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Upgrade risk in intraductal papillomas: A retrospective analysis of real-world data and predictive model development

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ABSTRACT

Background: In current practice, the traditional strategy of excising all IDPs has been replaced by more selective management. However, criteria for selecting patients for surveillance remain unclear, and no widely accepted predictive model exists.
Methods: We retrospectively analyzed real-world data from 325 cases of IDPs diagnosed via core needle biopsy (CNB) at a tertiary teaching hospital between 2010 and 2023. We assessed upgrade rates to malignancy and evaluated potential predictive factors. Two previously published models were applied to our cohort, and a new model was developed based on our data.
Results: Overall, 17% (55/325) of IDPs were upgraded to malignancy. Among lesions without atypia on CNB ($n = 215$), the upgrade rate was 8.8% (19/215), compared to 40% (23/58) in those with atypia ($p < 0.001$). Previously suggested models yielded modest results when applied to our study population. First model would have spared 11% (24/215) of patients from surgery, while the second model would have spared 17% (36/215), with one missed upgrade. Our model identified all upgraded cases and would have spared 33% (72/215) of non-atypical IDPs from surgery.
Conclusions: Atypia on CNB is a strong predictor of upgrade to malignancy. Existing models showed limited utility in reducing unnecessary surgeries. Our proposed model demonstrated improved performance and may support more individualized management of IDPs.

1. Introduction

Intraductal papillary lesions of the breast are classified as having uncertain malignant potential. [1,2]. They encompass a spectrum of conditions including papillomas with and without atypia and various malignant lesions. These malignant lesions can be further divided into subtypes, consisting of papillary ductal carcinoma in situ (DCIS), encapsulated papillary carcinoma (EPS), solid papillary carcinoma and invasive papillary carcinoma [3]. On core needle biopsy (CNB), intraductal papillary lesions are typically classified as B3 (lesions of uncertain malignant potential), although malignant papillary lesions are classified as B5 (malignant) and some completely excised benign papillomas may be classified as B2 (benign) [2,4]. Intraductal papillomas (IDPs) are proliferations of the breast ducts in which epithelial finger-like projections with fibrovascular cores protrude into the ductal lumen. [3,5]. Clinically, papillary lesions are often asymptomatic, but they may present with nipple discharge or palpable masses [5].

The diagnosis of IDPs involves a combination of clinical findings, radiological assessments and pathological findings. With the increasing use of screening mammography and advances in imaging and biopsy techniques, the number of diagnosed and incidentally detected IDPs has increased [1,6,7].

Traditionally, the recommended treatment approach for IDPs associated with atypia has been surgical excision [1,2,4,8]. The risk of a papilloma upgrading to malignancy or being associated with malignancy supports the decision to manage the lesions surgically [9]. Conversely, the recommendations regarding non-atypical IDPs have been updated since the introduction of vacuum assisted biopsy (VAB) -technique. Modern guidelines propose active surveillance in case of relatively small and non-atypical IDPs when a VAB yields complete excision verified with imaging control [1,2,8]. However, if a CNB reveals non-atypical IDP, further excision is indicated (VAB or diagnostic excision) especially if imaging and the CNB results are discordant [4,8].

Based on the current literature, the risk of IDPs progressing to

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malignancy varies considerably. IDPs exhibiting atypia have been associated with upgrade rates typically around 30%, with some studies reporting rates as high as 77%, although these high rates have been observed mainly in smaller sample studies [10,11]. In contrast, non-atypical IDPs demonstrate significantly lower upgrade rates, ranging from 0% to 33%, but most often less than 10% [6,10–12]. Because some studies have reported very low risk, some researchers have questioned the need for surgical excision when managing non-atypical IDPs, particularly in light of studies suggesting that, with proper predictive models, patients at low risk for malignancy could be managed with follow-up instead of surgery thus sparing women from surgical intervention [6,12–14]. However, no consensus has been reached on this issue.

The aim of our study was to investigate real-world data on the upgrade rate to malignancy of IDPs at a single university hospital, evaluate the diagnostic methods used, and identify predictive factors that could be applied to screening patients for elective surgery and optionally for follow-up. Additionally, we tested existing predictive models [6,12] within our study population to evaluate their accuracy and applicability.

2. Materials and methods

We performed a retrospective study of all IDPs diagnosed by CNB that underwent diagnostic excision between the years 2010 and 2023 at Turku University Hospital. This is the only public hospital in the district, serving a population of approximately 0.5 million, that provides surgical treatment, and thus the risk of selection bias should be minimal. The patients were referred to the hospital from primary health care, where the CNB was also performed.

The dataset includes all patients treated at Turku University Hospital during the study period, effectively constituting a consecutive patient series. Data were retrieved from the hospital's patient records system for all patients who had undergone a procedure with Nordic Medico-Statistical Committee (NOMESCO) code initiating with HAB (partial excision of mammary gland) without a documented cancer diagnosis, including all diagnostic breast procedures [15]. The primary data did not include diagnostic information, and therefore, information on the diagnosis was obtained by reviewing the patient records individually. Initially, the study cohort included patients with IDPs diagnosed by CNB, including cases with atypical histopathological features and cases with radiology-pathology discordance. We excluded patients who were diagnosed using ductography without subsequent CNB and those who presented with malignancies on CNB. Exclusion process is presented in Fig. 1. All patients for whom both the CNB and the final histopathological reports were available were included in the cohort, even if other data were missing. VAB did not become available at our institution until at the very end of our study period, therefore cases diagnosed with VAB were excluded. We conducted a review of referrals to our hospital, as well as appointment records, radiology, pathology, and surgery reports from our hospital.

Recorded clinical information included patient's age at the time of surgery, reason for referral to our hospital, lesion palpability, previous or concurrent breast cancer (BC), family history of breast cancer, body mass index (BMI), chest circumference, bra size, use of hormone replacement therapy (HRT), parity, smoking history and history of hysterectomy.

Documented imaging findings included the main finding on mammogram and ultrasound, presence of ductal dilatation, lesion shape, number of lesions, type of echo on ultrasound, presence of microcalcifications, lesion size, location on imaging and whether preoperative magnetic resonance imaging (MRI) was performed. Additionally, we recorded possible suggestion of diagnosis by a radiologist.

Documented histopathological findings from CNBs included presence of ductal hyperplasia, atypia, apocrine metaplasia and suspicion of malignancy. Atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS) were considered as atypical findings.

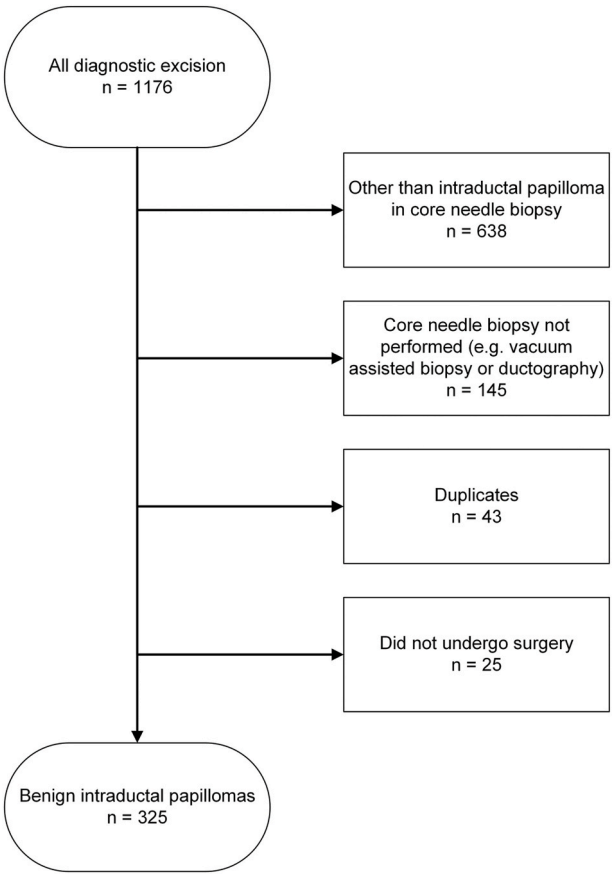

Fig. 1. Consort diagram of the exclusion process.

In a small number of cases, CNB demonstrated focal architectural or immunohistochemical features raising suspicion for malignancy (e.g. absence of myoepithelial cells), without cytological atypia or a definitive malignant diagnosis. These few cases were classified as non-atypical.

Considering the histopathological report of the subsequent excisional biopsy, we collected the information on final diagnosis of the lesion, lesion size and whether lesion was upgraded to malignancy. Upgrade to malignancy was defined as the presence of carcinoma in situ or invasive breast carcinoma. The detection of high-risk lesions, including ADH, ALH or LCIS, on excision was not considered an upgrade to malignancy.

The literature review identified two studies presenting predictive models for selecting patients for surgical intervention or surveillance. A model by Lee et al. [12] included the following factors: radiology-pathology discordance, palpable mass or nipple discharge as symptoms, age 60 years and older, lesion size 10 mm or over in imaging, and presence of four or more concurrent peripheral papillomas. Another model proposed by Zhang et al. [6] constituted of ten predictive factors including BI-RADS classifications 5, 4B and 4C, mass and calcifications on mammogram, symptom of bloody nipple discharge, radiologic-pathologic discordance, peripheral location of the IDP, palpable mass, microcalcifications and lesion size 10 mm or larger on imaging.

We evaluated these models within our study population by excluding cases in which one or more of the model criteria were present. Because both models were developed on benign, non-atypical IDPs, we evaluated the models only in the subset of our cohort without atypia on CNB. In the remaining cases, we calculated the risk of upgrade. This approach allowed us to theoretically examine what occurred in cases that would

not have been selected for surgical intervention based on the predictive models.

2.1. Ethics approval and consent to participate

This study was conducted retrospectively from data obtained for clinical purposes. The research protocol of the study was approved by the Hospital District of Southwest Finland (T981/2024). No additional preregistration was performed. No ethical approval was required for this retrospective study and informed consent was waived.

3. Statistical analysis

Continuous variables, which followed normal distribution, were described with mean and range. Variables that did not follow normal distribution were described using median and interquartile range (IQR). Categorical variables were summarized with counts and percentages. Categoric variables were compared between the upgrade and non-upgrade group using chi-square test or Fisher's exact test. The upgrade rate was defined by calculating the percentage of IDPs upgraded to malignancy at surgical excision from all IDPs diagnosed on CNB. Receiver Operating Characteristic (ROC) analysis was performed to evaluate the performance of the proposed predictive model. A significance level of 0.05 was used. All statistical analysis were performed with JMP®, Version 17.0 Pro (SAS Institute Inc., Cary, NC, 1989-2019.)

4. Results

A total of 325 IDPs diagnosed by CNB were included in this study. Overall, in 17% (55 of 325) of cases the IDP was upgraded to malignancy. Most frequent upgrades were to DCIS with 28 cases, to DCIS combined with IDC adding up to ten cases and to papillary carcinoma in situ with five cases. All upgraded cases, along with the number of discovered malignancies, are presented in Table 1.

In 215 cases the IDP had no atypical histopathological features on CNB, of which 8.8% (19 of 215) were upgraded to malignancy after surgical excision. Conversely, atypical features were present in 58 cases, with an upgrade risk of 40% (23 of 58). Thus, atypia was strongly associated with the risk of upgrade ($p < 0.001$). Histopathological findings are presented in Table 2. The presence of apocrine metaplasia was found to be associated with a lower risk of upgrade in IDPs with and without atypia ($p < 0.001$) as well as in non-atypical IDPs ($p = 0.006$). In five cases, CNB findings raised suspicion for malignancy without definitive atypia. All five cases were upgraded on surgical excision ($p < 0.0001$): two were diagnosed as DCIS, two as invasive ductal carcinoma, and one as papillary carcinoma in situ.

The clinical characteristics of the study population are presented in Table 3. We found that older age at the time of surgery was associated with higher risk of upgrade ($p < 0.001$). We also discovered that a history of hysterectomy ($p = 0.001$) and nulliparity ($p = 0.049$) were associated with the upgrade risk. For IDPs without atypia nulliparity was not associated with the upgrade risk. We found that a strong family history of breast cancer, defined as breast cancer appearing in siblings or the mother, was associated with a higher upgrade risk ($p = 0.032$). Lastly, clinically palpable mass was more common among the upgraded cases, but the association to upgrade did not reach statistical significance ($p = 0.252$).

Table 1
Malignancies of the upgraded IDPs.

Malignancy	N (%)
Ductal carcinoma in situ (DCIS)	28 (51)
DCIS with invasive ductal carcinoma (IDC)	10 (18)
Papillary carcinoma in situ (PCIS)	5 (9.1)
IDC	4 (7.3)
DCIS with PCIS	2 (3.6)
DCIS with encapsulated papillary carcinoma (EPC)	2 (3.6)
Invasive lobular carcinoma (ILC)	1 (1.8)
DCIS with ILC	1 (1.8)
DCIS with IDC and ILC	1 (1.8)
Metaplastic carcinoma	1 (1.8)
Total	55 (100)

Table 2
Association of histopathological features with upgrade to malignancy.

Feature	All (n = 325)	Not Upgraded (n = 270)	Upgraded (n = 55)	Upgrade Rate (%)	p-value
Atypia, % (n)					<0.001
Yes	18 (58)	13 (35)	42 (23)	40	
No	66 (215)	73 (196)	36 (19)	8.8	
Indeterminate	1.2 (4)	0.0 (0)	7.3 (4)	100	
Missing data	15 (48)	14 (39)	16 (9)	19	
Apocrine metaplasia, % (n)					<0.001
Yes	26 (85)	30 (80)	9.1 (5)	5.9	
No	59 (191)	56 (152)	71 (39)	20	
Nonspecific	0.62 (2)	0.0 (0)	3.6 (2)	100	
Missing data	14 (47)	14 (38)	16 (9)	19	

Imaging findings are comprised in Table 4. Shape of the lesion in mammogram and ultrasound was associated with risk of upgrade after excision in IDPs with and without atypia ($p = 0.011$) as well as in non-atypical IDPs ($p = 0.028$). In 192 (59 %) cases the shape of the lesion was not reported. Secondly, the presence of microcalcifications was associated with the risk of upgrade among IDPs with and without atypia ($p = 0.031$). However, for non-atypical IDPs the presence of microcalcifications did not associate with the risk of upgrade. In eight cases, the lesion was considered radiologically suspicious for malignancy. Of these, four cases (50%) were upgraded: three to DCIS and one to metaplastic carcinoma. Lastly, we found that lesion size was greater among the upgraded IDPs with and without atypia ($p = 0.014$) and that lesion size was associated with lesion palpability ($p = 0.005$).

We tested two predictive models within our study population by excluding cases in which one or more of the model criteria were present. In the remaining cases, we calculated the risk of upgrade.

By applying Lee et al.'s predictive model [12] to our dataset, only 11% (24/215) of patients would have been spared from surgery. Additionally, among these 24 cases, no upgrades were observed after surgical excision, indicating that all upgraded lesions were successfully identified using this model.

Secondly, according to the model by Zhang et al. [6], applying surgical treatment to cases with one or more of the model's criteria would have resulted in 17% (36 of 215) of non-atypical IDPs being spared from surgery. Among these 36 cases, one lesion was upgraded after excision, and it was reported to be a papilloma with adjacent DCIS in the final pathology report.

Based on the present data, previously published results by other researchers and clinical experience, we developed a predictive model by utilizing factors associated with a higher upgrade risk as exclusion criteria, as illustrated in Fig. 2. After empirically testing several variable combinations, the following five criteria remained: patient age being 60 years or older, a palpable mass in clinical exam, lesion size $\geq$20 mm in imaging exam, presence or unknown status of atypia on CNB and suspected malignancy according to radiology or pathology report.

If patients had been selected for surgery based on the presence of any of the five factors mentioned, 33% (72 of 215) of IDPs without atypia could have been spared using this model and no upgrades would have been left unidentified. This model reached an area under the curve (AUC) of 0.84, with the ROC curve presented in Fig. 3. Using a 10% cutoff probability, the model yielded a sensitivity of 50% (134/270) and a specificity of 95% (52/55). However, this threshold resulted in three missed upgrades, making the model presented in Fig. 2 the more

Table 3
Association of clinical characteristics with upgrade to malignancy.

Feature	All (n = 325)	Not Upgraded (n = 270)	Upgraded (n = 55)	Upgrade Rate (%)	p-value
Age at surgery in years, Mean (range)	59 (25–89)	57 (25-88)	67 (42-89)		<0.001
Body mass index, Median (Q1, Q3)	27.0 (24.0, 31.0)	26.8 (23.8, 31.0)	27.7 (24.3, 31.1)		0.218
Smoking history, % (n)					0.982
Smoker	9.5 (31)	9.6 (26)	9.1 (5)	19	
Previous smoker	8.0 (26)	8.2 (22)	7.3 (4)	15	
Never smoker	81 (263)	80 (217)	84 (46)	17	
Missing data	1.5 (5)	1.9 (5)	0.0 (0)	0.0	
Use of hormone replacement therapy, % (n)					0.073
Systemic	15 (48)	14 (39)	16 (9)	19	
Local	8.9 (29)	8.2 (22)	13 (7)	24	
Both	4.6 (15)	3.3 (9)	11 (6)	40	
Never	65 (212)	68 (183)	53 (29)	14	
Missing data	6.5 (21)	6.3 (17)	7.3 (4)	19	
Hysterectomy, % (n)					0.001
Yes	21 (67)	17 (47)	36 (20)	30	
No	79 (258)	83 (223)	64 (35)	14	
Nulliparous, % (n)					0.049
Yes	11 (37)	12 (33)	7.3 (4)	11	
No	79 (258)	77 (208)	91 (50)	19	
Missing data	9.2 (30)	11 (29)	1.8 (1)	3.3	
Prior or concurrent breast cancer, % (n)					0.080
Yes	3.4 (11)	2.6 (7)	7.3 (4)	36	
No	97 (314)	97 (263)	93 (51)	16	
Reported strong family history of breast cancer, % (n)					0.032
Yes	19 (62)	17 (47)	27 (15)	24	
No	62 (203)	62 (167)	65 (36)	18	
Missing data	18 (60)	21 (56)	7.3 (4)	6.7	
Reason for seeking care, % (n)					0.507
Palpable mass	16 (52)	15 (41)	20 (11)	21	
Nipple discharge	31 (102)	33 (89)	24 (13)	13	
Screening	38 (124)	37 (99)	45 (25)	20	
Incidental finding	7.1 (23)	7.4 (20)	5.5 (3)	13	
Other symptoms	6.1 (20)	6.7 (18)	3.6 (2)	10	
Missing data	1.2 (4)	1.1 (3)	1.8 (1)	25	
Lesion palpability, % (n)					0.252
Yes	24 (79)	22 (61)	33 (18)	23	
No	63 (206)	65 (176)	55 (30)	15	
Missing data	12 (40)	10 (33)	12 (7)	17	

Table 4
Association of imaging findings with upgrade to malignancy.

Feature	All (n = 325)	Not upgraded (n = 270)	Upgraded (n = 55)	Upgrade rate (%)	p-value
Lesion shape, % (n)					**0.011**
Round	16 (53)	14 (39)	25 (14)	26	
Spiculated	3.7 (12)	2.6 (7)	9.1 (5)	42	
Circumscribed, not round	21 (68)	23 (61)	13 (7)	10	
Nonspecific	59 (192)	60 (163)	53 (29)	15	
Number of lesions, % (n)					0.360
1	81 (263)	80 (215)	87 (48)	18	
2	11 (36)	11 (30)	11 (6)	17	
Multiple	7.1 (23)	8.1 (22)	1.8 (1)	4.4	
Missing data	0.92 (3)	1.1 (3)	0.0 (0)	0.0	
Microcalcifications, % (n)					0.031
Yes	24 (77)	21 (57)	36 (20)	26	
No	62 (203)	64 (172)	56 (31)	15	
Missing data	14 (45)	15 (41)	7.3 (4)	14	
Ductal dilatation, % (n)					1.00
Yes	20 (65)	20 (54)	20 (11)	17	
No	80 (258)	79 (214)	80 (44)	17	
Missing data	0.62 (2)	0.74 (2)	0.0 (0)	0.0	
Hypoechoic on ultrasound, % (n)					0.201
Yes	26 (84)	24 (66)	33 (18)	21	
Nonspecific	74 (241)	76 (204)	67 (37)	15	
Lesion size in millimeters, median (Q1, Q3)	9 (6.3, 14)	9 (6, 13)	10 (7, 19)		0.014
Location of lesion					0.399
Broad	1.5 (5)	1.5 (4)	1.8 (1)	20	
Peripheral	15 (49)	13 (36)	24 (13)	27	
Central	56 (181)	57 (153)	51 (28)	15	
Intermediate	9.9 (32)	10 (28)	7.3 (4)	13	
Missing data	18 (58)	18 (49)	16 (9)	16	
Suspected diagnosis by a radiologist, % (n)					0.130
Papilloma	34 (111)	35 (94)	31 (17)	15	
Fibroadenoma	7.7 (25)	8.5 (23)	3.6 (2)	8	
Cyst	2.5 (8)	3.0 (8)	0.0 (0)	0.0	
Malignancy	6.2 (20)	4.8 (13)	13 (7)	35	
Nonspecific	50 (161)	49 (132)	53 (39)	18	

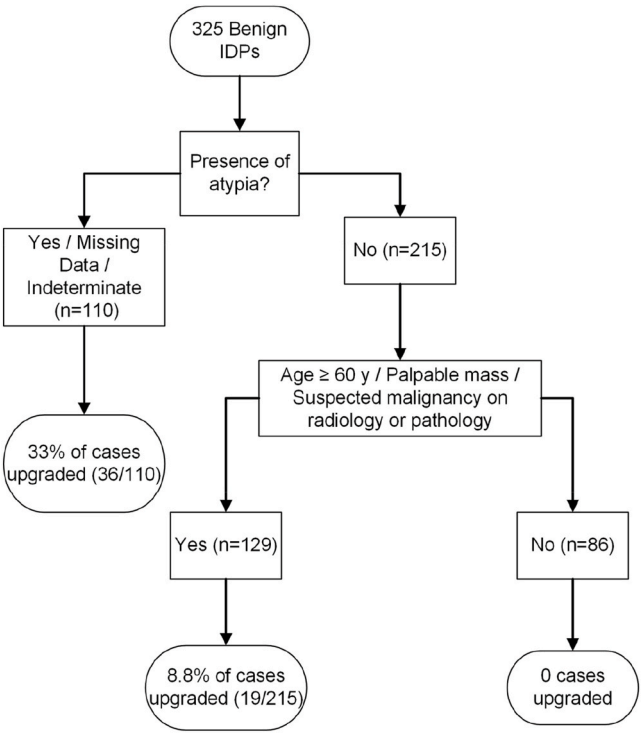

Fig. 2. Predictive model for current study population.

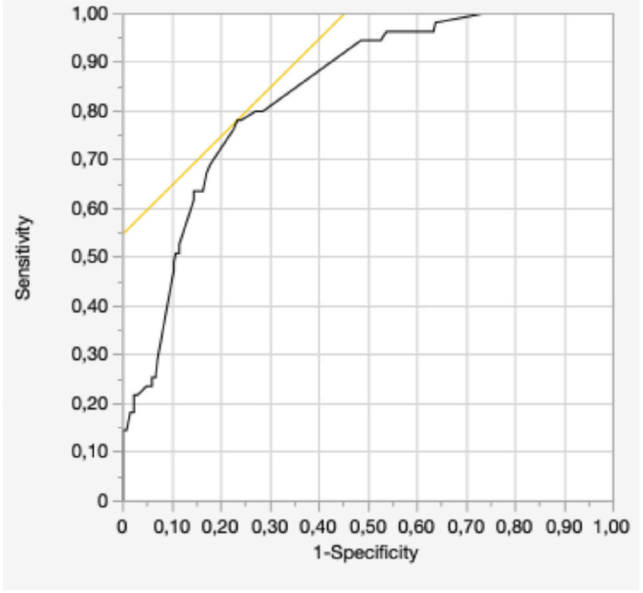

Fig. 3. Receiver Operating Characteristic (ROC) curve of the proposed predictive model, with the area under the curve (AUC) of 0.84.

favorable approach.

5. Discussion

In this study, the overall upgrade risk for all IDPs was 17%. For IDPs with atypia, the upgrade risk was 40%, which supports the consensus in the literature that atypical IDPs should be managed with surgical excision [2,11,16,17]. For IDPs without atypia, the upgrade risk was 8.8%, which is higher than reported in recent studies [10,12,17–19].

Lin et al. conducted a literature review of IDPs with and without atypia published between 2000 and 2019 [10]. The reported upgrade rate ranged from 0% to 33%, with a pooled rate of 6.1% across 38 studies. However, as Lin et al. state, the lack of standardized methods for patient selection and the differing definitions of upgrade among studies limits the reliability of comparative analysis. In addition, many of the studies included were small in sample size.

In a recent meta-analysis Keating et al. reviewed 13 studies reporting the upgrade rate of non-atypical and radio-pathologic concordant IDPs [19]. They found that the pooled upgrade rate was 1.4 % which is relatively modest result. Keating et al. state that surgical excision of non-atypical and radio-pathologic concordant IDPs would be considered overtreatment.

Because of the low upgrade risk for IDPs without atypia in some studies, management with follow-up has been suggested instead of routine surgical excision [1,13,20]. The NCCN guidelines state that if the CNB result is concordant with imaging results, IDPs without atypia could be treated with surveillance instead of surgical excision [8]. However, in the meta-analysis by Keating et al. it is pointed out that the definition of radiologic-pathologic concordance varies between studies [19], which should be considered when applying guidelines to clinical practice.

In this study, we evaluated two existing predictive models that could support decision-making regarding surgery versus surveillance in IDPs without atypia.

In their study, Lee et al. reported that 48% (294 of 612) of non-atypical IDPs would have been spared from surgical excision while all upgraded cases would have been identified [12]. In contrast, when applying the same model to our cohort, only 11% could have been spared, highlighting that models developed in specific populations may not be generalizable to others.

The model by Lee et al. utilized radiologic-pathologic discordance as a predictive factor. In our cohort, BI-RADS categories were not consistently documented in the imaging reports used in this study, and the reports rarely included explicit diagnostic proposals. However, radiological reports typically included a descriptive assessment of the detected lesion. Radiologic–pathologic discordance was defined as cases in which, based on the radiologist's interpretation of the descriptive findings, the lesion was not considered compatible with a benign IDP. This underscores the challenge that modern guidelines, such as the NCCN guidelines, may not always be directly applicable to routine clinical practice.

When applying the model by Zhang et al. [6] to our study population, 17% of IDPs without atypia would have been spared from surgical intervention. However, among these, there was one case in which the lesion was upgraded to DCIS adjacent to a papilloma after surgical excision. The patient was 60-year-old woman, with a 6 mm lesion detected in a surveillance mammography after previous DCIS in contralateral breast. After surgical excision, final pathology revealed a 16 mm intraductal papilloma with an adjacent 4.5 mm area of DCIS.

It is possible that because the model by Zhang et al. did not include patients' age, this particular case was not identified.

The model by Zhang et al. utilized BI-RADS classification, which could not be obtained in our data retrospectively. The information on microcalcifications was based solely on mammograms, and there may be interpretation discrepancy compared to the study by Zhang et al. Furthermore, in our data it was not specified whether the nipple discharge was bloody or not, and thus, we utilized the presence of any nipple discharge as a substitute factor.

Both models evaluated in this study included lesion size >10 mm as a criterion, as lesion size is widely regarded as an important predictor of upgrade in IDPs. In our cohort as well, larger lesion size was associated with a higher risk of upgrade. In our study population, using cut-off value of 10 mm did not provide adequate discriminatory performance. Only 25% (55 of 215) of IDPs without atypia could be spared from surgery with no upgrades missed. Therefore, we raised the limit to 20 mm or above to safely reach higher specificity. Notably, there was a strong association between lesion size and palpability and therefore, having both factors included in the model improves sensitivity and

specificity.

In previous literature, patient age has been suggested as a predictor of upgrade [21]. In our cohort, older age was significantly associated with an increased upgrade risk among all IDPs ($p < 0.001$). Lee et al. reported that the upgrade risk was substantially higher (5.6% vs. 0.7%) in patients aged 60 years and older compared to those under 60 [12]. Lin et al. proposed an even lower age threshold of 53 years [10]. In our data, no upgrades would have been missed when utilizing the threshold of 60 years. However, the optimal age cutoff for guiding surgical decision-making remains unclear [13,22,23].

While microcalcifications were associated with the upgrade risk regarding all IDPs in our study, this association was not observed in the subgroup of non-atypical IDPs. Prior studies have reported conflicting findings regarding microcalcifications as a predictive factor, further emphasizing the need for more standardized research [24,25].

This study has several limitations. The main limitation is the retrospective nature of the study, which introduces a risk of missing data and limitations in the interpretation of patient records and documentation intended for clinical use, and limited control over confounding variables. Secondly, over the 13-year study period, accuracy of the imaging and histopathological examinations and reporting at our hospital have evolved, and the completeness of the data was not as high at the beginning of the study period as it was at the end.

6. Conclusions

Our findings support surveillance instead of routine excision in cases of IDPs without atypia diagnosed on CNB in younger patients. Further research is needed to develop a robust and validated model.

CRediT authorship contribution statement

Jenni Kotola: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Anselm Tamminen:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Conceptualization.

Consent to publish

All authors of the manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript in accordance with ICMJE criteria. All authors have agreed to publish the article in Human Pathology.

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Declaration of competing interest

The authors declare no competing interests.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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