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Evaluation of The Value of Core Needle Biopsy in The Diagnosis of a Breast Mass

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ABSTRACT

Background: Core needle biopsy (CNB) with histological findings is regarded as one of the most important diagnostic measures that make preoperative assessment and planning for appropriate treatment possible. The aim of this study was to determine the sensitivity and specificity of core biopsy results in our patients with benign and malignant breast lumps, especially for borderline breast lesions, by using a classification method.

Methods: In this study, 116 patients who were referred to the Surgery Clinic of Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran with breast lump and underwent diagnostic procedures such as mammography and ultrasound were selected. Core needle biopsy (Tru-cut #14 or 16) was performed. After that, excisional biopsy was done. The benign, malignant and unspecified samples obtained by core needle biopsy were evaluated with the samples of the surgical and pathological findings. Then, false positive, false negative, sensitivity, specificity, and diagnostic accuracy of the core needle biopsy method were calculated. Also, the National Health Service Breast Screening Program (NHSBSP) classification was employed.

Results: The mean age of the participants in this study was 39±13.13 years and the mean tumor size was 2.7 cm. An average of 3.35 biopsies was taken from all patients. Most of the pathology samples taken from CNB and excisional biopsy were compatible with invasive ductal carcinoma. Of the B type classifications, B5 was the most frequent in both methods. Borderline lesions B3 and B4 had a change in their category after surgery. About 2.5% of the samples in core biopsy were inadequate. Skin bruising was the most common core biopsy complication reported. While, the most common complication of excisional biopsy was hematoma. Accuracy, sensitivity, specificity, positive and negative predictive values of the core needle biopsy procedure compared with excisional biopsy was 95.5%, 92.6%, 100%, 100%, and 91.8%, respectively.

Conclusions: Core needle biopsy has a high sensitivity and specificity with few side effects. Borderline classifications need more evaluation to rule out cancers.

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Introduction

Breast cancer is the most common cancer worldwide.[1, 2] Also, breast cancer is the most common cancer in Iranian women[3], and considering the fact that the majority of patients are referred with breast masses, selecting appropriate diagnostic and treatment method is very important.[1, 2] Today, biopsy

especially core needle biopsy (CNB) which can be used instead of open biopsy and breast surgery, has a special place in researches, particularly because it can be performed without hospitalization and therefore is not costly. In contrast, excisional biopsy, which requires surgery and an operating room and hospitalization, can increase the cost of treatment. Moreover, several studies have shown the possibility of using preoperative patient evaluations on core biopsy samples to create comprehensive treatment strategy.[4]

In core samples, genetic evaluation and assessment of hormone receptors and tumor markers can be done in addition to routine pathologic evaluation and if necessary, the clinician can discuss new treatment methods such as neo-adjuvant (pre-operative chemotherapy), sentinel lymph node biopsy (SLN), and immediate breast reconstruction after mastectomy.[3, 4] CNB can provide tissue specimens from the mass using various techniques with or without image guiding for non-palpable or palpable breast masses. This procedure can be performed either manually or with a biopsy gun.

Even if the mass is fixed on palpation, it could still be moved by the needle causing sample error. This can happen when the procedure is done manually. The use of ultrasound, even when we are dealing with palpable lesions, can be helpful for correct lesion insertion by the needle to obtain sufficient samples. A number of samples need to be collected from different parts of the lesion to ensure a sufficient amount of samples. If future follow up such as surgical resection is necessary, four to six lesions are desirable to place a marker on the lesion location.

Open biopsy is still a common method of the evaluation of a breast mass by some surgeons in our region with no national guidelines available in our country; these surgeon are not familiar with the procedure and do not use it in some cities so if our study shows good results, needle biopsy can be more popular as an available alternative method to open surgery. Also, acceptable results of our study can help to improve teamwork and interdisciplinary collaboration. In order to determine the borderline case sand diagnostic values of our core biopsies, we used the National Health Service Breast Screening Program classification (NHSBSP) (by dividing the results into five categories), for better management of borderline reports.[5] The aim of our study was to find the accuracy of our core biopsy method and to determine how the use of the NHSBSP classification method could help in the interpretation of biopsy results and evaluation of the patients for selecting a proper treatment method.

Methods

Patients referred to the Breast and Surgery Clinics of Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran with a complaint of breast mass and underwent diagnostic mammography and ultrasound procedures from May 2012 to June 2014 were selected to participate in this study.

Study inclusion and exclusion criteria

Patients included in this study had breast masses and underwent CNB biopsy. Furthermore, the benign cases had to undergo surgical biopsy (because of large-sized fibroadenomas, recurring cysts, being high risk for cancer, or the patient's desire to remove the lump).

Patients were excluded if they did not have the possibility for proper follow up and, those with benign masses or were not willing to have mass excision. After obtaining informed consent from the patients, their demographics and previous medical history (including biopsy, history of cancer, and cancer risk factors) were recorded.

Then, two surgeons who were familiar with the procedure did CNB by a 16 or 14-gauge Tru-Cut needle (TSK semiautomatic or automate needle biopsy). The procedure includes 3 to 4 mm incision and then the core needle is inserted and biopsies are taken. After that, the patients underwent an excisional biopsy or lumpectomy or mastectomy according to pathologic results. Borderline or unspecified results of the CNB sample were also evaluated by excisional surgery. Then, false-positive and false-negative rates were determined.

False negative was described when the results showed a benign lesion in core sample and a malignant lesion was reported in the final pathology. False positive was defined as the malignant report of the CNB sample but non-malignant results in the final pathology. The diagnostic value (predictive value) and, sensitivity and specificity of the core biopsy were also determined.

The complications of CNB such as infection, bleeding, hematoma, and pain were evaluated. Also, classification based on NHSBSP in all of the five result groups were determined as below[5]:

B1: Normal breast tissue like lipoma or hamartoma;

B2: Benign lesion like fibroadenoma, fibrocyctic, duct ectasia, and fat necrosis;

B3: Lesion of uncertain malignant potential like atypical ductal hyperplasia, papillary lesion, lobular neoplasia, and radial scar;

B4: Suspicious lesion like high grade atypical;

B5: Malignant lesion like *in situ* or invasive ductal or lobular carcinoma

The diagnostic value was determined in each group, especially in borderline cases.

Statistical analysis

With a study power of 90%, statistical significance set at 5% and assuming a sensitivity of 71% for carcinoma *in situ* according to Cipolla *et al*., the required sample size was at least 108 participants.[6] First, the population was classified based on demographic characteristics including age, tumor

size and type of tumor, left or right breast, the number of core biopsies, the percentage of inadequate samples, core biopsies and final pathology, tumor grade in core biopsy samples and pathological findings, and blind biopsy complications. Then, the association between complications and the number of biopsies were described in terms of frequency and p-value. Also, the false positive and false negative of this method were evaluated. Next, the relationship between false positive cases with the number of biopsies and tumor size was examined. Finally, the accuracy, sensitivity, and specificity of the CNB were determined.

Results

In this study, 116 patients with a mean age of 39±13.13 years ranging from 17 to 80 years were enrolled. About 56.9% of the patients had a mass on the right side and 43.1% on left side. The mean mass size was 2.77±1.52 cm, varying from 0.8 cm to 8 cm. The mass diameter mostly were categorized as T1 (0 to 2 cm). The number of biopsies taken from the patients varied from 1 to 7 with a mean of 3.35±1.24. In 3 cases (2.5%), core biopsy specimens were inadequate and their data were excluded from the final analysis.

Pathologic evaluation of 113 CNB samples showed that invasive ductal carcinoma was the most frequent with 59 cases (52.2%). According to the results of the excisional biopsy, invasive ductal carcinoma was the most frequent with 65 cases (57.5%). Other results in core samples were fibroadenoma (20.6%), fibrocyctic change (6.8%), mastitis (4.3%), invasive lobular carcinoma (2.5%), *in situ* carcinoma (0.8%), and granulomatousmastitis (2.5%). We had 3 inadequate specimens and 10 patients (8.6%) with other pathologies like papillary lesion, radial scar, ductal lesion with atypia, ductal ectasia, *etc*. Using the NHSBSP classification, it was found that 4(3.6%) patients were in the B3 and 2(1.8%) in the B4 group. After surgical excision, 5 of these challenging results showed malignancy. The frequencies of samples in each NHSBSP category are presented in table 1.

Of the 113 patients who underwent CNB, 31 cases of bruising, 3 of bleeding, 7 case of hematoma, one case of infection, and 7 cases of pain were reported. All complications were cured without hospitalization. The relationship between the number of biopsy samples taken and complications was studied. The number of biopsies was 4.43±1.13 in patients who had hematoma and 3.28±1.225 in other patients, which showed a significant difference (P = 0.019). Other complications had no significant relationship with the number of biopsies.

The mass status data obtained from the two series of CNB and surgical samples showed that among the 113 samples in 108 cases (95.5%), the condition in the two series was quite consistent. The 5 discordant cases (4.42%) were false negative cases in samples taken via CNB.The sensitivity, specificity, accuracy, and positive and negative predictive values of this technique to determine the status of breast masses were 92.6%, 100%, 95.5%, 100%, and 91.8%, respectively.

Table 1. Results of pathologic findings through core needle and excisional biopsy based on NHSBSP classification

NHSBSP categories	CNB N (%)	Excisional biopsy N (%)
B1	1 (0.8%)	0 (0%)
B2	43 (38.1%)	44 (39%)
B3	4 (3.6%)	1 (0.8%)
B4	2 (1.8%)	0 (0%)
B5	63 (55.7%)	68 (60.2%)
Total	113 (100%)	113 (100%)

Abbreviation: NHSBSP: National Health Service Breast Screening Program; CNB: core needle biopsy

Discussion

In recent years, the use of core needle biopsy for histopathological characterization of suspicious breast lesions has increased, which has reduced the number of surgical biopsies or intraoperative evaluation of the lumps.[7] The false negative cases of breast biopsy are very low; however, if the results are not concordant with the clinical picture or radiologic evaluations, rebiopsy is necessary.[8] The disadvantages of this technique include the need for inserting multiple needles, patient discomfort, moderate costs, and the lack of a complete set of features of the lesion.

Our aim was to determine the accuracy of needle biopsy and the rate of complications in our patients with breast mass and also to enhance decision making strategies in treatment by using a classification method. In 116 of our patients, a right mass was more prevalent and the mean size was 2.7 cm, but most of the patients had a tumor size between 0-2 cm that reduced errors in results because of the heterogenecity of larger tumors. In large size masses, core biopsy may not be reliable enough because it cannot provide adequate samples of the entire tumor; there may be malignancy in some parts of the mass where we do not have any samples for evaluation.

Several studies have reported a strong correlation between the results of CNB and surgical biopsies. In addition, it is helpful in some cases such as patients with ductal carcinoma in situ and lobular or atypical

hyperplasia.[9,10]

Cipolla *et al*. evaluated 195 patients with suspicious debris and reported that the correlation between core biopsy and final biopsy was 94.9% in infiltrative carcinoma and 71% in carcinoma in situ. The predictive value was 98.9% with a sensitivity of 96.1% and a specificity of 93.3%.[6]

In a study by Andrew *et al*., the CNB results were classified into five groups based on the NHSBSP. In a study of 3054 patients with B5 (malignant) and B4 (suspicious) tumor, the diagnostic value of core needle biopsy was 100% with no false positive cases; the negative predictive value in B2 (benign) was 97.3 % with a false negative of 3.5%.[6]. This classification of CNB results has been used by different pathologists.[11]

According to our results, the B4 lesion was reported malignant in the final surgery and half of B3 lesions were malignant, as well. So, it seems that surgical excision or rebiopsy in these categories is required.

Li and colleagues studied 177 patients and reported a sensitivity of 94.4%, false negative of 5.1%, specificity of 100%, false positive of 0%, positive predictive value of 100%, and negative predictive value of 85.4%.[12] Flegg *et al*. evaluated borderline breast lesions, ductal hyperplasia or non-atypical lobular, papillary lesions, carcinoma *in situ*. Comparison of the results of needle biopsy and surgical removal indicated 20% benign pathology, 55% borderline lesions, 17% non-invasive malignancy, and 7% invasive malignancy. The results suggested that further investigation of these lesions was required.[13]

In a systematic review study of various biopsy techniques, Bruening and colleagues discussed the best method of biopsy. In general, CNB has advantages over fine needle aspiration (FNA), including a lower number of suspected cases and determining cancer hormone receptors, while thin-needle biopsy (FNA) does not show invasion estimates. Papillary lesions in situ, fibroblasts, and less malignant cases of the epithelium can also be detected by CNB. Our CNB results also showed a good detection rate without false positive, but we did not compare the results with FNA in our patients.[14]

Ultrasound and core biopsy can be reliable diagnostic methods for benign lesions such as fibroadenoma.[15] Comparison of our results showed a good correlation between core and surgical biopsy. We only had 3 inadequate specimens, 110 patients (97.3%) had concordant core and surgical biopsy results with a sensitivity of 95% and a specificity of 100 % that was similar to other studies. CNB can provide the possibility of planning for sentinel lymph node biopsy before surgery in the early stages of cancer and pre-operative chemotherapy in advanced stages by detecting the cancer. The tumor response to chemotherapy agents is more reviewable than surgical biopsy cases.[16, 17] Moreover, breast biopsy core samples can be used for conducting genetics studies.[18]

According to Bilous, although biopsy gives a definitive answer in many cases or at least provides information that can be used to plan the treatment, there are still unresolved issues regarding the results, especially in potentially malignant lesions in which surgical removal is advised. However, more research is recommended in this regard.[19]

In a study done in Turkey in 2007, 201 patients who were supposed to have breast cancer and underwent CNB followed by surgical biopsy (lumpectomy or mastectomy) were evaluated. Then, by adjusting for factors such as size, number of biopsies, and the location of biopsy, concordant results were 82% regarding the tumor type and 68% regarding the breast grade between the two methods of CNB and surgical biopsy. According to the results of this study, CNB was recommended as a beneficial method for treatment planning. To increase the accuracy of the results, they suggested performing the procedure under the ultrasound guide.[20]

In a study in 2009 in South Korea, 104 CNB breast cancer samples were examined. The conformity of the two methods of CNB and surgical biopsy in determining the tumor type and grade was reported to be 100% and 81%, respectively. Therefore, the CNB method was found to be of use for predicting the tumor grade before surgery.[21]

In 2011, a study was conducted on 209 patients with breast cancer in the United States. The accuracy of CNB was compared with surgical biopsy and the result for tumor diagnosis was 93%. Grade determination was 86%. The samples were taken under the ultrasound guide or via stereotaxy, and four to six biopsies were available for each tumor. The results showed that CNB was not a reliable method for determining the breast tumor grade in all cases.[22]

Jangjoo *et al.* studied 30 patients with primary breast cancer who underwent CNB followed by definitive surgery. He found that CNB was a reliable method in determining the tumor pathology, grading, and also the estrogen and progesterone receptor status. Prognostic factors of breast cancer including the estrogen receptor, progesterone receptor, HER-2, P53 were concordant in the two methods (97%, 90%, 63%, and 77% respectively).[23]

Karimian assessed the value of CNB as a first approach in the management of palpable breast masses. In this study, 112 patients with palpable breast masses participated and, adequate samples were prepared in 103 cases (91.9%). In 78 (69.6%) cases in whom malignancy was reported, the results were consistent with samples obtained from surgical biopsy. In 34 (30.4%) patients, CNB with benign samples was reported and after three years of follow-up, 25 (73%) of these patients underwent surgical

biopsy and in one case (3%) malignant tumors were confirmed.[24] We did not include follow up patients in our study because of some ethical considerations as patients with benign masses may not be willing to undergo excision. It may be our limitation so further studies with more patients are needed to evaluate the follow up of patients. Also, 2.5% of the samples in core biopsy were inadequate which were excluded. In our study, the diagnostic accuracy, sensitivity, specificity, false positive, false negative, and positive and negative predictive values of CNB as compared with surgery were 97.3%, 94%, 100%, 2.7% 0%, 96%, and 100%, respectively. Moreover, the relationship between the number of biopsies, the size of the mass, and false positive was not significant. We also had a low rate of complications, and the number of biopsies was significant in association with the rate of hematoma (p=0.019). This study recommends CNB as an appropriate first step in the evaluation of breast masses.[24]

In conclusion, core needle biopsy has a good predictive value and has few complications for evaluating a breast mass. Considering the fact that core needle biopsy does not need any anesthesia and hospitalization, it is a suitable method to diagnose benign or malignant breast lumps. The use of the NHSBSP classification for the evaluation of the core results can help with making better decisions in borderline reports.

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