patients were under the age of 50 and had papillary lesions of <2 cm in size without atypia. Among these patients, 5 (4.7%) were upgraded to malignancy. As the value of 4.7% can be acceptable, non-atypia papillary lesions <2 cm in women under the age of 50 can be managed with clinical and radiological follow-up. However, close follow-up is necessary to avoid overlooking 4.7% of cases.

Several previous studies tried to identify the factors associated with the upgrade of papillary breast lesions without atypia (9,10,13–18). These studies reported that palpable lesions (14,15), larger lesion size (cutoff, 1–1.5 cm) (10,16,17), older age (cutoff, 50–54 years), peripheral lesion, higher Breast Imaging Reporting and Data System score, and pathological–radiological discordance (17) were associated with upgrading to malignancy.

Some authors thought the upgrading was associated with the sampling method and reported that vacuum-assisted breast biopsy was a more efficient method than the usual CNB (18–20). Vacuum assisted excision can be a good option for management of papillary lesion without atypia in CNB and can produce better cosmetic outcome (21). However, no long-term prospective studies have been conducted on benign papillary lesions diagnosed using CNB. Thus, prospective long-term studies on benign papillary lesions diagnosed using CNB in a larger number of patients are mandated. This study was a retrospective cross-sectional study with a relatively small number of patients, which is a source of its inherent limitations. Breast imaging and pathologic result were reported according to Breast Imaging Reporting and Data System and World Health Organization Classification of Tumours of the Breast. However there could be interobserver variability,

Table 2 Univariable/multivariable analysis of clinicopathological factors associated with upgrading

Variables	Upgrading		Univariable analysis			Multivariable analysis		
	No (N=160)	Yes (N=19)	OR	95% CI	P value	OR	95% CI	P value
Age (years)								
Mean ± SD	43.7±9.8	52.2±11.2	1.1	1.0–1.1	0.001*			
<50	127 (93.4%)	9 (6.6%)						
≥50	33 (76.7%)	10 (23.3%)	4.3	1.6–11.4	0.004*	4.6	1.5–14.1	0.008*
Menopause								
Pre	127 (92.7%)	10 (7.3%)						
Post	33 (78.6%)	9 (21.4%)	3.5	1.3–9.2	0.013*			
Size								
<2 cm	141 (93.4%)	10 (6.6%)						
≥2 cm	19 (67.9%)	9 (32.1%)	6.7	2.4–18.5	<0.001*	6.4	1.9–21.1	0.002*
Palpability								
No	115 (93.5%)	8 (6.5%)						
Yes	45 (80.4%)	11 (19.6%)	3.5	1.3–9.3	0.011*			
Nipple discharge								
No	133 (88.7%)	17 (11.3%)						
Yes	27 (93.1%)	2 (6.9%)	0.6	0.1–2.7	0.482			
Multifocality								
No	133 (91.7%)	12 (8.3%)						
Yes	27 (79.4%)	7 (20.6%)	2.9	1.0–8.0	0.043*	2.1	0.6–7.1	0.241
Location								
Peripheral	113 (90.4%)	12 (9.6%)						
Central	47 (87.0%)	7 (13.0%)	1.4	0.5–3.8	0.504			
Atypia (on CNB)								
No	146 (92.4%)	12 (7.6%)						
Yes	14 (66.7%)	7 (33.3%)	6.1	2.1–17.9	0.001*	5.1	1.5–18.2	0.011*

*, statistically significant. OR, odds ratio; CI, confidence interval; CNB, core-needle biopsy.

Table 3 Upgrade rate after surgical excision of benign papillary lesion diagnosed in core-needle biopsy: published results

Study (year)	Needle gauge	Type of biopsy	No. of lesions excised	No. of lesions upgraded to malignancy/total No. of lesions (%)
Puglisi <i>et al.</i> (7) [2003]	14	Ultrasound, stereotactic	31	2/31 (6.5)
Mercado <i>et al.</i> (4) [2001]	11 and 14	Ultrasound, stereotactic	36	2/36 (5.6)
Rizzo <i>et al.</i> (8) [2008]	11	Stereotactic	86	9/86 (10.5)
Jaffer <i>et al.</i> (9) [2009]	14–20	Ultrasound, stereotactic	104	9/104 (8.7)
Chang <i>et al.</i> (10) [2011]	11 and 14	Ultrasound	64	2/64 (3.1)
Chae <i>et al.</i> (11) [2016]	Not available	Ultrasound	329	42/329 (12.8)
This study	14	Ultrasound	179	19/179 (10.6)

which is also the limitation of this study.

In conclusion, upgrading to malignancy in patients with benign papillary lesions in CNB was associated with age ≥ 50 years, lesion size ≥ 2 cm, and atypia. Benign papillary lesions diagnosed using CNB in women under the age of 50, which are small lesions without atypia, can be observed but require close observation with clinical and radiological follow-up.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/gs-20-310>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional review boards of Inha University Hospital (approval number: INHAUH 2017-10-016) and waived the requirement for informed consent.

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