ORIGINAL ARTICLE

SUSPICIOUS MICROCALCIFICATIONS ON FULL-FIELD DIGITAL MAMMOGRAPHY AND ITS CORRELATION WITH RISK OF MALIGNANCY: ASSESSMENT OF POSITIVE PREDICTIVE VALUE

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ABSTRACT

OBJECTIVES: To evaluate retrospectively the positive predictive value of suspicious microcalcifications diagnosed on full-field digital mammography (FFDM) and establish the likelihood of malignancy using stereotactic biopsy results as gold standard. **STUDY DURATION AND SETTINGS:** Retrospective study was conducted at the department of Diagnostic Radiology, Dallah hospital, Riyadh, Saudi Arabia. Study duration was 2.3 year (January 2018-March 2020). **MATERIAL AND METHODS:** The study included 60 female patients with microcalcification on mammogram who underwent stereotactic guided biopsy between January 2018 and March 2020. The sample size was calculated using the WHO calculator. Non probability consecutive sampling was used for selection of patients. Ethical approval was taken. Patients underwent digital mammography with tomosynthesis and stereotactic biopsy. The morphology and distribution of microcalcifications was assessed on mammogram and subsequently BI-RADS (Breast Imaging-Reporting and Data System) descriptors were recorded. Finally, correlation with histopathology was performed. Data was analysed using SPSS version 24. Chi-square and Pearson s correlation was applied. P value ≤ 0.05 was considered significant. **RESULTS:** Total 60 biopsies were included in this study. Mean age of women was 50 years – 30.1SD. There were 30 (50%) women in the age group 30-40 years and 30 (50%) women in the age group of 40-50 years. In mammography, microcalcification is seen in the right breast in 20 (33.3%) cases and in the left breast in 38 (63.3%) cases. Of the 60 microcalcification lesions biopsied, 33 were benign and 27 were malignant, representing an overall positive predictive value of 45% for the microcalcification on mammogram The morphologic characteristics of the suspicious microcalcifications were as follows: amorphous in 13 (22.0%) of the 60 cases, coarse heterogeneous in 14 (23.3%), Pleomorphic in 25(41.6%) and linear microcalcifications in 8 (13%). Among the 60 cases, the distribution of the suspicious microcalcifications was classified as grouped in 51 (85%), as segmental in 8 (13.3%), and as regional in 1 (1.6%). The 22 malignant lesions consisted of 2 cases of DCIS (9.1%) and 20 (90%) cases of invasive ductal carcinoma. In our study 63% of patients with a BIRADS score of 4 to 5 had microcalcifications associated with benign tissue. **CONCLUSION:** Suspicious microcalcifications (BIRADS category 4 and 5) on digital mammography had high positive correlation with histopathological findings. Appropriate screening for high risk patients leads to early diagnosis and lowers the disease progression.

Key words: Stereotactic biopsy, FFDM, VABB, Suspicious microcalcification, DCIS, BI-RADS.

Introduction

Breast calcifications are common findings on mammography and their frequency increases with the age of the patient. While the majority of microcalcifications that occur are benign, some specific grouped patterns

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can be caused by malignant disease or high risk lesions.[1] It is important to differentiate the microcalcifications of benign origin from those that are suspicious, since 55% of non-palpable cancers are diagnosed by the presence of microcalcifications.[2] Microcalcifications are the main form of manifestation of ductal carcinoma in situ (DCIS).[3] Some of these calcifications not only correspond to pure DCIS, but correspond to the intraductal portion of infiltrating carcinomas.[4]

Benign calcifications tend to be larger, present a characteristic appearance and do not require magnification. Whereas the suspicious ones tend to be smaller and their characterization should be studied with magnified images.

The density difference between the benign and malignant calcifications is mainly given by the various chemical compounds prevailing in each one. While benign calcifications are composed mainly of calcium oxalate, malignant calcifications are composed predominantly of calcium phosphate.[5]

The incorporation of digital mammography systems has allowed for an improvement in the investigation of microcalcifications. The Vestfold study, in 2008, found a significantly increased detection of DCIS using digital mammography.[6] It should be noted, however, that even in these systems the requirement of complementary magnified images remains in effect. Tomosynthesis still exhibits a debatable usefulness in the detection of microcalcifications. Some studies show detection rates similar to or somewhat lower for tomosynthesis compared with digital mammography.[7-9] The vast majority of microcalcifications are not visible by ultrasound (US) and it only detects large ones or those that are associated with nodules or cysts.[10]

Mammographically visible microcalcifications are present in approximately 55% of nonpalpable breast malignancies[11] and are responsible for the detection of 85-95% of cases of ductal carcinoma in situ (DCIS) by screening mammography.[12] The American College of Radiology BI-RADS (Breast Imaging-Reporting and Data System) includes descriptors of the morphology and distribution of microcalcifications.[13] Each morphology descriptor places the described lesion into a category that helps predict the malignant potential of the lesion. These categories include typically benign, intermediate concern, and higher probability of malignancy.[13] For example, amorphous calcifications have been reported to represent malignancy in 13-25% of biopsies.[14-18] They are therefore currently placed into the intermediate concern group. Calcifications in the higher probability of malignancy group described as fine linear/branching or fine pleomorphic have rates of malignancy as high as 92% and 67%, respectively.[18]

Classification type	BIRADS Category
Vascular calcifications, skin calcifications popcorn calcifications, milk of calcium calcifications, thick linear calcifications, popcorn calcifications dystrophic calcifications, round, scattered or isolated calcifications, ring calcifications, suture calcifications	BI-RADS 2
Round grouped calcifications	BI-RADS 3
Coarse, rough, heterogeneous calcifications	BI-RADS 4A
Amorphous calcifications	BI-RADS 4B
Fine pleomorphic calcifications	BI-RADS 4B
Linear or branched linear calcifications	BI-RADS 4C
Linear and new branching linear and segmental distribution	BI-RADS 5

Table 1: Classification of calcifications according to BI-RADS categories.[15]

The goal of this study was to assess the predictive value of the likelihood of malignancy for suspicious microcalcifications i.e. BI-RADS 4 and 5 microcalcification in the full field digital mammography (FFDM). The earlier studies that assessed and stratified the risk of malignancy for suspicious microcalcifications were performed before the widespread use of full-field digital mammography.[18,19]

Material and Methods

A retrospective study was conducted at the department of Diagnostic Radiology, Dallah Hospital Riyadh, Saudi Arabia. Study duration was 2.3 years (March 2018-March 2019). This study was performed with the approval of the institutional review board. The study included 60 biopsies from women who underwent stereotactic VABB (Vacuum assisted breast biopsy) for suspicious microcalcifications. The women were 30-80 years old at the time of biopsy (mean age 50 years). Pathologic analysis results from stereotactic core needle biopsies of the suspicious

lesions to determine the presence or absence of malignancy. All stereotactic biopsies were performed using an 11-gauge vacuum-assisted device, and at least 10 samples were obtained for each biopsy. The exclusion criteria included patients with implants, augmentation or reduction mammoplasty, Mammograms with additional findings of associated masses, architectural distortion, benign BIRADS 2 microcalcifications and mammograms without microcalcifications. A sample size of 60 biopsies was calculated with 7% absolute precision, 9% prevalence and 95% confidence interval using WHO calculator.

Patients underwent digital mammography and stereotactic biopsy. Digital mammographic examinations were performed with a Selenia Dimensions((Hologic) full-field digital mammography unit by GE Healthcare. Two projections (craniocaudal and mediolateral oblique views) for mammogram with tomosynthesis were obtained for analysis. CC and ML magnification views were also obtained for microcalcifications. Images were interpreted at a high-resolution workstation by radiologists experienced in breast imaging using BI-RADS descriptors. BI-RADS final assessment categorization (categories 4A, 4B, 4C, and 5) of each lesion was performed by one of the interpreting radiologists. Final assessment categories were scored using lexicon definitions as follows: Category 4A for lesions with a low likelihood of malignancy (2 10%); category 4B for lesions with an intermediate likelihood of malignancy (11 - 50%); category 4C for lesions with a moderate likelihood of malignancy (51 - 95%); and category 5 for lesions highly suggestive of malignancy (> 95%).

Core biopsies were performed with VABB and 11-gauge needle on Hologic MultiCare Platinum Biopsy machine by GE. Data was analysed using SPSS version 24. Mean and standard deviation was calculated for quantitative data. Percentage and frequencies were calculated for qualitative data. Chi-square and Pearson s correlation was applied. P value ≤ 0.05 was considered significant.

Results

Total 60 biopsies were included in this study. Mean age of women was 50 years – 30.1SD. There were 30 (50%) women in the age group 30-40 years and 30 (50%) women in the age group of 40-50 years. In mammography, microcalcification was seen in the right breast in 20 (33.3%) cases and in the left breast in 38 (63.3%) cases.

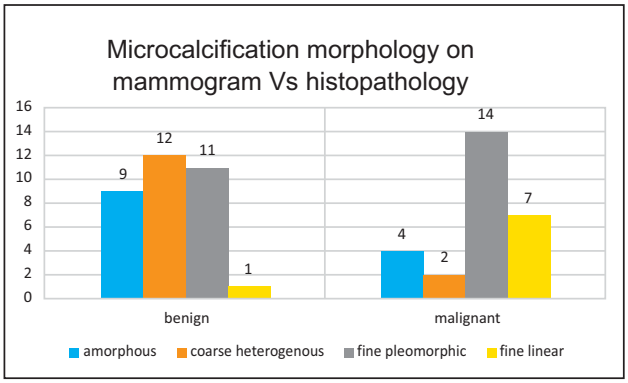
Of the 60 microcalcification lesions biopsied, 33 were benign and 27 were malignant, representing an overall positive predictive value of 45% for the microcalcification on mammogram. The morphologic characteristics of the suspicious microcalcifications were as follows: amorphous, in 13 (22.0%) of the 60 cases, coarse heterogeneous in 14 (23.3%), pleomorphic in 25 (41.6%) and linear microcalcifications in 8 (13%). Among the 60 cases, the distribution of the suspicious microcalcifications was classified as grouped in 51 (85%), as segmental in 8 (13.3%), and as regional in 1 (1.6%). The 22 malignant lesions consisted of 2 cases of DCIS (9.1%) and 20 (90%) cases of invasive ductal carcinoma.

In our study 63% of patients with a BIRADS score of 4 to 5 had microcalcifications associated with benign tissue.

A high positive correlation was found between BIRADS 4 and 5 microcalcifications and stereotactic biopsy (p=0.00).

	Amorphous microcalcifications n	Coarse heterogeneous microcalcifications n	Fine pleomorphic microcalcifications n	Fine linear microcalcifications n
Benign	9	12	11	1
Malignant	4	2	14	7

Table 2: Association between morphology of microcalcification on mammogram and pathological type (on the basis of stereotactic biopsy)



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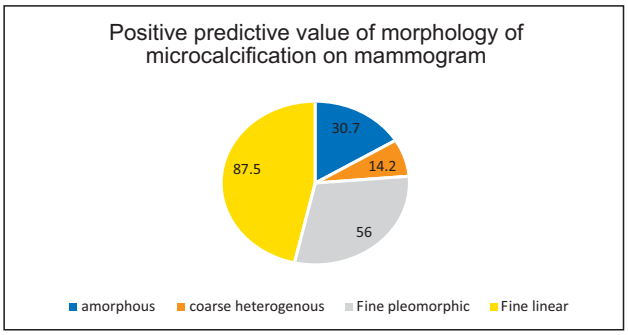
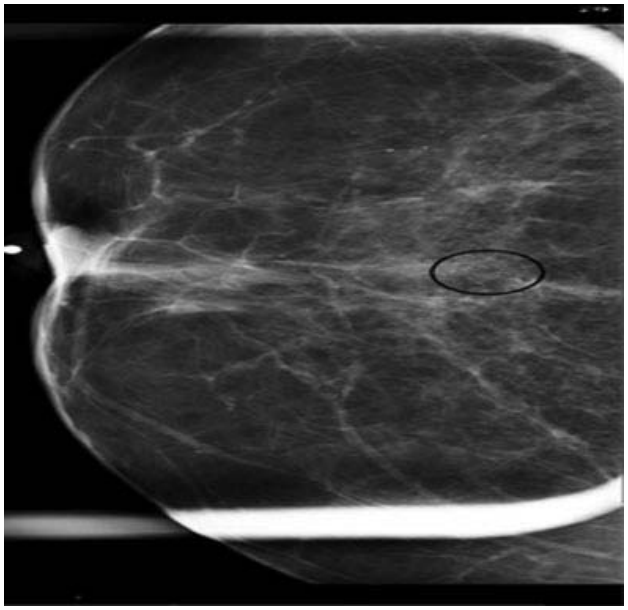
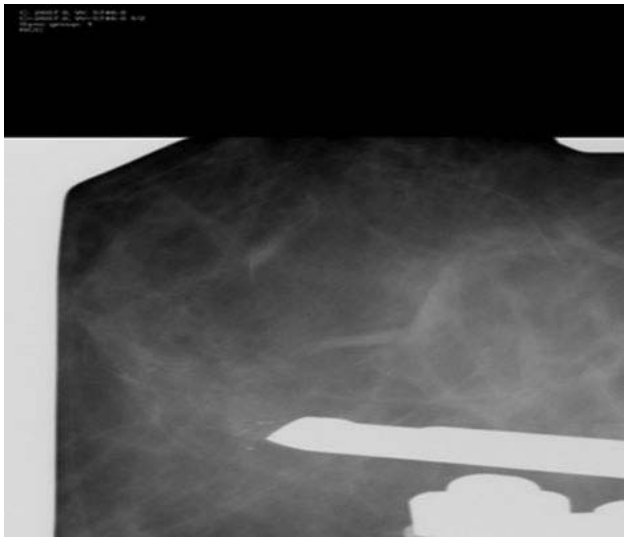


Figure 2: Positive predictive value of morphology of microcalcification on mammogram





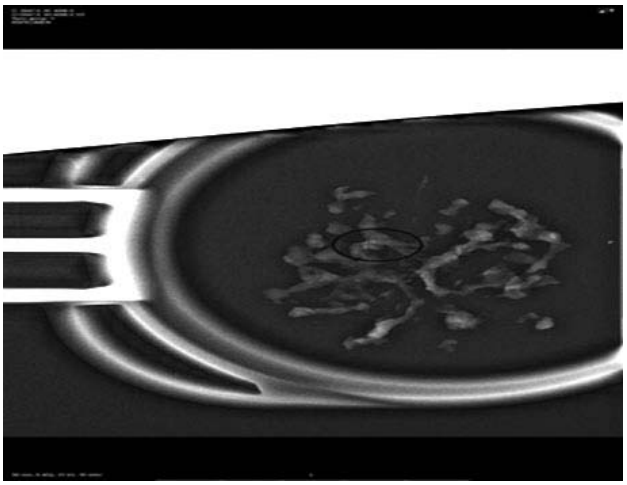
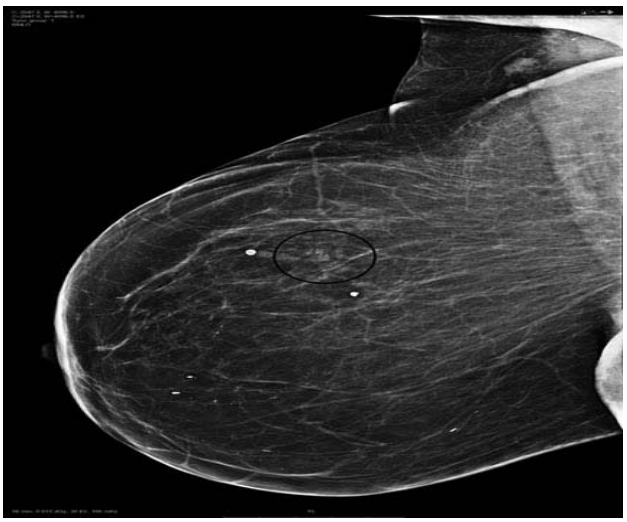
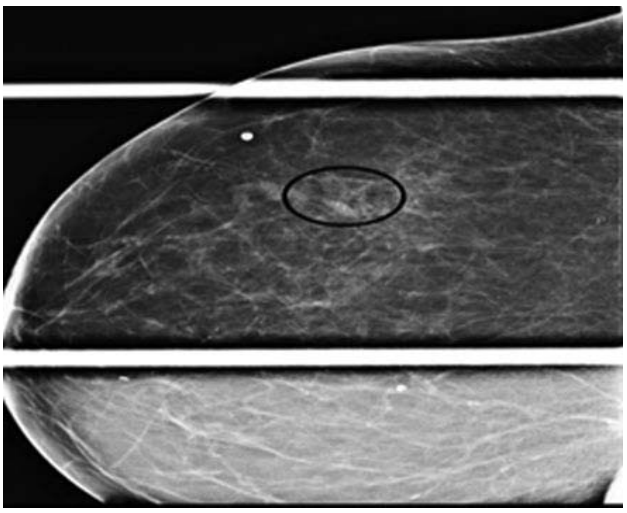


Figure 3: Right breast of 65 years female mediolateral oblique and magnified craniocaudal views mammograms show grouped fine pleomorphic microcalcifications. Post stereotactic images showing calcifications. Histopathology shows invasive ductal carcinoma.





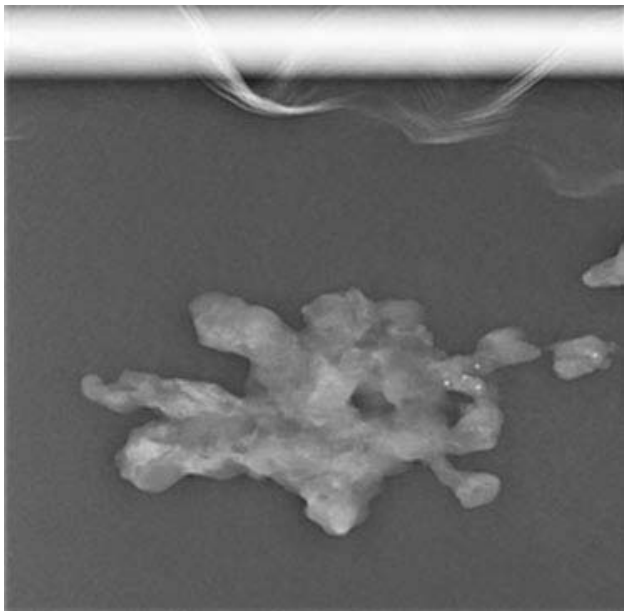


Figure 4: Right breast of 50-year-old woman. Mediolateral/magnified craniocaudal mammogram shows grouped amorphous calcifications. Pathologic diagnosis at stereotactic core needle biopsy revealed DCIS.

Discussion

The finding of indeterminate or malignant-appearing MCs on mammography presents a diagnostic challenge. Small clusters of calcifications are easy to miss and difficult to interpret. An aggressive approach to investigate may result in high rates of benign biopsies, but reducing the number of females recalled is likely to mean some significant changes are not investigated. The benefit of biopsy is early diagnosis, meaning treatment can be easier and more effective, with a mortality benefit.

The results of our study are consistent with those of other groups. Our data showed that the overall positive predictive value for biopsy was 45%, which is consistent with the overall positive predictive value for biopsy found in previous studies of 21-42%.[15-17,20] Of the malignancies found, 9.1% represented DCIS, whereas the remaining 90% represented invasive carcinoma. The frequency of these histopathologic results is similar to previously reported findings.[16,17] In this study, morphology descriptors progressively stratified the risk of malignancy as follows: coarse heterogeneous, amorphous, fine pleomorphic and fine linear/branching. Overall, this progressively increasing risk of malignancy supports the current categorization of microcalcification descriptors into intermediate concern and higher probability of malignancy categories. Microcalcifications of fine linear morphology in our study represented a statistically significant increased risk of malignancy, compared with all other morphologies.

The positive predictive value for fine linear microcalcifications in our study was 87% that is consistent with previously reported values of 81-92%.[16,17] Furthermore, the positive predictive values of amorphous and pleomorphic microcalcifications in our study were 31% and 56%, respectively. Previously published data show that the rate of malignancy of amorphous calcifications is 13-26%,[14-17] which is lower but not inconsistent with our findings. Compared with the 7% positive predictive value reported by Burnside et al.,[16] the risk of malignancy in our study for coarse heterogeneous calcifications was higher i.e.14%.

In another study[21] overall positive predictive values of biopsies was 28.8%, which is lower compared to our study. The individual morphological descriptors for each microcalcification morphology predicting the risk of malignancy however was consistent with our study.

Our study has certain limitations. Our patient sample was small and limited to a single centre, and not all patients in whom surgical excision was recommended underwent the procedure. Our study population sampled only patients recommended for biopsy of suspicious microcalcifications. Furthermore, interobserver variability is inherent in the practice of radiology. Moreover, there is no consensus on the use of the term amorphous, which could lead to differences among treatment centres in terms of the rates of detection and underestimation of malignancy.

Conclusion

Suspicious microcalcification on digital mammography has high positive correlation with histopathological findings. The fine linear and pleomorphic microcalcifications diagnosed on FFDM correlate strongly with risk of malignancy and a radiologist can successfully stratify lesions by malignant potential by using the morphology and distribution of microcalcifications according to BIRADS scoring.

Conflict of Interest: None

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