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Occurrence and Positive Predictive Value of Additional Nonmass Findings for Risk Stratification of Breast Microcalcifications in Mammography

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Abstract

Purpose: To assess the occurrence and positive predictive value of additional nonmass findings to stratify the risk of breast microcalcifications.
Methods: This retrospective evaluation included 278 lesions with vacuum- or image-guided hook-wire biopsy for suspicious microcalcifications. The lesions were categorized into exclusive microcalcifications and microcalcifications with focal asymmetry, tubular density or architectural distortion (ie, nonmass findings). To evaluate the utility of additional nonmass findings for risk stratification, outcome variables were positive predictive values and odds ratios for malignancy and invasive carcinoma.
Results: Forty-five of 278 microcalcification lesions (16%) were associated with nonmass findings: 28 focal asymmetries, 2 tubular densities, and 15 focal asymmetries in conjunction with tubular densities. Architectural distortion was observed in 28 of these cases. The odds ratio for additional nonmass findings relative to exclusive microcalcifications was 5.9 and was statistically significant ($P < .00001$). Architectural distortion was the most specific indicator for malignancy and invasiveness, with odds ratios of 6.5 ($P = .0072$) and 5.6 ($P = .0214$), respectively.
Conclusions: Microcalcifications with nonmass findings were less frequent than exclusive microcalcifications but were more predictive for malignancy. Architectural distortion demonstrated the highest risk of malignancy and invasiveness. Assessment of additional nonmass findings might be useful for further risk stratification of microcalcifications, indications for additional imaging, and pretreatment considerations.

Résumé

Objet : Évaluer la fréquence et la valeur prédictive positive des résultats supplémentaires de rehaussement sans masse afin de stratifier les risques de microcalcifications mammaires.
Méthodes : L'évaluation rétrospective englobait 278 lésions ayant fait l'objet d'une biopsie pour des microcalcifications suspectes, soit par aspiration, soit suite à la mise en place d'un harpon stéréoguidé. Les lésions ont été classifiées en microcalcifications isolées et en microcalcifications avec asymétrie focale, densité tubulaire ou distorsion architecturale (c.-à-d. rehaussement sans masse). Dans le but de mesurer l'utilité des résultats supplémentaires de rehaussement sans masse à des fins de stratification des risques, les résultats ont été établis comme valeurs prédictives positives et comme rapports de cotes de la malignité et du carcinome invasif.
Résultats : Parmi les 278 lésions présentant des microcalcifications, 45 (16%) étaient associées à un rehaussement sans masse, dont 28 cas d'asymétrie focale, 2 cas de densité tubulaire et 15 cas d'asymétrie focale assortie de densité tubulaire. Une distorsion architecturale a été observée dans 28 de ces cas. Le rapport de cotes pour les résultats supplémentaires de rehaussement sans masse par rapport aux microcalcifications isolées était de 5,9 et était statistiquement significatif ($P < 0,00001$). La distorsion architecturale s'est avérée l'indicateur de malignité ou de cancer invasif le plus précis, présentant un rapport de cote de 6,5 ($P = 0,0072$) et de 5,6 ($P = 0,0214$), respectivement.
Conclusions : Les microcalcifications présentant un rehaussement sans masse étaient moins fréquentes que les microcalcifications isolées, mais détenaient une valeur prédictive plus élevée au chapitre de la malignité. La distorsion architecturale a par ailleurs démontré le risque de malignité ou de cancer invasif le plus élevé. L'évaluation des résultats supplémentaires de rehaussement sans masse pourrait servir à stratifier

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les risques des microcalcifications de manière plus exhaustive, à indiquer le besoin d'examens supplémentaires et à analyser les diverses considérations entourant le prétraitement.

Type and distribution descriptors of microcalcifications are generally used for risk stratification of breast malignancy [1]. The use of focal asymmetry, tubular density, and architectural distortion in the context of microcalcifications for risk stratification has received less attention. Studies of proven ductal carcinoma in situ (DCIS) alone are reporting the occurrence of focal asymmetry and architectural distortion in conjunction with DCIS [2,3]. Stomper et al [3] found that the spectrum of soft-tissue abnormalities associated with clinically occult DCIS appears to have 2 major pathologic correlations: a direct manifestation of the tumour with tumour-filled ducts and the presence of periductal fibrosis or elastosis, which creates an irregular or spiculated mass. By using subgross histology and large-section histology, Tabár et al [4] explained tumour-forming DCIS by the induction of dense and disorganized duct-like structures. The presence of a basement membrane classifies these structures as an in situ process.

In a large study, Venkatesan et al [5] examined the positive predictive value of specific mammographic findings. Focal asymmetry exhibited the lowest predictive value for malignancy. Architectural distortion demonstrated a low prevalence but was highly predictive of invasive cancer. Calcifications were similarly predictive of invasive cancer and DCIS in their cohort. Combinations of mammographic findings were not analysed in this study. If associated with suspicious microcalcifications, then tubular structures were considered significant by the standards presented by the American College of Radiology Breast Imaging-Reporting and Data System (BI-RADS), 4th edition, [1]. We noticed a lack of studies that quantify the positive predictive value for malignancy of suspicious microcalcifications in conjunction with nonmass findings: focal asymmetry, tubular density, and architectural distortion. Therefore, we evaluated the occurrence and positive predictive value for malignancy and invasiveness of suspicious microcalcifications with and without additional nonmass findings.

Materials and Methods

Study Design

This retrospective study includes the results of 324 consecutive x-ray—guided biopsies (vacuum-assisted stereotactic biopsy or open surgery with hook-wire guidance) performed in 284 women because of nonpalpable suspicious microcalcifications on mammograms between January 2002 and December 2003 at an academic hospital before the introduction of an official and nationwide screening program, and were part of a 7-year follow-up. The mammograms were retrospectively reevaluated by 2 subspecialty-trained breast imagers in accordance (E.V.S., M.B.R.). The readers were blinded for histopathology, medical record, and previous description of microcalcifications. The analysis of additional mammographic findings included focal asymmetry, tubular density (tubular structure), and architectural distortion [1]. The exclusion criteria for this retrospective analysis with special focus on microcalcifications with nonmass lesions were as follows: (a) microcalcifications were not identified in the histologic specimen (1 case of vacuum biopsy; all other 108 vacuum biopsies were technically successful), (b) 2 or more synchronous or asynchronous separate accumulations of microcalcifications in the same quadrant (1 case of asynchronous microcalcifications in the same quadrant), and (c) mammographic images that showed a combination of microcalcifications with spherical mass (44 cases; 9 complex lesions, and 35 cases selected for x-ray—guided biopsy because of small, invisible, or not clearly detectable spherical mass lesions on prior focused ultrasound). Thus, 278 mammographic lesions (either pure microcalcifications or microcalcifications with nonmass findings) were further analysed in regard to the positive predictive value for malignancy and invasiveness.

Patients

The institutional review board approved this study and waived the requirement for informed consent. The women were 25-83 years of age (mean age [SD], 54.5 ± 11.3 years). All included mammographic lesions were nonpalpable breast lesions. Twenty-six women with 31 included mammographic lesions were followed-up because of a history of breast cancer (prior histologic examination: 4 women with pure DCIS and 22 women with invasive carcinoma with or without a DCIS component). Fourteen women (14 lesions, 1 woman with a history of breast cancer) showed a suspicious palpation within a different quadrant, and 7 women (7 lesions; 2 women with a history of breast cancer) manifested with nipple discharge. Hence, 3 women had a history of breast cancer and were symptomatic women. Thus, 229 of 278 mammographic lesions were screen-like detected lesions in asymptomatic women (206 asymptomatic women without a history of breast cancer).

Mammograms and Readings

Examinations were made by using the dedicated screen-film technique. During the 2-year study period, a total of 7878 mammograms were evaluated. Craniocaudal, mediolateral

oblique, true lateral, and magnification views were retrospectively evaluated. Only images obtained before biopsy were used. The minimum number of suspicious microcalcifications was more than 5 per 1 mL, with a maximum size below 1 mm in width. Focal asymmetry in the context of this study was a dense structure that was irregular, observed in 2 planes (although probably less well in 1 of the 2 planes), and more ill defined and less dense than a spherical mass. An asymmetry seen in only one view was considered irrelevant for this study because of the general workup protocol for microcalcifications of 3 planes and magnification views. Only tubular, dense structures that point to and from microcalcifications with or without microcalcifications inside were considered as tubular densities. Architectural distortion was defined as thin lines or spiculations that radiated from the microcalcification lesion or within close vicinity. Type descriptors of suspicious microcalcifications of intermediate concern were the following: amorphous or indistinct, coarse heterogeneous, and suspicious round or punctate. Distribution descriptors of lower concern were the following: clustered, regional, and diffuse. Small lesions were microcalcification lesions with less than 2 cm of greatest diameter.

Biopsies

One hundred and eight lesions in 108 patients were confirmed by vacuum-assisted stereotactic biopsy on a digital prone table (Mammotest; Fischer Imaging, Denver, CO) with 11-gauge vacuum probes. One hundred and seventy lesions in 132 patients were primarily treated by open surgery. The average time between mammography and final histologic verification was 20 days (range, 0-217 days). Radiography was performed for all surgical specimens. Nowadays, all women with suspicious breast lesions undergo image-guided percutaneous assessment.

Histologic Examination

Histologic examination was performed in-house, in accordance with generally accepted histologic standards. Definitive histologic analysis of the surgical specimens allowed grouping of the results into 3 classes, according to the pathology codes of the BI-RADS, 4th edition [1]: benign, malignant (DCIS and/or invasive carcinoma), and malignant subgroup invasive (invasive carcinoma only with or without a DCIS component). Atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ were classified under the rubric benign lesions. If there were multiple histologic findings within 1 specimen, then the most suspicious histopathology was considered to be the final histologic result.

Statistics

For statistical analysis, we used the software R (The R Project for Statistical Computing, www.r-project.org, version 2.15.0) and Excel (Excel 2000; Microsoft, Redmond, WA). To calculate the positive predictive value for invasiveness

and malignancy, the proportion of invasive or malignant (DCIS and invasive carcinomas) lesions of all the lesions of the subtype were considered. For odds ratio calculation, microcalcifications without additional findings were considered as the baseline risk group. The difference between exclusive microcalcifications and additional nonmass findings was tested with the Fisher exact test. To assess the contribution of each individual additional nonmass finding, as well as the other risk factors together with additional nonmass finding, to the risk of malignancy and invasiveness logistic regression was used. *P* values less than .05 were considered statistically significant.

Results

Occurrence of Microcalcifications With Nonmass Lesions

Two hundred and thirty-three of 278 lesions (84%) were pure microcalcifications. The remaining 45 lesions (16%) exhibited additional nonspherical-mass lesions: 28 focal asymmetries, 2 tubular densities, and 15 focal asymmetries in combination with tubular densities. Architectural distortion was identified in 28 of 45 microcalcifications with associated nonspherical mass lesions (62%): 17 of 28 with focal asymmetries (61%), 1 of 2 tubular densities (50%), and 10 of 15 focal asymmetries with tubular densities (67%). The occurrence of microcalcifications with nonmass findings of clinically asymptomatic, screen-like detected lesions was 33 of 229 mammographic lesions (14%). Two examples of microcalcifications with additional nonmass findings are included for illustration (Figures 1 and 2).
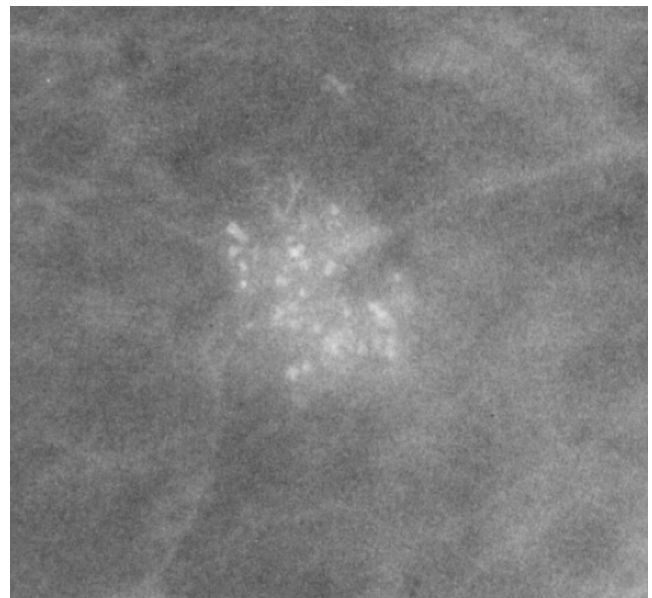

Figure 1. A 64-year-old woman with intraductal carcinoma, demonstrating suspicious microcalcifications with focal asymmetry on the craniocaudal magnification view of her right breast.
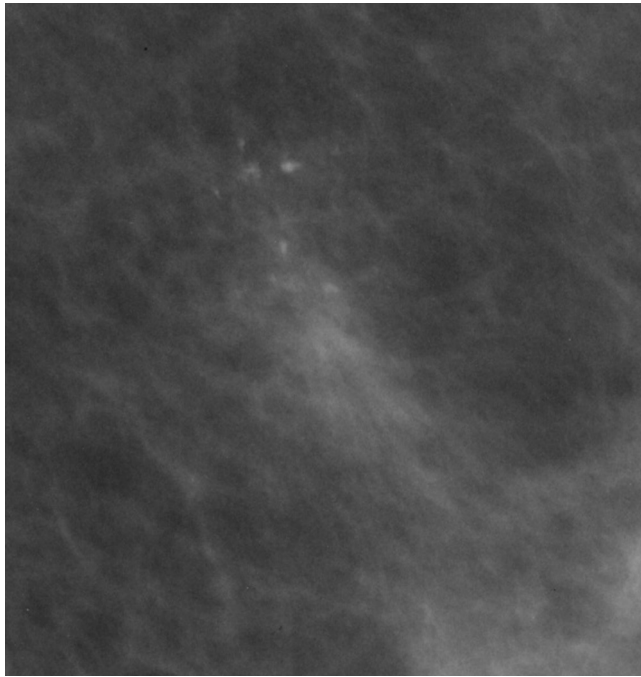
Figure 2. A 61-year-old woman with invasive carcinoma, demonstrating suspicious microcalcifications with focal asymmetry and architectural distortion in close vicinity on the mediolateral oblique magnification view of her left breast.

Positive Predictive Value for Malignancy and Invasiveness of Microcalcifications With and Without Nonmass Findings

Fifty-five of 233 exclusive microcalcifications (24%) were malignant. Twenty-nine of 45 microcalcifications (64%) with a nonmass finding were malignant, as were 16 of 28 microcalcifications with focal asymmetry (57%) (8 DCIS and 8 invasive carcinoma), both with tubular density (both DCIS); 11 of 15 with combined focal asymmetry and tubular density (73%) (3 DCIS and 8 invasive carcinoma); and 22 of 28 with architectural distortion (79%) (8 DCIS and 14 invasive carcinoma). The respective proportions of DCIS of malignant cases of the cohort were 63% (53/84), exclusive microcalcifications 73% (40/55), and microcalcifications with additional nonmass findings 45% (13/29). The positive predictive value for malignancy of the subgroup of clinically

asymptomatic, screen-like detected microcalcifications with additional nonmass findings was 21 of 33 mammographic lesions (64%) (9 invasive carcinoma, 12 DCIS) and, for microcalcifications alone, 42 of 196 lesions (21%) (11 invasive carcinoma, 31 DCIS). The positive predictive value for malignancy of microcalcifications with focal asymmetry without architectural distortion was 36% (4/11) (2 invasive cancer and 2 DCIS) and for the subgroup of clinically asymptomatic, screen-like detected lesions was 30% (3/10) (1 invasive cancer and 2 DCIS). Positive predictive values and odds ratios for malignancy and invasiveness of breast microcalcifications with and without additional nonmass findings and for subgroups with and without architectural distortion are listed in detail in Table 1. The respective odds ratios for malignancy and invasiveness of all microcalcification lesions with additional nonmass findings relative to exclusive microcalcifications were 5.9 and 8.0, and were statistically significant ($P < .00001$). Further logistic regression analysis of the individual nonmass findings demonstrated significantly increased odds ratios for malignancy and invasiveness in case of architectural distortion (Table 2). Positive predictive values and odds ratios for malignancy and invasiveness with and without additional findings in regard to screen-like detected lesions, type descriptors of intermediate concern, distribution descriptors, and size are listed in Table 3. Further logistic regression analysis showed that nonmass findings are an additional significant factor for risk stratification of malignancy and invasiveness, which is independent from the presence of screening, type, and distribution descriptors as well as size (both $P < .0001$) (Table 4).

Discussion

Soft-tissue abnormalities were observed by Barreau et al [2] on the mammograms of 255 of 909 lesions with DCIS (28%). These included indistinct, well-defined, ill-defined, and spiculated lesions, focal asymmetry, and architectural distortion with and without microcalcifications. Stomper et al [3] studied the surrounding tissue of 100 clinically occult DCIS lesions detected with mammography: 72% of these lesions appeared as microcalcifications, 10% as soft-tissue abnormalities, and 12% as a combination of the two. Tabár

Table 1
Occurrence, positive predictive values, and odds ratios of microcalcifications for malignancy (DCIS and/or invasive carcinoma) and invasiveness (invasive carcinoma only) with and without additional nonmass findings

Microcalcifications	n	No. malignant lesions	Positive predictive value for malignancy, % (95% CI)	No. invasive lesions	Positive predictive value for invasiveness, % (95% CI)	OR for malignancy (95% CI)[a]	OR for invasiveness (95% CI)[a]
Pure microcalcifications	233	55	23.6 (18.3-29.6)	15	6.4 (3.6-10.4)	—	—
Microcalcifications with nonmass findings	45	29	64.4 (48.8-78.1)	16	35.6 (21.9-51.2)	5.9 (3.0-11.6)	8.0 (3.6-17.9)
With architectural distortion	28	22	78.6 (59.0-91.7)	14	50.0 (30.6-69.4)	11.9 (4.6-30.7)	14.5 (5.9-36.0)
Without architectural distortion	17	7	41.2 (18.4-67.1)	2	11.8 (1.5-36.4)	2.3 (0.8-6.2)	1.9 (0.4-9.3)

CI = confidence interval; DCIS = ductal carcinoma in situ; OR = odds ratio.
[a] Pure microcalcifications as baseline.

Table 2
Contribution of each individual additional nonmass finding for risk stratification of microcalcifications

	β	OR (95% CI)	*P* value
Risk of malignancy			
Focal asymmetry	0.2288	1.26 (0.4-3.8)	.6993
Tubular density	1.1334	3.11 (0.8-14.2)	.1134
Architectural distortion	1.8768	6.53 (1.8-28.2)	.0072
Risk of invasiveness			
Focal asymmetry	0.7081	2.0 (0.4-7.8)	.3337
Tubular density	0.8060	2.2 (0.6-8.1)	.2167
Architectural distortion	1.7220	5.6 (1.4-28.6)	.0214

CI = confidence interval; OR = odds ratio.

et al [4] correlated the soft-tissue abnormalities of DCIS with subgross and large-section histologic examination, and explained the presence of focal asymmetry and architectural distortion with DCIS by using the theory of neoductgenesis. Focal asymmetry corresponded to unnaturally high concentrations of duct-like structures within a limited area. Many of these were surrounded by desmoplastic reaction and lymphocytic infiltration. The investigators observed overexpression of Tenascin C around the newly formed ducts. Tenascin C is a complex multifunctional protein that promotes angiogenesis, tumour growth, and invasion [6]. The theory of neoductgenesis and defect of the basement membrane is supported by a recent study of magnetic resonance imaging that shows intrusion of gadolinium inside and along neoplastic mammary ducts in a murine model [7].

In our cohort, which excluded typical mass findings, the occurrence of microcalcifications with additional nonmass findings was 16%. Distended ducts with only inside microcalcifications were, with 2 cases, a rare finding and specific for DCIS. The proportion of DCIS of all malignant lesions of

our cohort was 63%, which is in the range of other studies that have excluded typical mass findings from their cohort [8—11]. The proportion of DCIS of malignant cases of our study was 73% for microcalcifications alone compared with 45% with associated nonmass findings. One-fourth of all proven DCIS lesions in this study exhibited a combination of microcalcifications and nonmass findings. This proportion was higher, as indicated by previously published studies [2,3].

This study found a significantly higher positive predictive value for malignancy of 64% and invasiveness of 36% for all microcalcifications with additional nonmass findings compared with exclusive microcalcifications, which had a positive predictive value for malignancy of only 24% and invasiveness of 6%. We found that nonmass findings increased the positive predictive value for malignancy and invasiveness independent from history, size of lesion, type, and distribution descriptors. Focal asymmetry was the most common nonmass finding and was commonly found in conjunction with other nonmass findings. However, the positive predictive value for malignancy of microcalcifications with focal asymmetry alone was only 36% (for the subgroup of clinically asymptomatic, screen-like detected lesions in women, 30%); the odds ratio of logistic regression was not significantly different from microcalcifications alone. The results are in accordance with the study of Burrell et al [12]. In their cohort, the positive predictive value for malignancy of microcalcifications alone (45%) did not vary versus microcalcifications with a density (44%). However, within their subgroup of screen-detected lesions, the positive predictive value for malignancy of microcalcifications with densities was higher than of microcalcifications alone (67% vs 46%). Tubular dense

Table 3
Occurrence, positive predictive values, and odds ratios of microcalcifications for malignancy (DCIS and/or invasive carcinoma) and invasiveness (invasive carcinoma only) without (pure microcalcifications) and with additional nonmass findings for screen-like detected, asymptomatic lesions, intermediate concern type descriptors (amorphous or indistinct, coarse heterogeneous, and suspicious round/punctate), non—high-risk distribution descriptors (clustered, regional, diffuse), and small size (<2 cm)

	History	Microcalcification characteristics		
	Screen-like detected, asymptomatic lesions (n = 229)	Intermediate concern type descriptors (n = 171)	Non—high-risk distribution descriptors (n = 237)	Small size (n = 204)
Pure microcalcifications				
Total no.	196	150	197	170
No. malignancies	42	19	41	31
Positive predictive value for malignancy, % (95% CI)	21.4 (15.9-27.8)	12.7 (7.8-19.1)	20.8 (15.4-27.2)	18.2 (12.7-24.9)
No. invasive malignancies	11	7	10	6
Positive predictive value for invasive malignancy, % (95% CI)	5.6 (2.8-9.8)	4.7 (1.9-9.4)	5.1 (2.5-9.1)	3.5 (1.3-7.5)
Microcalcification lesions with additional nonmass findings				
Total no.	33	21	40	34
No. malignancies	21	11	24	22
Positive predictive value for malignancy, % (95% CI)	63.6 (45.1-79.6)	52.4 (29.8-74.3)	60.0 (43.3-75.1)	64.7 (46.5-80.3)
No. invasive malignancies	9	5	12	12
Positive predictive value for invasive malignancy, % (95% CI)	27.3 (13.3-45.5)	23.8 (8.2-47.2)	30.0 (16.6-46.5)	35.3 (19.7-53.5)
OR for malignancy (95% CI)[a]	6.4 (2.9-14.1)	7.6 (2.8-20.3)	5.7 (2.8-11.7)	8.2 (3.7-18.4)
OR for invasiveness (95% CI)[a]	6.3 (2.4-16.8)	6.4 (1.8-22.5)	8.0 (3.2-20.3)	14.9 (5.1-43.7)

CI = confidence interval; DCIS = ductal carcinoma in situ; OR = odds ratio.

[a] Without additional nonmass findings as baseline.

Table 4
Contribution of each individual risk factor and additional nonmass finding for risk stratification of microcalcifications

	β	OR (95% CI)	*P* value
Risk of malignancy			
High-risk type descriptor[a]	1.57	4.8 (2.6-8.9)	<.0001
High-risk distribution[b]	1.01	2.7 (0.9-8.3)	.0693
Non−screen-like asymptomatic[c]	0.90	2.5 (1.2-5.2)	.0170
Non-small size[d]	0.15	1.2 (0.5-2.8)	.7431
Additional nonmass finding	1.77	5.9 (2.8-12.7)	<.0001
Risk of invasiveness			
High-risk type descriptor[a]	0.93	2.5 (1.1-6.3)	.0364
High-risk distribution[b]	1.33	3.8 (0.9-18.1)	.0738
Non−screen-like asymptomatic[c]	1.34	3.8 (1.5-10.1)	.0063
Non-small size[d]	0.21	1.2 (0.3-4.1)	.7436
Additional nonmass finding	2.09	8.0 (3.4-20.0)	<.0001

CI = confidence interval; OR = odds ratio.
[a] Fine pleomorphic, and fine linear or fine-linear branching.
[b] Segmental and linear.
[c] History of breast cancer or symptomatic woman.
[d] Size ≥ 2 cm.

structures without inside microcalcifications may be due to neoduct- or neoangiogenesis. Logistic regression analysis found significantly increased odds ratio of microcalcifications in conjunction with tubular densities for malignancy. The most important predictor for malignancy and invasiveness of microcalcifications was architectural distortion, which is in line with the study by Venkatesan et al [5] that examined single mammographic findings and found architectural distortion to be the most indicative predictor for malignancy and invasiveness.

To our knowledge, this is the first study to provide detailed results of the frequency of occurrence, positive predictive value for malignancy, and invasiveness of microcalcifications with associated focal asymmetry, tubular density, and architectural distortion. Type and distribution descriptors of microcalcifications stratify the risk of malignancy; however, they lack the ability to stratify the risk for invasiveness [8,11,13]. The assessment of additional nonmass findings might be helpful for further risk stratification of microcalcifications, an indication for additional imaging, and pretreatment considerations. There were several limitations to this study. Challenging interobserver, intraobserver, and interinstitution variabilities are inherent to all mammographic descriptors. Gross pathology (for the exact correlation of additional nonmass findings with histopathology) was unavailable to our institution. The cohort was based on screen-film mammography, and digital mammography might be more accurate [14]. Therefore, our results must be confirmed by others, and further research is encouraged.

In conclusion, this study found that breast microcalcifications in conjunction with nonmass lesions were an infrequent mammographic finding. Compared with pure microcalcifications, the presence of additional nonmass findings significantly increased the risk for malignancy in microcalcification lesions. The most important predictor of malignancy and invasiveness was architectural distortion.

References

[1] American College of Radiology. Breast Imaging Reporting and Data System (BI-RADS). 4th ed. Reston (VA): American College of Radiology; 2003.

[2] Barreau B, de Mascarel I, Feuga C, et al. Mammography of ductal carcinoma in situ of the breast: review of 909 cases with radiographic-pathologic correlations. Eur J Radiol 2005;54:55−61.

[3] Stomper PC, Connolly JL, Meyer JE, et al. Clinically occult ductal carcinoma in situ detected with mammography: analysis of 100 cases with radiologic-pathologic correlation. Radiology 1989;172:235−41.

[4] Tabár L, Tot T, Dean PB. Breast Cancer: Early Detection With Mammography: Crushed Stone-like Calcifications: The Most Frequent Malignant Type. Stuttgart, Germany: Thieme; 2008.

[5] Venkatesan A, Chu P, Kerlikowske K, et al. Positive predictive value of specific mammographic findings according to reader and patient variables. Radiology 2009;250:648−57.

[6] Guttery DS, Hancox RA, Mulligan KT, et al. Association of invasion-promoting tenascin-C additional domains with breast cancers in young women. Breast Cancer Res 2010;12:R57.

[7] Jansen SA, Paunesku T, Fan X, et al. Ductal carcinoma in situ: x-ray fluorescence microscopy and dynamic contrast-enhanced MR imaging reveals gadolinium uptake within neoplastic mammary ducts in a murine model. Radiology 2009;253:399−406.

[8] Liberman L, Abramson A, Squires F, et al. The breast imaging reporting and data system: positive predictive value of mammographic features and final assessment categories. AJR Am J Roentgenol 1998;171:35−40.

[9] Kettritz U, Morack G, Decker T. Stereotactic vacuum-assisted breast biopsies in 500 women with microcalcifications: radiological and pathological correlations. Eur J Radiol 2005;55:270−6.

[10] Akita A, Tanimoto A, Jinno H, et al. The clinical value of bilateral breast MR imaging: is it worth performing on patients showing suspicious microcalcifications on mammography? Eur Radiol 2009;19:2089−96.

[11] Bent CK, Bassett LW, D'Orsi CJ, et al. The positive predictive value of BI-RADS microcalcification descriptors and final assessment categories. AJR Am J Roentgenol 2010;194:1378−83.

[12] Burrell HC, Pinder SE, Wilson ARM, et al. The positive predictive value of mammographic signs: a review of 425 non-palpable breast lesions. Clin Radiol 1996;51:277−81.

[13] Burnside ES, Ochsner JE, Fowler KJ, et al. Use of microcalcification descriptors in BI-RADS 4th edition to stratify risk of malignancy. Radiology 2007;242:388−95.

[14] Perry NM, Patani N, Milner SE, et al. The impact of digital mammography on screening a young cohort of women for breast cancer in an urban specialist breast unit. Eur Radiol 2011;21:676−82.