Ultrasound-Guided Needle Biopsy of Suspected Microcalcifications in the Breast

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ABSTRACT

Background: Sonography plays an important role in characterizing breast masses and in guiding needle core biopsies and wire localizations of suspicious sonographic abnormalities. Objective: The aim of this study was to show the possibilities of high frequency ultrasound devices in the presentation of microcalcifications of the breast, and the use of these possibilities in performing needle biopsy under ultrasound control. Methods: This was a retrospective study conducted from May 2017 to December 2020 on 32 women, 29-86 years of age using mammograms and ultrasound to show suspected microcalcifications (radiological findings of BI RADS 4B and 4C), and needle biopsy led by ultrasound that confirmed the diagnosis of breast cancer. Patients with suspected microcalcifications on mammography that had previously had the diagnosis of breast cancer confirmed in the same or contralateral breast were excluded from the study. Histology results from each core biopsy and surgical excision were reviewed. The positive predictive values of sonography and mammography for this population were calculated, and the sensitivity, specificity, and negative predictive value of sonography were determined. For analysis of the agreement of ultrasound findings with mammography the McNemar x²-test for dependent samples was used. Results: The sensitivity of mammography in the detection of microcalcifications in this study was 100%. The sensitivity of the ultrasound apparatus with a high frequency probe in the detection of microcalcifications after mammography examination in this study was 87.55%, while the specificity was 42.85%. Conclusion: Ultrasonic devices with high-frequency probes enable the display of accumulations of microcalcifications previously verified by mammography, and thus enable the performance of needle biopsy of suspected microcalcifications under ultrasonic control. An alternative is the much more complicated and significantly more expensive stereotactic biopsy under the control of mammography. Keywords: Ultrasound, ultrasound-guided needle biopsy, mammography, microcalcifications, breast cancer.

1. BACKGROUND

Sonography plays an important role in characterizing breast masses and in guiding needle core biopsies and wire localizations of suspicious sonographic abnormalities (1, 2). Recently, the emphasis has been on the complementarity of these diagnostic procedures, which is especially evident when the findings of mammography and ultrasound are observed in parallel. This leads to diagnostic accuracy in interpretation of findings of up to 98% (3). Among the most obvious shortcomings of ultrasound are its poor results in the registration of microcalcifications whose presence is associated with intraductal cancer, although there are papers showing that highresolution ultrasound devices can be used to detect microcalcifications in nonpalpable breast lesions (4). In the mid- to late 1990s, the advent of high-frequency transducers, increased computing power, and digital signal processing resulted in improved sonographic resolution and contrast. Using this most modern technology, radiologists are now identifying microcalcifications more frequently by sonography (5-7).

Ductal carcinoma in situ (DCIS) is manifested on mammography by clusters of microcalcifications, usually without associated soft tissue lesions (8, 9). Patients with suspected microcalcifications present on mammography are subjected to stereotactic biopsy under
mammographic control in further processing. Stereotactic wide-needle biopsy (core or vacuum biopsy) under mammographic supervision is significantly more complex, time-consuming and more difficult to perform than ultrasound guided biopsies (10). Mammography guided biopsies require several images of the breast from different projections, thus exposing the breast to additional ionizing radiation, which carries known risks for the development of harmful repercussions. The patient is uncomfortable, with a compressed breast, and with a significant sensation of pain and discomfort (11). During a biopsy performed in a sitting position on a rotating chair, women relatively often collapse. Anterior and prepectoral lesions are common, which are not possible to biopsy. Mammographic stereotactic equipment, especially MR stereotactic equipment, is extremely expensive and the procedures are time-consuming and technically very demanding and complicated (12). Needle biopsy under ultrasound control is performed with the patient in the supine position on their back or side, and it is possible to change the patient’s position. Unlike stereotactic biopsy, the breast is not compressed and it is not exposed to ionizing radiation. Ultrasound-guided needle biopsy can be used for lesions located in any quadrant of the breast. The direction of the needle is monitored under ultrasound control. The time required to perform is significantly shorter. The test is cheaper and more accessible. In the same act, biopsy of several lesions from one breast can be performed, i.e. biopsy of lesions from both breasts.

2. OBJECTIVE

The aim of the study were: a) to show the possibilities of high frequency ultrasound devices in the presentation of mammographically verified microcalcifications of the breast; b) the use of these possibilities in performing needle biopsy under ultrasound control which is of particular importance for Centers that do not have the ability to perform expensive and complicated stereotactic biopsy.

3. PATIENTS AND METHODS

The study was retrospective and was conducted on 32 women, 29–86 years of age, in the period from May 2017 to December 2020. Patients with suspected microcalcifications in the breast on mammography (radiological findings in accordance with the Breast Imaging Reporting and Data System as BI RADS 4B and 4C) underwent ultrasound examination with a high resolution probe and a high frequency of 12 MHz. In those patients in whom a hyperechoic glandular parenchyma, hypoechoic echoes, oval or irregular area with echogenic foci, or dilated milk ducts with echogenic foci in the area of the suspected microcalcifications on mammography, an ultrasound-guided needle biopsy was performed. Patients with suspected microcalcifications on mammography whose ultrasound findings were features underwent magnetic resonance imaging. Patients younger than 40 years of age underwent mammographic examination of the breasts after an ultrasound finding showing suspected microcalcifications.

If, after a needle biopsy of suspected microcalcifications guided by ultrasound, the expected diagnosis of breast cancer was not confirmed pathohistologically, the patients were referred to the Department for Plastic and Maxillofacial Surgery for excisional biopsy after markings were made under ultrasound control.

Mammography and breast ultrasound examinations were performed at the Department of Radiology and Nuclear Medicine, Tuzla Clinical Center. Mammography was performed using analog mammography updated to digital Siemens Mammmomat 5000 NOVA with cassette sizes 18x24 cm. Standard mammographic projections were performed: craniocaudal and mediolateral.

Ultrasound examinations were performed using a “TOSHIBA” Xario 100 breast ultrasound with linear probes measuring 12 MHz. Core needle biopsies (CNB) were taken after the administration of 2% Lidocaine, using a biopsy gun needle (14G diameter- Pro-Mag). At least three cores were taken from each lesion.

For technical reasons, the cylinders obtained by needle biopsy under ultrasound control could not be radiographed.

Mammography and breast ultrasound findings were interpreted by one radiologist.

After the HP diagnosis was obtained, the patients are presented to the Breast Oncology Board for further treatment. According to the decisions of the Breast Oncology Board, the patients were referred to the Plastic and Maxillofacial Surgery Department for surgery.

Statistical analysis

For statistical analysis, we applied standard methods of descriptive statistics, such as relative numbers (%), measures of central tendency, and measures of variability. For the analysis of the agreement of ultrasound findings with mammography the McNemar \( \chi^2 \)-test for dependent samples was applied.

4. RESULTS

The study included 32 patients with average age of 55.34 ± 15.77 years. Mammographic findings for 10 (31.25%) patients were concluded as BI RADS 4B, and for 22 (68.75%) patients as BI RADS 4C. Taking into account the density of breast shadowing according to the ACR classification of mammographic findings, 8 patients (25%) were classified in ACR category a breast shadowing, 15 (46.25%) as ACR B, 1 (3.125%) as ACR c and 10 (31.25%) as ACR category d. In 18 patients (56.25%) suspected microcalcifications were verified in clusters on mammography, in 10 patients (31.25%) in

| Total number of patients | Glandular parenchyma density according to ACR classification | Morphological characteristics of microcalcifications | Distribution of microcalcifications |
|--------------------------|------------------------------------------------------------|-----------------------------------------------------|----------------------------------|
| 32 (100%)                | ACR a = 8 (25%) ACR b = 13 (40,625%) ACR c = 1 (3,125%) ACR d = 10 (31,25%) | Amorphous - 5(15,625%) Pleomorphic- 22 (68,75%) Gross heterogeneous - 5(15,625%) | Cluster=18 (56,25%) Segmental=10(31,25%) Regional= 4 (12,5%) |

Table 1. Distribution of patients with respect to glandular parenchyma density, distribution and morphological characteristics of microcalcifications
Ultrasound-guided needle biopsy of suspected microcalcifications in the breast

Table 1. Distribution of patients with regard to ultrasound characteristics

| Ultrasound characteristics | Patients |
|----------------------------|----------|
| Hyperechoic glandular parenchyma | 2 (6.25%) |
| Hypoechoic echoes | 9 (28.125%) |
| Irregular hypoechoic area with echogenic foci | 11 (34.375%) |
| Echogenic foci | 8 (25%) |
| Dilated milk ducts | 2 (6.25%) |
| Table 2. Distribution of patients with regard to ultrasound characteristics |

| Number of patients | CORE biopsy | Excisional surgery |
|-------------------|-------------|-------------------|
| 4 (12.5%) | DCIS | Atypical ductal hyperplasia |
| 10 (31.25%) | DCIS | DCIS |
| 2 (6.25%) | Fibrocystic dysplasia | Fibrocystic dysplasia |
| 2 (6.25%) | Carcinoma intraductale | Carcinoma intraductale |
| 1 (3.125%) | Inflammatory infiltrate | Inflammatory infiltrate |
| 8 (25%) | DCIS | Carcinoma ductale microinvasivum |
| 1 (3.125%) | DCIS | Carcinoma ductale invasivum |
| 1 (3.125%) | Carcinoma ductale microinvasivum | Carcinoma ductale invasivum |
| 1 (3.125%) | Carcinoma papillare in situ | Carcinoma ductale invasivum |
| 1 (3.125%) | Carcinoma ductale precipue micropapillare „low grade“ | Carcinoma ductale invasivum |
| 1 (3.125%) | Carcinoma ductale invasivum | Carcinoma mixtum (micropapillare et ductale invasivum) |

Table 3. PHD needle biopsy and excisional surgery

Segmental distribution, and in 4 patients (12.5%) in regional distribution. Morphologically, the most common were pleomorphic microcalcifications verified in 22 patients (68.75%), followed by gross heterogeneous verified in 5 (15.625%) patients and amorphous also verified in 5 (15.625%).

Ultrasound examination of 2 patients (6.25%) with suspected microcalcifications on mammography verified hyperechoic glandular parenchyma and hypoechoic echoes were verified in 9 patients (28.125%). An irregular hypoechoic area with echogenic foci was verified in 11 patients (34.375%) and echogenic foci were verified in 8 patients (25%), noting that in 4 patients echogenic foci were verified by second look ultrasound, only upon examination after magnetic resonance imaging, and dilated milk ducts were verified in 2 patients (6.25%).

The pathohistological diagnosis after ultrasound-guided needle biopsy was ductal carcinoma in situ in 23 patients (71.875%), intraductal carcinoma in 2 patients (6.25%), fibrocystic dysplasia in 2 patients (6.25%), inflammatory infiltrate in 1 (3.125%), Ca ductale microinvasivum in 1 patient (3.125%), Ca ductale invasivum in 1 (3.125%), Ca papillare in situ in 1 (3.125%) and Ca micropapillare in 1 patient (3.125%). The presence of atypical ductal hyperplasia was found in 4 (12.5%) patients after surgical excision of PHD. PHD findings in 15 (46.875%) patients were confirmed after surgical excision. In 14 (43.75%) patients the PHD findings were upgraded to invasive cancers.

The sensitivity of mammography in the detection of microcalcifications in this study was 100%. The sensitivity of the ultrasound apparatus with a high frequency probe in the detection of microcalcifications after mammography examination in this study was 87.55%, while the specificity was 42.85%. The positive predictive value was 100% while the negative predictive value was 42.85%.

5. DISCUSSION

In this study, mammograms and ultrasound examinations of the breasts were performed in all patients before ultrasound-controlled needle biopsies. Four patients underwent a first ultrasound examination of the breast, after which the presence of microcalcifications was suspected, which was confirmed by mammography. Major strides have been made in the past decade in improving resolution and contrast in breast sonography, allowing better and more frequent visualization of breast microcalcifications (13-16). Although mammography examination revealed highly suspicious accumulations of microcalcifications in 4 patients (MMG findings concluded as BI RADS 4C), the first ultrasound examination did not detect any microcalcifications, which is explained by the fact that all 4 patients have breasts with a glandular structure. These patients underwent magnetic resonance imaging. The magnetic resonance finding accurately localized the pathological process, after which an ultrasound second look examination was performed.
for all 4 patients which localized accumulation of microcalcifications as echogenic foci within the dense glandular parenchyma. In the prospective study by Soo et al., 23% of microcalcifications without other mammographic findings were identified on sonography, and sonographic guidance was used successfully to guide the biopsy using core biopsy or wire localization techniques. A few false-positive sonograms have a specificity of 89%. The mammographic features of the microcalcifications that were most predictive of sonographic identification included the large size of the microcalcification group, a large number of calcific particles in the group, BI-RADS category 5 lesions, and segmental distribution of microcalcifications (15).

In a prospective study by Teh WL et al., forty-one patients (93%) had ultrasound abnormalities corresponding to mammographic calcification. USCB was performed on 37 patients. In 29/37, USCB obtained a definitive result (78.4%). USCB was non-diagnostic in 4/9 benign (44.4%) and 4/28 (14.3%) malignant lesions biopsied. The complete absolute sensibilities for malignancy using USCB were 85.7% (24/28) and 81% (25/31), respectively. USCB correctly identified invasive disease in 12/23 (52.2%) cases. There was no significant difference in the presence of abnormal flow on PD between benign and malignant lesions. However, abnormal PD vascularity was present in 43.5% of invasive cancers and was useful in directing successful biopsy in eight cases (17). In this study, in 15 patients (40.625%) PHD after needle biopsy under ultrasound control was more favorable than after surgical excision. This underestimation is explained by the fact that in 11 patients (34.357%) the breast was densely glandular, and in 2 patients (6.25%) the accumulations of microcalcifications were drowned in the glandular parenchyma, even though breast shadowing was ACR category b. Also, a possible reason for this underestimation is the fact that ultrasound-guided needle biopsies are done with smaller 14-gauge needles.

In the study by Soo et al., showed less underestimation of the disease when core biopsy was performed with sonographic guidance, compared with lesions using stereotactically guided biopsy, despite the fact that smaller 14-gauge needles were used in sampling 28% of cases with sonographic guidance and larger 11-gauge probes were used in all stereotactically guided biopsies. The smaller 14-gauge needles used with the multipass automated gun technique have previously been reported to result in more underestimation of disease than the 11-gauge probes used with the vacuum assisted technique, on the basis of data from a series of stereotactic biopsy cases (18, 19).

6. CONCLUSION

Ultrasound is a simple, reliable and widely accepted method for performing broad-needle biopsies and is an alternative to more complicated, expensive and patient-tolerant stereotactic biopsies under the control of mammography. Our study, despite its limitations—the small number of patients examined in one Center, without the possibility of post-procedural mammographic control of samples, still indicates the possibility of high-resolution ultrasound probes in the verification of microcalcifications registered by mammography.

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**REFERENCES**

1. Jackson VP. The role of ultrasound in breast imaging. Radiology. 199; 177: 305-311.
2. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. Radiology. 1995; 196: 123-124.
3. Fajdić I, Drinković I, Brkljačić B, Rainer S. Ultrazvuk dojke. Suvremena dijagnostika bolesti dojke. Medicinska naklada, Zagreb. 2001; 101-102.
4. Budan N. Algoritam dijagnostičkih postupaka prije početka liječenja raka dojke. Suvremena dijagnostika bolesti dojke. Medicinska naklada, Zagreb. 2001; 1-2.
5. Anderson ME, Soo MSC, Bentley RC, Trahey GE. The detection of breast microcalcifications with medical ultrasound. J Acoust Soc Am. 1997; 101: 29-39.
6. Yang WT, Suen M, Abuja A, Metreweli C. In vivo demonstration of microcalcification in breast cancer using high resolution ultrasound. Br J Radiol. 1997; 70: 685-690.
7. Moon WK, Im J-G, Koh YH, Noh D-Y, Park I.A. US of mammographically detected clustered microcalcifications. Radiology. 2000; 217: 849-854.
8. Lewin JM, Hendrick RE, D’Orsi CJ, et al. Comparison of full-field digital mammography with screen-film mammography for cancer detection: results of 4,945 paired examinations. Radiology. 2001; 218: 873-880.
9. Nyström L, Rutqvist LE, Wall S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials. Lancet. 1995; 341: 973-978.
10. Čikara I. Mogućnosti ultrazvuka visoke rezolucije u prikazu i nadzoru bolesti dojke. Suvremena dijagnostika bolesti dojke. Medicinski časopis, Zagreb. 2012; 6.
11. Bauer M, Tontsch P, Schulz-Wendtland R. Fine-needle aspiration and core biopsy. Radiological diagnosis of breast diseases, Springer, Berlin. 2000; 291-298.
12. Kuhl C. Current status of breast MRI: clinical applications. Radiology. 2007; 244(3): 672-691.
13. Soo MS, Baker JA, Rosen EL, Vo TT. Sonographically guided biopsy of suspicious microcalcifications of the breast: a pilot study. AJR. 2002; 178: 1007-1015.
14. Moon WK, Im J-G, Koh YH, Noh D-Y, Park I.A. US of mammographically detected clustered microcalcifications. Radiology. 2000; 217: 849-854.
15. Anderson ME, Soo MSC, Bentley RC, Trahey GE. The detection of breast microcalcifications with medical ultrasound. J Acoust Soc Am. 1997; 101: 29-39.
16. Yang WT, Suen M, Abuja A, Metreweli C. In vivo demonstration of microcalcification in breast cancer using high resolution ultrasound. Br J Radiol. 1997; 70: 685-690.
17. Teh WL, Wilson ARM, Evans AJ, Burrell H, Pinder SE, Ellis IO. Ultrasound-guided core biopsy of suspicious mammographic calcifications using high frequency and power Doppler ultrasound. Clin Radiol. 2000; 55: 390-394.
18. Liberman L, Smolkin JH, Dershaw DD, Morris EA, Abramson AF, Rosen PP. Calcification retrieval at stereotactic, 11-gauge, directional, vacuum-assisted breast biopsy. Radiology. 1998; 208: 251-260.
19. Jackman RJ, Burbank F, Parker SH, et al. Stereotactic breast biopsy of nonpalpable lesions: determinants of ductal carcinoma in situ underestimation rates. Radiology. 2001; 218: 497-502.