Original Article

The value of imaging combined with clinicopathological features in the diagnosis of high-risk breast lesions

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Background: The upgrade of high-risk breast lesions (HRLs) is closely related to subsequent treatment, but the current predictors for upgrade are limited to intratumoral features of single imaging mode.

Methods: We retrospectively reviewed 230 HRLs detected by mammography, ultrasound, and magnetic resonance imaging (MRI) before biopsy at the Fudan University Cancer Hospital from January 2017 to March 2018. The clinical features, imaging data according to the Breast Imaging Reporting and Data System (BI-RADS) lexicon, and tumor upgrade situation were received. Based on the different risks of upgrade reported, the lesions were classified into high-risk I [HR-I, with atypical hyperplasia (AH)] and high-risk II (HR-II, without AH). We analyzed the association between clinicopathological and imaging factors and upgrade. We used the receiver operating characteristic (ROC) curve to compare the efficacy of three imaging modes for predicting upgrade.

Results: We included 230 HRLs in 230 women in the study, and the overall upgrade rate was 20.4% (47/230). The upgrade rate was higher in HR-I compared to HR-II (38.5% *vs.* 4.1%, P<0.01). In patients with AH, estrogen receptor-positive (ER+) patients accounted for 81.0% (64/79). For all HRLs and HR-I, in clinical characteristics, age, maximum size of lesion, and menopausal status were significantly associated with upgrade (P<0.05). In imaging factors, MRI background parenchymal enhancement (BPE), signs of MRI and ultrasound were significantly correlated with upgrade (P<0.05). Patients with negative MRI or ultrasound manifestations had lower upgrade rates (P<0.01). For HR-II, only BPE showed a significant difference between groups (P=0.001). Multifactorial analysis of all HRLs showed that age and BPE were independent predictors of upgrade (P<0.01). The areas under the ROC cure (AUCs) for predicting upgrade in mammography, ultrasound, and MRI were 0.606, 0.590, and 0.913, respectively, indicating that MRI diagnosis was significantly better than mammography and ultrasound (P<0.001).

Conclusions: HRLs with AH had a higher rate of upgrade and increased ER expression. Among three imaging modes, MRI was more effective than ultrasound and mammography in diagnosing the upgrade of HRLs. Older age and moderate to marked BPE can indicate malignant upgrade. MRI can provide a certain value for the diagnosis and follow-up of HRLs.

Keywords: Breast neoplasm; high-risk breast lesions (HRLs); magnetic resonance imaging (MRI); mammography; breast ultrasound

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Introduction

High-risk breast lesions (HRLs) are a group of morphologically and biologically heterogeneous diseases with an increased risk of breast cancer during follow-up after diagnosis (1-3). The high-risk lesions mainly include atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), flat epithelial atypia (FEA), papillary lesions, sclerosing adenosis (including radial scarring and complex sclerosing adenosis), and mucocele-like lesions (4-7). Currently, high-risk lesions are found mainly through image-guided biopsies, but because of sampling volume limitations or suboptimal targeting, there is a risk of upgrading to ductal carcinoma in situ (DCIS) or invasive malignancy at the time of surgical excision (8). As a result, surgical excision is often recommended (3). To some extent, this results in excessive treatment and unnecessary surgery.

The follow-up management of HRLs remains controversial, mainly because of the wide range of reported upgrade rates (9). If the upgrade rates of HRLs can be accurately predicted by combining various characteristics of lesions, we can guide clinical decision-making better and manage patients individually. At present, many scholars have discussed the factors affecting the upgrade rate of HRLs, including clinical, pathological, imaging, and other aspects. Previous studies have found that some characteristics are closely associated with upgrade, including age, menopausal status, lesion size, mode of biopsy, and imaging characteristics (10-14). Despite these efforts, there are still no definite characteristics that can reliably distinguish lesions requiring surgical excision from those that can be monitored. Current studies have some limitations. For example, the imaging characteristics used in the studies were limited to a single mode, and only the tumor's imaging features were analyzed, whereas the background parenchyma features were ignored. Our study included clinicopathological features and imaging features of three modes [breast ultrasound, mammography, and magnetic resonance imaging (MRI)], comparing the value of different features in predicting the upgrade of HRLs to better stratify the risk of upgrade and assist in clinical decisions. Furthermore, we analyzed the background parenchymal enhancement (BPE) of MRI to study the effect of breast parenchymal features on the upgrade. We present the following article in accordance with the STARD reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-155/rc).

Methods

Study population

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of Fudan University Shanghai Cancer Center, Shanghai, China (No. 1507149-8), and individual consent for this retrospective analysis was waived. We continuously retrospectively analyzed patients who met the following inclusion criteria in the Fudan University Cancer Hospital from January 2017 to March 2018: (I) the pathology of the biopsies (including hollow-core needle biopsy, vacuum-assisted biopsy, and open biopsy) showed HRLs, including ADH, ALH, sclerosing adenosis (including radial scarring and complex sclerosing adenosis), intraductal papilloma, mucocele-like lesions, and FEA; (II) complete imaging data of the three modes—breast ultrasound, mammography, and MRI—are available; (III) all imaging examinations were performed before biopsy; and (IV) short-term follow-up was performed for 6 months to 1 year. The exclusion criteria included (I) poor image quality, and (II) lack of follow-up. Information about the patients' age, maximum diameter of lesion, menopausal status, history of benign and malignant breast lesions, family history of malignant tumors, and clinical manifestations was collected from the clinical case system, and the image information before biopsy was obtained from the picture archiving and communication system.

Histopathologic analysis

Breast specimens were analyzed by an associate chief physician specializing in breast diagnosis in the Department of Pathology. The histologic analysis was based on the microscopic analysis of tissue sections stained with hematoxylin-eosin (H&E). Histological types were defined according to the fifth edition of the World Health Organization's (WHO's) pathological classification of breast tumors (15). Immunohistochemical methods were used to determine the expression of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2), and the Ki-67 antigen. The pathologist was blinded to the results of the imaging examination.

High-risk lesion upgrade was defined as the presence of DCIS or invasive ductal carcinoma components at subsequent surgery based on histopathology (16). Based on

their risk of upgrade reported in the literature (17-19), the lesions were categorized in order of severity as high-risk I (HR-I) (ADH, ALH, atypical papilloma, and sclerosing adenosis with atypical hyperplasia) and high-risk II (HR-II) (sclerosing adenosis, benign papilloma, mucocele-like lesions, and FEA). Although FEA is accompanied by atypical hyperplasia (AH), as the literature reports (3), the upgrade rate of FEA is much lower than that of other AH, so FEA was classified as HR-II.

Image interpretation

Because of the significant difference in the upgrade rates between HR-I and HR-II lesions, we researched the relationship between the imaging features and the upgrade rates of all HRLs, HR-I, and HR-II lesions, respectively. Two breast radiologists (with 6 and 15 years of experience in breast imaging diagnosis, respectively) reviewed these cases independently and reached a consensus after consultation. The analysis and evaluation of imaging manifestations of breast lesions were based on standards from the Breast Imaging Reporting and Data System (BI-RADS) proposed by the American College of Radiology (20). Mammographic features of lesions included mass, calcification, architectural distortion, and asymmetry; MRI features included mass, non-mass enhancement (NME), and BPE (minimal to mild or moderate to marked); and ultrasound features were divided into mass and other manifestations (such as heterogeneity, ductal dilation, and calcification). According to the BI-RADS lexicon (20) and clinical application, MRI BI-RADS 4 was still diagnosed as 4 A–C, and pathological results were taken as the gold standard to compare the efficacy of different imaging modes in diagnosing the upgrade of HRLs.

Statistical analysis

Independent sample *t*-tests and chi-square tests were used to compare the clinical features and imaging signs between the upgraded and non-upgraded group of HRLs. According to BI-RADS classification, seven points (1, 2, 3, 4A, 4B, 4C, and 5) were assigned as ordered classification variables. Using the pathological results as the gold standard, the diagnostic efficacy of mammography, ultrasound, and MRI for the upgrade rate of HRLs was compared by the receiver operating characteristic (ROC) curve. Binary logistic regression analysis was used to compare the relationship between the upgrade rate of HRLs and the clinical and imaging signs. $P<0.05$ indicated a significant difference. Statistical analyses were conducted using SPSS (version 26) and MedCalc software (version 20.0.3).

Results

Clinicopathological features

During the study period, 274 HRLs in 274 patients were diagnosed by biopsy. Of these lesions, 10 were excluded for poor image quality, and 34 were excluded for lack of follow-up. Therefore, 230 HRLs in 230 women were included in the study. The mean patient age was 48.3±10.6 years, and the mean maximum diameter of the lesions was 15.6±8.9 mm. According to the main pathological features, there were 43 cases of ADH, 6 cases of ALH, 89 cases of sclerosing adenosis, 87 cases of intraductal papilloma, 4 cases of mucocele-like lesions, and 1 case of FEA. One hundred twenty patients underwent surgery after biopsy, and the interval between biopsy and surgery was less than seven days. One hundred ten patients were confirmed complete resection of the lesion at biopsy, and they did not undergo surgery. Of 230 lesions, a total of 47 (20.4%) cases upgraded to cancer during follow-up surgery: 22 (9.5%) DCIS and 25 (10.9%) invasive. *Table 1* shows the upgrade situation of different pathological types. There were statistical differences in age, maximum diameter of lesions, and menopausal status of HRLs between the upgraded group and the non-upgraded group (*Table 2*).

HR-I patients (N=42/109, 38.5%) were significantly more likely to upgrade compared to HR-II (N=5/121, 4.1%, $P<0.01$). There were no significant differences in mean age (49.0±11.0 *vs.* 47.5±10.2 years old, $P=0.3$) and mean maximum diameter (15.59±8.01 *vs.* 15.53±9.72 mm, $P=0.9$) between HR-I and HR-II patients. In HR-I, there were also statistical differences in age, maximum diameter of lesions, and menopausal status between the upgraded group and the non-upgraded group (*Table 2*).

It has been reported that ER expression in breast epithelium is associated with AH, and ER percent staining and intensity are significantly increased in AH (21). Immunohistochemical examinations were performed in 126 of all 230 lesions. ER status analysis showed that of 79 cases associated with AH, ER+ accounted for 81.0% (64/79), and ER expression >70% accounted for 65.8% (52/79). Of 47 cases without AH, ER+ accounted for 95.7% (45/47), and ER expression >70% accounted for 55.3% (26/47). Among these 47 cases without AH, there were 34 benign intraductal

Table 1 The pathological types and upgrade situations of all high-risk breast lesions

Histopathologic type	Number of cases	Number of upgrades	Upgrade rate, %
Atypical ductal hyperplasia	43	13	30.2
Atypical lobular hyperplasia	6	3	50.0
Papillary lesion	87	19	21.8
Sclerosing adenosis	89	11	12.4
Mucocele-like lesions	4	1	25.0
Flat epithelial atypia	1	0	0.0
Total	230	47	20.4

Table 2 Clinical features of HRLs in the non-upgraded group and the upgraded group

Features	All HRLs (n=230)			HR-I (n=109)			HR-II (n=121)		
	Non-upgraded (n=183)	Upgraded (n=47)	P	Non-upgraded (n=67)	Upgraded (n=42)	P	Non-upgraded (n=116)	Upgraded (n=5)	P
Age, years	47.2±10.5	52.3±10.3	0.003*	46.6±10.7	52.8±10.6	0.004*	47.6±10.3	48.0±7.55	0.926
Maximum diameter, mm	14.96±8.95	17.89±8.58	0.044*	13.96±7.15	18.19±8.69	0.007*	15.54±9.82	15.40±7.92	0.974
Side			0.240			0.820			0.262
Left	107	23		32	21		75	2	
Right	76	24		35	21		41	3	
Menopausal status			0.020*			0.015*			0.526
Post-	60	24		21	23		39	1	
Pre-	123	23		46	19		77	4	
Benign breast history			0.954			0.656			0.493
Yes	20	5		10	5		10	0	
No	163	42		57	37		106	5	
Malignant breast history			0.791			0.677			0.742
Yes	32	9		15	8		17	1	
No	151	38		52	34		99	4	
Family history of cancer			0.208			0.145			0.031*
Yes	13	6		2	4		11	2	
No	170	41		65	38		105	3	
Clinical symptoms			0.165			0.374			0.371
Discharge	10	4		5	4		5	0	
Mass	122	36		43	31		79	5	
Negative	51	7		19	7		32	0	

Numerical data are presented as the mean ± SD. Nonnumerical data are presented as the number of patients. *, P<0.05. HRLs, high-risk breast lesions.

Table 3 Imaging features of HRLs in the non-upgraded group and the upgraded group

Features	All HRLs (n=230)			HR-I (n=109)			HR-II (n=121)		
	Non-upgraded (n=183)	Upgraded (n=47)	P	Non-upgraded (n=67)	Upgraded (n=42)	P	Non-upgraded (n=116)	Upgraded (n=5)	P
Mammography			0.362			0.670			0.843
Mass	50	17		20	16		30	1	
Calcification	72	14		24	12		48	2	
Architectural distortion	21	4		7	3		14	1	
Asymmetry	18	8		7	7		11	1	
Negative	22	4		9	4		13	0	
MRI			0.016*			0.041*			0.549
Mass	76	26		29	23		47	3	
NME	81	21		29	19		52	2	
Negative	26	0		9	0		17	0	
MRI BPE			<0.001*			<0.001*			0.001*
Minimal to mild	155	16		61	15		94	1	
Moderate to marked	28	31		6	27		22	4	
Ultrasound			0.015*			0.024*			0.190
Mass	92	27		33	25		59	2	
Other manifestations	45	17		15	14		30	3	
Negative	46	3		19	3		27	0	

*, P<0.05. HRLs, high-risk breast lesions; MRI, magnetic resonance imaging; NME, non-mass enhancement; BPE, breast parenchymal enhancement.

papillomas in ER+ and 17 benign intraductal papillomas in ER >70%.

Imaging features

The correlation of imaging features in relation to the rate of upgrade among all HRLs, HR-I, and HR-II lesions is shown in *Table 3*. In all HRLs and HR-I lesions, MRI BPE (P<0.001; P<0.001), MRI manifestations (P=0.016; P=0.041) and ultrasound manifestations (P=0.015; P=0.024) were predictive of the upgrade. We further analyzed the specific manifestations of MRI (mass, NME, or negative) in the upgraded group and the non-upgraded group and found that none of the 26 MRI negative lesions had upgraded; the difference was statistically significant (χ^2=7.53, P=0.006). We further analyzed the specific manifestations of ultrasound (mass, other manifestations, or negative) in the two groups compared and found that the upgrade rate of the 49 cases with the negative manifestation was significantly lower than those with non-negative manifestations; the difference was statistically significant (χ^2=7.85, P=0.005). In the HR-II lesions, only MRI BPE was significantly different between the upgraded and non-upgraded groups (P=0.001). There was no statistical difference in mammographic signs between the upgraded and non-upgraded groups. MRI BPE was effective in predicting the upgrade of HRLs in all three subgroups and had a greater diagnostic value than ultrasound and mammography.

Univariate and multivariate analysis of the upgrade of HRLs

Univariate analysis was conducted on the clinical and imaging features related to the upgrade. As a result, age, the maximum diameter of the lesion, and moderate to marked BPE were the positive correlation factors for predicting the

Table 4 Univariate and multivariate analyses of features associated with HRLs

Features	Univariate analysis			Multivariate analysis		
	OR	95% CI	P	OR	95% CI	P
Age	1.045	1.014–1.007	<0.01*	1.070	1.006–1.139	0.031*
Maximum diameter of lesions	1.034	1.000–1.069	<0.05*	1.017	0.973–1.062	0.459
Premenopausal	0.467	0.244–0.895	<0.05*	0.381	0.084–1.720	0.209
MRI-negative	0.858	0.809–0.910	<0.01*	0	0	0.998
MRI-moderate to marked BPE	10.725	5.193–22.151	<0.01*	31.562	10.158–98.069	<0.01*
Ultrasound-negative	0.210	0.064–0.728	<0.05*	0.376	0.094–1.501	0.166

*, P<0.05. HRLs, high-risk breast lesions; MRI, magnetic resonance imaging; BPE, breast parenchymal enhancement; OR, odds ratio; CI, confidence interval.

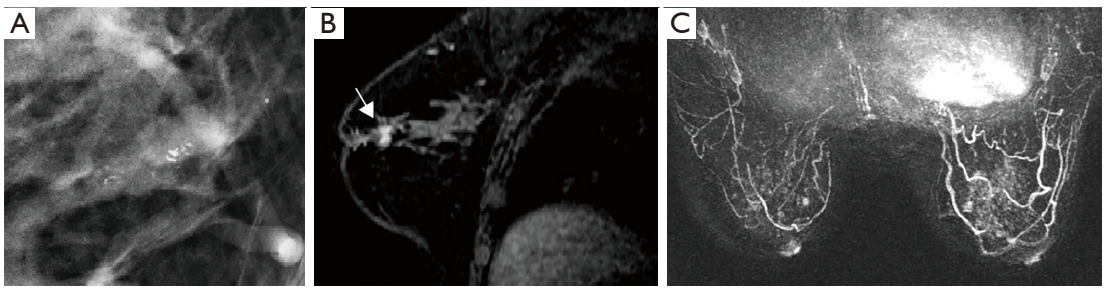

Figure 1 Female, 61 years old, found a mass in left breast for 1 month. (A) The magnified partial craniocaudal image of a left mammogram, showing line-like amorphous calcification in the posterior area of the left areola, BI-RADS 4A. (B) An MRI sagittal enhanced recombination image, showing the enhanced area in the left posterior areola area, basically consistent with the distribution range of calcification (↑). (C) The MIP of MRI, showing moderate to marked BPE in the left breast and several small, enhanced masses in the medial part of the left posterior areola with linear distribution, BI-RADS 4B. The pathology of the core needle biopsy revealed an intraductal papillary tumor with high ductal epithelial hyperplasia, which was upgraded to a papillary lesion with middle-grade DCIS after surgery. BI-RADS, Breast Imaging Reporting and Data System; MRI, magnetic resonance imaging; MIP, maximal intensity projection; BPE, background parenchymal enhancement; DCIS, ductal carcinoma in situ.

upgrade of HRLs, while pre-menopause, negative MRI, or ultrasound diagnosis were the negative correlation factors for predicting the upgrade of HRLs. The factors associated with upgrade in univariate analysis were introduced into multivariate logistic regression analysis. Age and BPE of MRI were found to be independent factors in predicting the upgrade of HRLs. The rate of upgrade of HRLs increased with age and MRI BPE (*Table 4*; *Figures 1*,*2*).

The efficacy of imaging diagnosis

According to the Youden index, when BI-RADS 4A was used as the cut-off point, mammography, ultrasound, and MRI had the highest diagnostic efficacy in evaluating the upgrade of HRLs. Their sensitivities were 40.4%, 68.1%, and 93.6%; specificities were 78.69%, 53.0%, and 86.3%; and the areas under the ROC curve (AUCs) were 0.606, 0.590, and 0.913, respectively (*Figure 3*). The diagnostic value of MRI for HRLs was significantly higher than that of mammography and ultrasound (P<0.001; *Figure 4*).

Discussion

In the diagnosis of HRLs, our study is unique because it combined clinical features, histological features, and multimodal imaging features, making it more comprehensive than previous studies. In terms of clinical features, we found that age, the maximum diameter of the lesions, and the menopausal status of the patients with HRLs were significantly correlated with upgrade, which

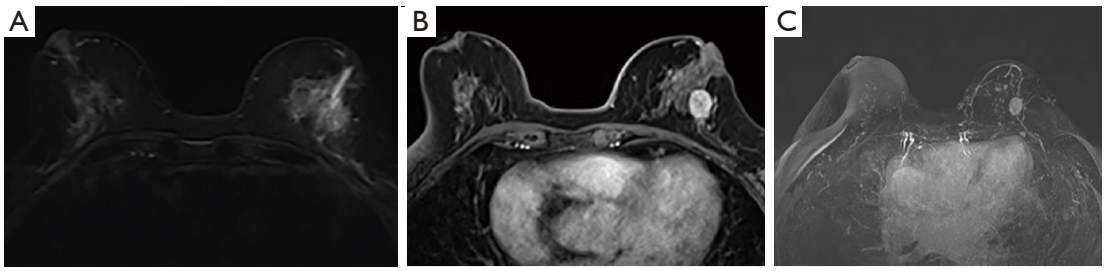

Figure 2 Female, 71 years old, 6 years after the operation for right intraductal papilloma, found left lacteal discharge for one month. T2WI of MRI (A) showed a slightly hyperintense lesion in the lateral posterior region of the left breast with an anterior dilated catheter. The MRI obtained in the post-contrast phase (B) showed annular enhancement of the left lateral breast mass, BI-RADS 4B. The MIP of the MRI (C) showed mild BPE in the left breast. The pathology of the core needle biopsy showed an intraductal papillary tumor with atypical ductal hyperplasia; the pathology was not upgraded after surgery. T2WI, T2-weighted image; MRI, magnetic resonance imaging; BI-RADS, Breast Imaging Reporting and Data System; MIP, maximal intensity projection; BPE, background parenchymal enhancement.

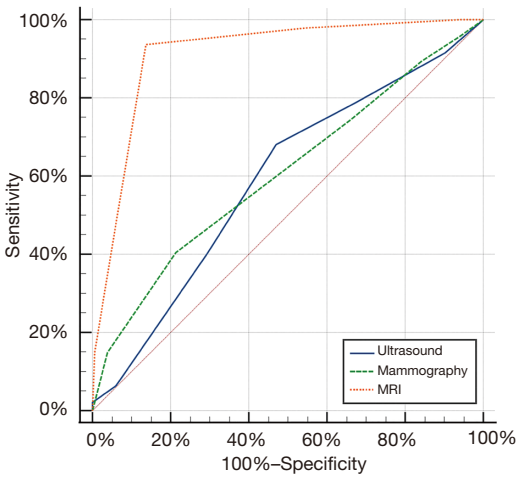

Figure 3 ROC curves for predicting the upgrade of HRLs by mammography, ultrasound, and MRI. The areas under the ROC curve were 0.606, 0.590, and 0.913, respectively. ROC, receiver operating characteristic; MRI was superior to mammography and ultrasound in diagnosing HRLs. MRI, magnetic resonance imaging; HRLs, high-risk breast lesions.

was consistent with previous studies. Giuliani *et al.* found that the older the patients were, the higher the risk they had of the HRLs being upgraded (14), and Cheeney *et al.* found that the maximum diameter of the lesions was larger in upgraded HRLs (10).

In terms of histological features, we once again demonstrated that AH is an important factor associated with the upgrade of HRLs. Rakha *et al.* proposed to classify B3 lesions into B3a (without AH) and B3b (with AH) according to their AH components (17). Mayer *et al.* found that the upgrade rate of B3b lesions by biopsy was higher, and it was more meaningful to perform surgery (18). Our results are consistent with previous reports that the likelihood of upgrade in HR-II was significantly reduced (17-19), suggesting that the evaluation of AH components could be useful in guiding the follow-up management of HRLs. Because the upgrade rates of HR-I and HR-II are very different, it is important to select the correct follow-up management. We further investigated the factors influencing the upgrade in the HR-I and HR-II groups and found that only BPE of MRI had predictive value in both groups, which can guide the clinical selection of surgery or follow-up.

ER is reported to be positive in almost all breast AH (22), and ER expression is increased in AH (21). In this study, the positive rate of ER in HRLs with AH was 81.0%, and the ER expression >70% accounted for 65.8%, which was consistent with the report. The positive rate of ER in HRLs without AH was 95.7%, and ER >70% accounted for 55.3%. This may be due to the large number of benign intraductal papillomas in HRLs without AH. The pathogenesis of intraductal papillomas is related to the long-term proliferation of breast tissues under the dominant effect of estrogen, which promotes the proliferation of normal breast cells through ER (23). Therefore, there are more ER+ cases in intraductal papillomas, and the further increase of ER in AH may be one of the reasons why its hyperplasia degree is more active than that of normal hyperplasia.

In terms of imaging features, for mammography, Nguyen *et al.* linked calcification to the upgrade of HRLs (13). In our study, calcification was the most common X-ray sign,

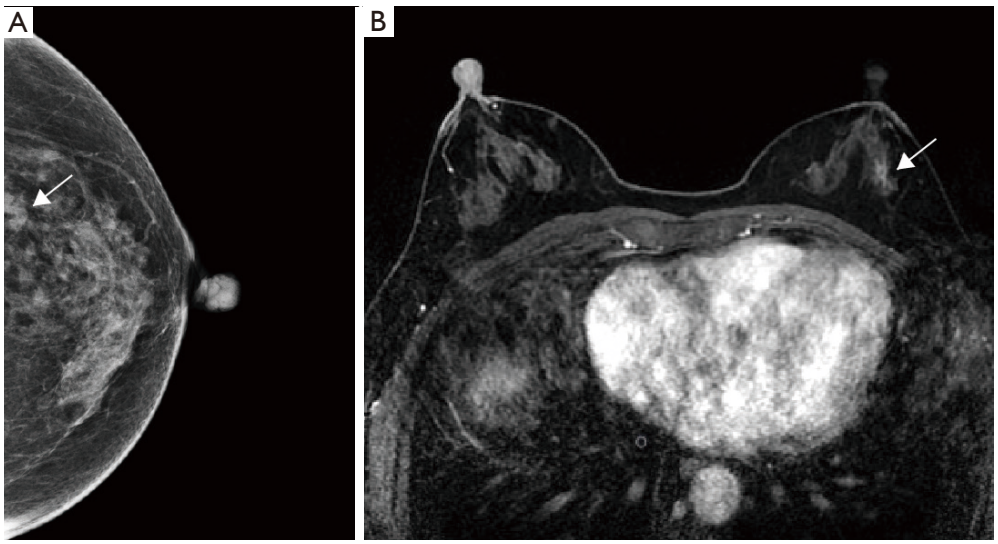

Figure 4 Female, 58 years old, with negative ultrasound finding. The mammography craniocaudal image (A) showed local architectural distortion in the deep lateral part of the left breast, BI-RADS 0. The MRI obtained in the post-contrast phase (B) showed a small, patchy enhanced area at three points in the left breast with local architectural distortion, which was consistent with the mammography, BI-RADS 4A. The pathology was confirmed to be sclerosing adenosis with low-grade DCIS. BI-RADS, Breast Imaging Reporting and Data System; MRI, magnetic resonance imaging; DCIS, ductal carcinoma in situ.

followed by mass, but the value of different X-ray signs for upgrading diagnosis was not found. For MRI, Preibsch *et al.* found the upgrade rates of NME and large lesions (>20 mm) were lower (11), whereas Okamoto *et al.* believed that the size and MRI features of lesions had no diagnostic value for the upgrade rate (24). Unlike previous research, the data in this study showed that the upgrade rate of HRLs with negative MRI findings was lower and the upgrade rate of HRLs with moderate and marked BPE was higher, but mass and NME had no diagnostic value for the upgrade of HRLs. For ultrasound, Giuliani *et al.* found that HRLs presenting as masses had a higher rate of upgrade (14). Our study found that HRLs with negative ultrasound manifestations had a lower rate of upgrade, while mass or other positive manifestations were not significantly associated with upgrade. In terms of diagnostic efficacy, we found that MRI was superior to mammography and ultrasound in diagnosing HRLs. MRI BPE was an independent factor in evaluating the upgrade of HRLs. A previous research has shown that BPE is influenced by hormone levels associated with age and the menstrual cycle and is a predictor of breast cancer risk (25). We found that BPE was a positive correlation indicator of the upgrade of HRLs, indicating that it could also indicate the correlation between HRLs and breast cancer risk, which could provide a reference for clinical decision-making in the follow-up treatment of HRLs.

In brief, our study has the following three advantages compared with other studies. First, we combined three imaging modes of mammography, ultrasound, and MRI for analysis, comparing the prediction efficiency of each mode. We found that MRI had the highest predictive efficacy, suggesting the importance of MRI follow-up for patients with HRLs. Second, we added features of breast parenchyma and found that BPE was an independent factor in predicting upgrade. Third, previous studies have proved that HRLs with AH are more likely to upgrade (17-19). To better determine the need for surgery, we further analyzed the factors that predicted the upgrade of HR-I and HR-II. We found that BPE was the only predictor of both groups and the odds ratio of BPE was highest. Based on this, we can infer that HR-I lesions with moderate to marked BPE are more suitable for surgery, and HR-II lesions with minimal to mild BPE can be considered for regular follow-up.

A limitation of our study is its retrospective design. We only included short-term follow-up data from 6 months to 1 year. Long-term follow-up monitoring of HRLs is still in progress. In addition, mammography in this study had no diagnostic value for the upgrade of HRLs. The reason may be that the analysis of image features is limited to the

main signs, such as mass and calcification. The density, margin, morphology of the mass, and the distribution and characteristics of calcification were not targeted. In the future, more detailed research will focus on 1 or 2 features.

Conclusions

In conclusion, our study showed an increased rate of upgrade and ER expression in HRLs with AH. For different modes of imaging examination, MRI had better diagnostic efficacy than ultrasound and mammography for the upgrade of HRLs. Age and the BPE of the MRI can be used as independent factors to predict the upgrade of HRLs. The imaging features and diagnosis of HRLs still need further testing and will depend on clinical, pathological, and imaging multidisciplinary cooperation.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-22-155/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-22-155/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-155/coif). The authors have no conflicts of interest to declare.

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 Medical Ethics Committee of Fudan University Shanghai Cancer Center, Shanghai, China (No. 1507149-8), and individual consent for this retrospective analysis was waived.

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