Indian Journal of Surgery (August 2023) 85(4):883–889
https://doi.org/10.1007/s12262-022-03591-1

ORIGINAL ARTICLE

# Clinical, Radiological and Pathological Correlation of Papillary Lesions of the Breast

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Received: 12 April 2022 / Accepted: 15 October 2022 / Published online: 8 November 2022


**Abstract**
Papillary lesions of the breast are a heterogenous group of neoplasms having varied clinical and radiological presentations and variable management and prognosis. They are difficult to diagnose leading to management dilemmas. This study aims to analyse the clinical presentations, radiological features and pathological characteristics of the patients with papillary breast lesions. This is a retrospective study of patients with papillary lesions of the breasts who underwent surgery in our institute. Medical records were retrieved, and clinical, radiological presentations were correlated with histopathological findings. In this study, 37 patients with 40 papillary lesions of breast (3 bilateral) were operated in 4 years. Median age was 62 years. Final histopathological diagnosis was benign papillary in 27 lesions (67.5%), atypical ductal hyperplasia in 3 lesions (7.5%) and malignancy in 10 lesions (25%). The radiological findings were concordant with pathological findings in 34 out of 40 lesions (85%) with a significant $p$ value of 0.006. However, malignancy was not accurately predicted using imaging alone (sensitivity 50%, specificity 96.67%, PPV 83.33% and NPV 85.29%). Core biopsy was inaccurate in 21.7% of lesions and showed a sensitivity of 62.5%, specificity of 100%, PPV of 100% and NPV of 83.33% in the diagnosis of malignancy. Though there is a good correlation between imaging modalities and histopathology findings in papillary lesions of the breast, upgrade rates to malignancy cannot be ignored. The underestimation rates of core biopsy are also high. Hence, surgical resection should be done for palpable papillomas and papillomas with atypia and also lesions with pathology-imaging discordance. Incidental and clear cut benign papillomas may be followed up with an individualised decision for resection.

**Keywords** Breast · Papillary lesions

## Introduction

Breast papillary lesions are rare tumours and have a wide spectrum of pathological features ranging from benign intraductal papillomas to high-grade invasive papillary carcinomas. Their heterogeneity makes an accurate diagnosis difficult leading to dilemmas in the management. They constitute less than 10% of benign breast lesions and less than 1% of malignant breast neoplasms [1–3]. Benign forms include intraductal papillomas and papillomatosis. Malignant papillary lesions include in situ forms (intraductal or intracystic papillary carcinoma) or invasive (invasive papillary carcinoma) [3].

Although the WHO has classified the papillary lesions differently, in this study, we have used the broader classification [4] in Table 1 in order to correlate with the imaging findings.

The presentation of papillary lesions in the breast is variable clinically, radiologically and pathologically. Clinically, a palpable mass or nipple discharge (bloody or serous) may [5] or may not [6] be present in papillary lesions.

On mammography, patients might have single or multiple bilateral lesions with or without microcalcifications. Mammography has a sensitivity and specificity of 78% for detecting papillary lesions by itself, and these increase to 91%

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**Table 1** Papillary breast lesion classification as used in our study

| | |
|---|---|
| Benign papillary lesions | 1. Intraductal papilloma (solitary)<br>2. Intraductal papillomatosis |
| Atypical papillary lesions | 1. Intraductal papilloma with atypical ductal hyperplasia |
| Malignant papillary lesions | In situ:<br>1. Papillary DCIS<br>2. Encapsulated papillary ca in situ<br>3. Solid papillary ca in situ<br>Invasive:<br>1. Invasive papillary ca<br>2. Solid papillary carcinoma with invasion<br>3. Encapsulated papillary carcinoma with invasion |

when ultrasound is also performed [7]. On ultrasound, the lesions can present as a complex intracystic lesions, homogeneous solid lesions or small intraductal lesions.

Fine-needle aspiration cytology is not useful in differentiating these lesions. Image-guided core biopsy is a better diagnostic modality. However, it can also be inaccurate as it may fail to pick up the subtle differences. Core biopsy may underestimate malignancy in up to 38% of cases [8]. Vacuum-assisted biopsy gives larger volume of tissue for more accurate characterization. However, a detailed examination of the whole lesion may be necessary because small foci of carcinoma in situ or an area of abruption of the myoepithelial layer might not be targeted in core/VAB biopsy. Hence, surgical excision may be required in most of the cases.

In this study, we evaluated the histologic findings, the clinical outcome and the radiologic features of patients with histologically proven papillary lesions and their role in the management of these patients.

### Aims and Objectives

This study aims to analyse the clinical presentations, radiological features and pathological characteristics of the patients of papillary breast lesions and to correlate these findings.

## Patients and Methods

This is a case series analysis of 37 female patients with 40 papillary breast lesions (3 patients had bilateral) diagnosed and operated in our institute from March 2017 to March 2021. Details regarding the clinical features, imaging findings and pathological reports were collected from medical database of our institution.

The following variables were evaluated—age, clinical presentation, imaging studies, histopathology reports and type of surgery performed.

Data analysis was performed by using SPSS (Statistical Package for Social Sciences) Version 27:0. Qualitative data variables were expressed by using frequency and percentage. Quantitative data variables were expressed by using Mean and SD, etc. Chi-square test was used to find the association between BIRADS score with histopathological outcome. Sensitivity, specificity, positive predictive value, negative predictive value (%), Kappa coefficient and diagnostic accuracy were calculated to find the concordance between radiological and histopathological findings for malignancy. A $p$-value $< 0.05$ was considered as significant.

## Results

During the 4-year period, a total of 37 female patients with 40 lesions (3 bilateral) with diagnosis of papillary lesions of breast were admitted for treatment in our institute.

The median age was 62 (range 27–88 years). Majority of the patients (77.5%) were older than 50 years of age.

Malignant invasive lesions were found in patients aged 60–73 years (median age 63.5) and in situ lesions were found in age group 57–73 years (median age 62.5). Benign lesions were seen in patients with median age of 62 (age group: 30–88 years). There was no significant correlation of age with malignancy in papillary lesions.

### Clinical Presentation

Out of the 37 patients, 36 were symptomatic, 1 patient had come for routine check-up. Out of 40 lesions, 14 (35%) were associated with only bloody nipple discharge, 20 (50%) were associated with only painless lump in the breast, 3 (7.5%) were associated with both bloody nipple discharge and lump and 2 (5%) were associated with painful lump.

None of the clinical features had any correlation with malignancy as seen in Table 2A ($p$ value = 0.411).

### Radiological Findings

Mammography was done for 23 patients, and sonography was done for all 40 lesions.

**Table 2** Correlation of clinical symptoms, imaging findings and radiological diagnosis with histopathological diagnosis

| | Histopathology | | | |
|---|---|---|---|---|
| A: Clinical symptoms | Malignant | atypical | Benign | Total |
| Painless lump | 6 | 2 | 12 | 20 |
| Bloody nipple discharge | 3 | 1 | 10 | 14 |
| Painful lump | 1 | | 1 | 2 |
| Lump + bloody nipple discharge | | | 3 | 3 |
| B: Imaging findings | | | | |
| Solid lesion | 3 | 2 | 7 | 12 |
| Complex solid cystic lesion | 1 | | 3 | 4 |
| Dilated ducts with intraductal lesion/debris | 3 | 1 | 12 | 16 |
| Complex cysts | 0 | | 3 | 3 |
| Asymmetrical density | 2 | | 2 | 4 |
| Solid spiculated lesion | 1 | | | 1 |
| Microcalcifications | 4 | | 6 | 10 |
| Hypervascularity | 4 | | 2 | 6 |
| Microcalcifications + hypervascularity | 2 | | | 2 |
| C: Radiological diagnosis | | | | |
| Malignant (BIRADS 5) | 5 | 0 | 1 | 6 |
| Suspicious for malignancy (BIRADS 4a and 4b) | 4 | 1 | 12 | 17 |
| Benign (BIRADS 2,3) | 1 | 2 | 14 | 17 |

*p* value for this data is 0.006 which shows significant radiologic-pathological correlation

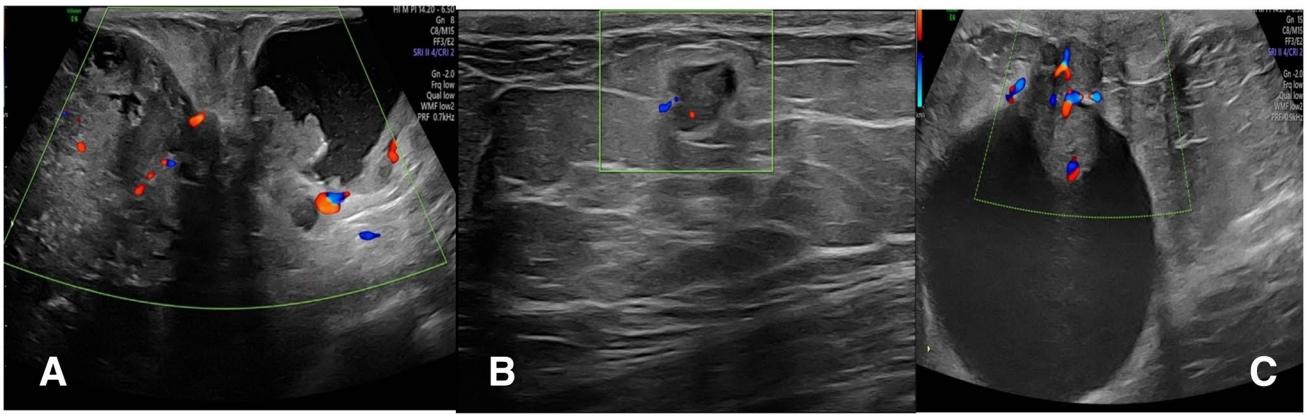


**Fig. 1** **A** USG of left breast showing large solid cystic complex lesion with solid component showing irregular margins, calcifications and vascularity BIRADS 5; **B** USG of right breast showing solid hyperechoic asymmetrical density and perilesional oedema with prominent vascularity within. BIRADS 4b; **C** USG showing evidence of well-circumscribed bilobed solid cysts in contact with nipple with vascularity within s/o intracystic papillary tumour, BIRADS 4b

On imaging (mammography + sonography), 12 lesions (30%) were purely solid, 4 lesions (10%) were solid cystic lesions (Fig. 1C), 3 lesions (7.5%) were complex cysts, 16 lesions (40%) were associated with dilated ducts with debris/intraductal lesions, 4 lesions (10%) were asymmetrical densities (Fig. 1B) and 1 lesion was solid spiculated (Fig. 2B).

Apart from these primary radiological features, few additional characteristics were assessed. Ten lesions (25%) had microcalcifications, 6 lesions (15%) had increased vascularity (Fig. 1C) and 2 lesions (5%) had both microcalcifications and hypervascularity (Fig. 1A) on imaging and were found to be malignant on hpe (Table 2B).

MRI was done for only 1 patient in our study which was suggestive of multiple papillomas (MRRADS 3).

## BIRADS Categorization

Out of 37 patients with 40 lesions, 6 lesions (15%) were estimated to be malignant in radiological evaluation

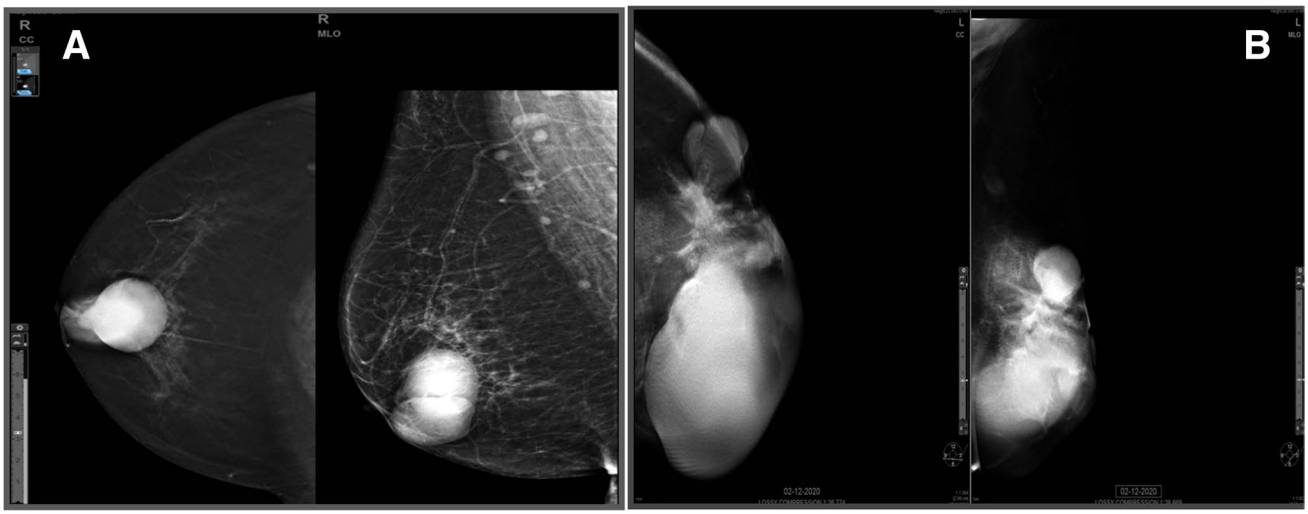


**Fig. 2** **A** Mammography showing a well-circumscribed high-density bilobed solid cystic lesion in the retroareolar region in right breast with no associated microcalcifications; **B** mammography image of left breast showing large high-density well-circumscribed lesion with foci of coarse microcalcifications in UOQ. Focal spiculated lesion with skin involvement seen. BIRADS 5

**Table 3** Comparison of radiological diagnosis with histopathological diagnosis

| | Histopathology | | |
|---|---|---|---|
| Radiology | Malignant | Atypical + benign | Total |
| Malignant | 5 | 1 | 6 |
| Suspicious + benign | 5 | 29 | 34 |
| Total | 10 | 30 | 40 |

(BIRADS 5) (Fig. 2B), 17 lesions (42.5%) were suspicious for malignancy (BIRADS 4a and b) (Fig. 2A) and the rest 17 lesions (42.5%) had benign radiological findings (BIRADS 2 and 3). There were no patients characterized as 4c.

When comparison was done between BIRADS reporting and final histopathological diagnosis, among all BIRADS 4 cases (17), 4 upgraded to malignancy, 1 had atypia and 12 downgraded to benign. Out of all BIRADS 2 and 3 cases (17), 1 upgraded to malignancy and 2 upgraded to atypia (Table 2C).

The sensitivity, specificity, NPV and PPV for the radiology have been calculated using Table 3. We have combined the atypical with benign lesions as the treatment for both remains the same.

Sensitivity of breast imaging (mammography and sonography) in diagnosis of papillary lesions of breast is 50%, specificity is 96.67%, PPV is 83.33% and NPV is 85.29%. Kappa value for the correlation of radiological and histopathological findings is 53.84. Diagnostic accuracy of the imaging modality is 85%.

## Pathological Diagnosis

In our study, for preoperative diagnosis, USG-guided core biopsy was done for 23 lesions, and 9 lesions were treated with microdochectomy after imaging without a core biopsy since they were too small to biopsy. Three lesions underwent FNAC, 1 lesion underwent VAB resection, intraoperative frozen section done for 2 lesions, 1 patient was incidentally diagnosed on abscess wall biopsy and 1 USG-guided lumpectomy was done for diagnosis.

The postoperative histopathological diagnosis was benign papillary (papilloma (Fig. 3A)/papillomatosis) in 27 lesions (67.5%), atypical, i.e. papilloma with atypical ductal hyperplasia in 3 lesions (7.5%), and malignant in 10 lesions (25%), which includes malignant in situ in 6 lesions (i.e. papilloma with foci of DCIS (Fig. 3C): 3, solid papillary carcinoma in situ (Fig. 3B): 3) and invasive in 4 lesions (i.e. invasive papillary carcinoma: 1, solid papillary invasive ductal carcinoma: 2, encapsulated papillary carcinoma with invasion: 1).

IhC was performed using combination markers (ER p63, HMWCK and calponin) to classify lesions to respective categories.

Out of the 23 lesions for which core biopsy was done, 5 were reported to be malignant, and 18 were reported to be benign. Out of the 18 benign lesions, 3 upstaged to be malignant on final histopathology and 2 reported as benign on core biopsy were found to be atypical on final hpe. When comparing the pathologic core biopsy result with surgical tissue, it was observed that core biopsy was discordant with final diagnosis in 21.73% cases.

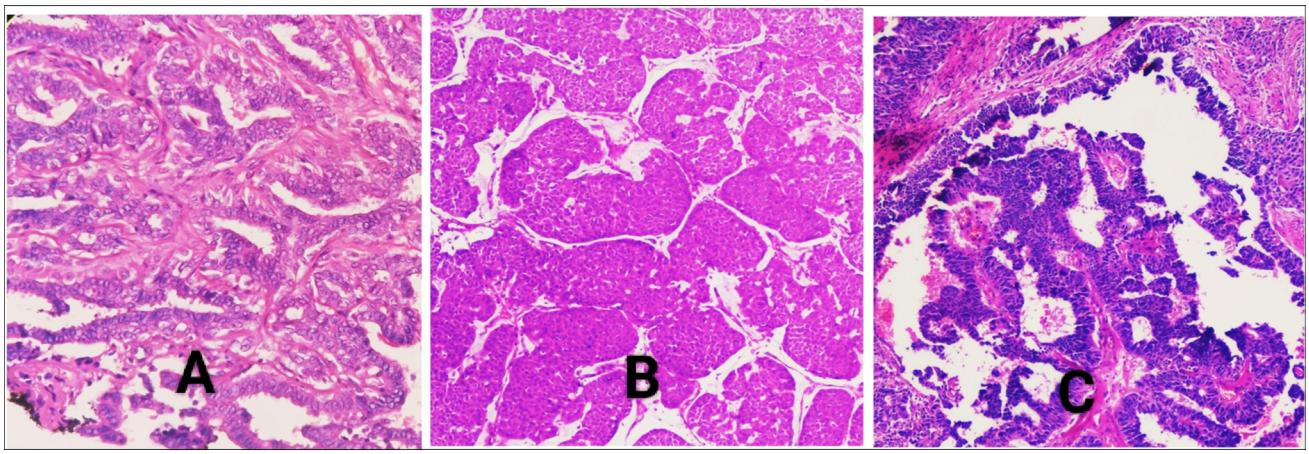


**Fig. 3** **A** Benign intraductal papilloma-epithelial and myoepithelial cells (vacuolated) are present in papillary area. **B** Solid papillary carcinoma—circumscribed, large cellular nodules separated by bands of dense fibrosis network of fibrovascular cores, but discrete papillae are not identified (H&E 40×); **C** papillary DCIS-papillary fronds containing prominent fibrovascular septa projecting into duct lumen (H&E 40×)

Out of 3 lesions for which FNAC was done, 2 were reported as benign and 1 as malignant, and out of the 2 reported benign, 1 upstaged to malignancy. Out of 8 microdochectomy specimens, 1 microdochectomy specimen was found to be malignant, and 1 was found to be atypical.

### Treatment

On imaging we had 6 malignant lesions for which 5 breast conservative surgeries were done and 1 modified radical mastectomy was done.

For 2 lesions, initially presenting with complains of nipple discharge, microdochectomy was done, but as in the final hpe, there was a component of ductal carcinoma in situ; they underwent completion mastectomy.

Two patients had initially undergone lumpectomy in view of benign radiology, but as the final hpe report was invasive carcinoma, they underwent revision surgery (breast conservation surgeries with sentinel node biopsies).

For benign lesions, 12 lump excisions were performed for palpable lump, 1 simple mastectomy was done for large benign lump, 7 microdochectomies were performed for benign papillomas, 3 segmental resections were done for multiple papillomas, 1 breast abscess incision and drainage was done (wall biopsy was benign papilloma), 2 Hadfield's procedures were performed for multiple papillomas and 1 vacuum assisted biopsy resection was done for a benign papilloma.

For atypical lesions, 1 microdochectomy was done, 2 lumpectomies were performed based on benign radiology, and as they were atypical on final histopathology, they were followed up closely.

Adjuvant treatment was given in all malignant cases according to their staging and biology. Chemotherapy was given to high-risk patients with node positive, larger tumours, especially with hormone receptor negative status. Radiotherapy was given to all breast conservative surgery patients and mastectomy patients who had T3 or node-positive tumours. Hormone therapy was given to all hormone receptor-positive patients.

## Discussion

Papillary lesions of the breast comprise a vast spectrum of diseases, leading to confusion in diagnosis and management. The reported upgrade rates to malignancy among benign papilloma vary widely from 0 to 33% [9–15]. Hence, their treatment is controversial. There is a consensus that papillomas with atypical pathological features justify surgical excision, because they are associated with a high rate of coexisting carcinomas [16]. However, there is no consensus on the optimal treatment of simple papillomas without atypia [17–21].

Atypical papillary lesions are more difficult to diagnose and treat and are pathologically defined as papillomas with few or absent myoepithelial cells and having a focus of monotonous cells along with features of low-grade ductal neoplasia [22]. Immunohistochemistry is useful to make distinctions regarding the extent of atypia [23]. Sampling errors, limited amount of material and heterogeneity of the tissue, make histological distinction between benign and atypical lesions difficult [24].

Papillary carcinomas accounts for fewer than 2% of all breast cancers (classified as invasive and non-invasive) [25]. Non-invasive papillary carcinomas are subdivided into encapsulated papillary carcinoma, solid papillary carcinoma

and papillary ductal carcinoma in situ. The invasive types are divided into invasive papillary carcinoma, solid papillary invasive ductal carcinoma and encapsulated papillary carcinoma with invasion [26]. It is important to differentiate between invasive and non-invasive types because of the prognostic significance [27]. Papillary ductal carcinoma in situ (non-invasive) is associated with extensive disease but low risk of invasion. Encapsulated papillary carcinoma has high risk of local recurrence but low risk of invasion. Solid papillary carcinoma has good prognosis; low risk of invasion and metastasis is rare. Invasive papillary carcinoma has good prognosis [28].

In our hospital, 2548 patients had visited the breast clinic in 4 years of our study, out of which 37 patients underwent surgery for papillary lesions of breast (incidence = 1.45%). This incidence appears low because these are only operated cases. There would be many patients with papillary lesions of the breast who would have been put on follow-up considering they were clear cut benign (clinically, radiologically and core biopsy proven) or patient not willing/not fit for surgery. Some patients were lost to follow-up after being advised surgery, for which accurate data is not available and thus are not included.

In our study, there was no path gnomic feature for malignancy on imaging. All patients had abnormal imaging with most frequent finding being that of BIRADS 4 (42.5%) consistent with published literatures [29]. Among these BIRADS 4 lesions, there was an upgrade rate of 23.5% for malignancy. Other authors have also reported similar upgrade rates [29]. Also, it is interesting to note that 70.5% of BIRADS 4 lesions downgraded to benign pathologies after final histopathology report. This is probably due to the fact that they were BIRADS 4 a and b and not c.

From our data, the sensitivity, specificity, PPV and NPV of breast imaging (mammography and sonography) in diagnosis of papillary lesions of breast is 50%, 96.67%, 83.33% and 85.29%, respectively. Kappa value for the correlation of radiological and histopathological findings is 53.84. Diagnostic accuracy of the imaging modality is 85%. These results indicate a good correlation between imaging and histopathology diagnosis, but the significant upgrade rates have to be considered.

When comparing the core biopsy result with that of final surgical tissue biopsy, an underestimation of malignant lesions was observed. In our study, the core biopsy underestimated malignancy/atypia in 21.73% cases. Rizzo et al. reported on 101 cases, an underestimation of malignant lesions in 24.5% of the cases [30]. In a series of Jaffer et al., out of 104 patients with core biopsy diagnosis of breast papillomas without atypia, 16.4% showed atypia or malignancy on surgical biopsy [31].

The frequency of malignancy in our study of papillary lesions was 25%. It is comparable to the study by Dahiana Pulgar Boin et al. of 70 patients which reported a high frequency of malignancy (21.4%). Similarly in a study by Valdes EK et al., 19 out of 80 lesions (24%) that underwent surgical excision were found to be malignant [29]. Hence, the findings of all these studies including ours imply that surgical resection should be recommended for papillary breast lesions [32].

This study is an attempt to better understand the clinical features, imaging findings and histopathological correlation of papillary lesions of the breast. Also, there is very limited Indian data on papillary breast lesions which makes it a good reason to do this study on Indian patients.

Our study has a few limitations. Since the sample size is small due to the rarity of the disease, it is difficult to draw conclusions. We have included only those patients in our study who have undergone surgical excision, and hence the final histopathology report is available. There would also be many benign cases who would have had conservative treatment/follow-up and thus would have been missed.

## Conclusion

Diagnosis of papillary lesions of the breast is extremely challenging preoperatively. Imaging modalities are very good for detection but not sensitive enough to differentiate between benign and malignant papillary lesions accurately. Though there is a good correlation between imaging modalities and histopathology findings in papillary lesions of the breast, upgrade rates to malignancy cannot be ignored. The underestimation rates of core biopsy are also high. Hence, surgical resection should be done for palpable papillomas and papillomas with atypia and also lesions with pathology-imaging discordance. Incidental benign papillomas may be followed up with an individualized decision to excise according to risk factors and symptoms.

#### Declarations

I am submitting a manuscript entitled "Clinical, Pathological and Radiological Correlation of Papillary Lesions of Breast", for consideration of publication in Indian Journal of Surgery.
I affirm that it has not been published elsewhere and that it has not been submitted simultaneously for publication elsewhere.
This study compares the clinical, radiological and pathological characteristics of patients with papillary lesions of breast. It emphasizes the need for surgical management of patients presenting with papillary lesions of breast. We believe that these findings will be of interest to readers of your Journal.
We have no conflict of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome. As corresponding author, I confirm that the manuscript has been read and approved for submission by all the named authors.

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