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EPIDEMIOLOGY

Is core needle biopsy effective at diagnosing male breast lesions?

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Abstract

Purpose The objective of this study was to examine the diagnostic accuracy of sonographically guided core needle biopsy (CNB) of breast lesions in men.

Methods This was a retrospective study where we analyzed consecutive sonographically guided 14-gauge CNB results on 234 male breast lesions. The CNB accuracy is determined by the comparison between the CNB and its corresponding excisional biopsy or to long-term follow-up imaging.

Results Sonographically guided CNB was effective to collect satisfactory samples from all 234 lesions. Out of those, 58.55% (137/234) were benign, 38.0% (89/234) were malignant, 1.71% (4/234) were papilloma with atypia and 1.71% (4/234) were atypical ductal hyperplasia lesions. Underestimation occurred in 3.4% (8/234) of the lesions. As for the detection of breast malignancy, the sensitivity of the CNB is 98.9%, specificity is 100%, negative predictive value is 99.3%, positive predictive value is 100%, false positive is 0% and false negative is 1.1%. The overall accuracy of sonographically guided CNB as a diagnostic tool is 99.6%.

Conclusion Sonographically guided 14-gauge CNB is an accurate, reliable and low invasive procedure for assessing breast lesions in men. Triple tests and follow-up checks of benign cases are essential for a successful breast biopsy program in men.

Keywords Male lesions · Breast neoplasm · Core needle biopsy · Breast ultrasonography · Male breast cancer

Introduction

The importance of preoperative histological diagnosis in the assessment of breast lesions in women is widely recognized. However, histological diagnosis is performed in men who present with breast lesions in a limited number of cases. Male breast cancer is a rare disease, accounting for < 1% of all men's breast cancers and < 1% of all cancer deaths annually [1]. Even if the incidence of male breast cancer has risen significantly for the last two decades. The management of male breast cancer patients has been generalized from the management of breast cancer in women because of its scarcity and lack of population-based screening and randomized trials [2, 3].

Breast cancer in women is generally diagnosed by core needle biopsy (CNB), which has a high diagnostic accuracy. Histological subtype, molecular markers including hormone receptor status and human epidermal growth factor receptor 2 status can be assessed reasonably well on CNB [4]. However, fine needle aspiration (FNA) is the principal mode of diagnosis in the management of breast lesions in male patients. A small number of series of FNA of the male breast have been reported [5–9]. FNA yields a high percentage of unsatisfactory samples (15%) [8]. There are few studies have been published on the use of CNB for male breast lesions [10–13]. Little is known about the clinical value of CNB in male breast lesions.

The aim of this study is to investigate the diagnostic accuracy of CNB performed for suspicious breast lesions in a cohort of Chinese male patients in our single-center experience.

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Materials and methods

This is a retrospective study of all consecutive core biopsies performed at Fudan University Shanghai Cancer Center (FUSCC) over a 10-year period. From January 1st 2007, to January 1st, 2017, 234 sonographically guided CNB were performed in 233 male patients in our center. Among these patients, 233 had biopsy of one lesion, one had biopsy of bilateral lesions. Informed consent was obtained from each patient before biopsy had been performed.

We recommended ultrasound-guided CNB for all sonographically visible solid breast lesions that required tissue diagnosis. All CNB were performed using a Monopty disposable automated 14-gauge cutting needle with a 22-mm throw (Bard Peripheral Technologies, Covington, GA). Freehand sonography using an HDI 3000 scanner (Philips-ATL, Bothell, WA) guided by a 5–10-MHz linear-array transducer was used during this procedure. The patient was placed in supine position. A small skin incision (4 mm) was made and the probe was positioned into the lesion by ultrasound guidance. The acquisition of tissue was performed in different ways and from different angles, as needed. The number of samples varied according to lesion size. A mean of four CNB specimens per lesion (range 2–7) was obtained. All core specimens were placed in 10% neutral buffered formalin and sent for pathologic analysis. The specific recommendations for follow-up were made to the patients whose histopathologic biopsy results were correlated with the imaging findings. Patients with malignant lesions revealed by CNB were immediately referred for surgery. We recommended excisional biopsy in cases of undetermined pathologic findings on CNB. In addition, if radiological and pathological findings were not consistent, repeat biopsy (open surgical excision) was performed. Patients diagnosed with benign conditions were followed up at 6-month intervals. Two-year routine follow-up is the recommendation for lesions with benign biopsy results. The mean follow-up duration was 4.2 years (range 2–9.6 years).

Because adequate number of lesion samples were included, it is meaningful to show the accuracy of CNB in identification of lesions. Therefore, the sensitivity, specificity, negative and positive predictive values, false positive, false negative, accuracy were calculated. Underestimation was considered when high-risk lesions including atypical ductal hyperplasia (ADH) and papilloma with atypia diagnosed at CNB was found during surgical procedure to be carcinoma, or ductal carcinoma in situ (DCIS) diagnosed at CNB was upgraded to invasive carcinoma. False negatives were considered when DCIS or invasive carcinoma were found during surgical procedure or follow-up, after CNB had shown benign results. For this analysis, patients with definitive diagnosis (surgery or follow-up imaging) of ADH and papilloma with atypia were considered in the group of patients with benign lesions.

Results

Two hundred and thirty three patients with 234 lesions were submitted to sonographically guided 14-gauge core needle biopsy procedure in the study period. The average age of the patients was 55.1 years, ranging between 18 and 83 years old. The average size of the lesions was 22 mm, ranging between 6 and 45 mm. All biopsies obtained sufficient tissue for histological analysis. Histological diagnoses are summarized in Table 1.

Adequate tissue samples for histopathologic evaluation were obtained from all 234 sonographically guided CNB procedures. Out of these, 58.55% (137/234) were benign, 38.0% (89/234) were malignant, 1.71% (4/234) showed papilloma with atypia and 1.71% (4/234) were ADH lesions. The histopathologic diagnosis is shown in Table 1. Sonographically guided CNB revealed malignancy in 89 (38%) of the 234 lesions (Table 1). Sonographically guided CNB showed breast-invasive carcinoma in 80 (34.2%) of the 234 lesions (Table 1). One patient is with bilateral breast-invasive carcinoma. Histopathologic findings after definitive surgical treatment were concordant with the CNB diagnoses in

Table 1 Pathological results of core needle biopsy of 234 lesions in 233 male patients

Status	Diagnosis	Number of patients
Malignant		89 (38.0%)
	Invasive ductal carcinoma	80
	Ductal carcinoma in situ	6
	Lymphoma	1
	Metastases	1
	Dermatofibrosarcoma protuberan	1
High-risk lesions		8 (3.4%)
	Atypical ductal hyperplasia	4
	Papilloma with atypia	4
Benign		137 (58.55%)
	Gynecomastia	90
	Inflammation (mastitsi)	12
	Adenosis	15
	Lipoma	9
	Benign nonspecific (normal tissue)	6
	Hemangioma	2
	Epidermal cyst	2
	Fibroadenoma	1

the 79 lesions that were excised. The remaining one patients in this group had no further surgical treatment because of multiple bone metastases and old age. He was treated with tamoxifen.

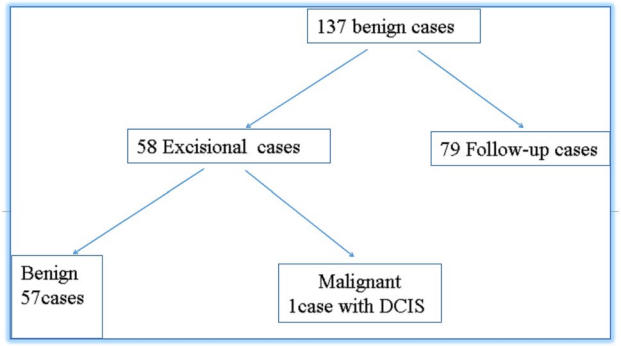
Sonographically guided CNB showed DCIS in only 6 (2.56%) of the 234 lesions (Table 1). Subsequent surgical excision confirmed DCIS only (no evidence of invasion) in two of these six lesions. Among the six patients with six DCIS lesions found on core needle biopsy, four previously sampled sites (66.7%) were upstaged to infiltrating ductal carcinoma after surgical excision (Table 2).

Sonographically guided CNB showed high-risk lesions including ADH and papilloma with atypia in 8 (3.42%) of the 234 lesions (Table 1). Subsequent surgical excision of these lesions showed that four of eight high-risk lesions (50%) on core needle biopsy were found to harbor carcinoma on surgical excision. One patient was found to have DCIS, and three patients were found to have infiltrating ductal carcinoma (Table 2).

One metastatic lesion occurred in a patient with a previous diagnosis of melanoma. We also found one primary diffuse large B cell lymphoma, and one dermatofibrosarcoma protuberan.

137 (58.5%) of the CNB specimens were diagnosed as specific benign lesions, including gynecomastia ($n=90$), inflammation (mastitsi, $n=12$), adenosis ($n=15$), lipoma ($n=9$), benign nonspecific (normal tissue) ($n=6$), hemangioma ($n=2$), epidermal cyst ($n=2$), and fibroadenoma ($n=1$). From the benign lesions ($n=137$), 58 underwent excisional biopsy due to discordance between the histological reports, the disagreement between radiologic and pathologic findings and patient or surgeon preference. Only in one case, DCIS was observed during surgical procedure. In the remaining 79 lesions, that underwent long-term imaging follow-up (> 2 years). During the follow-up period no women presented with carcinoma at the site of the prior CNB (Fig. 1).

The sensitivity of sonographically guided 14-gauge CNB for the diagnosis of breast malignancy was 98.9%, specificity 100%, negative predictive value 99.3%, positive predictive value 100%, false positive 0% and false negative 1.1%. The overall accuracy of the procedure was 99.6% (Table 3).



DCIS: ductal carcinoma in situ

Fig. 1 Further treatments and pathological results for cases identified as benign by core needle biopsy

Discussions

To our knowledge, our study represents the largest reported series on CNB as an initial diagnostic procedure for suspicious male breast lesions. All 234 samples contained sufficient tissue for diagnosis, and there were no procedure-related complications. We confirmed that 14-gauge CNB is a safe and effective method for assessment of male breast lesions.

The goal of image-guided breast biopsy is to increase the accuracy distinguishing benign and malignant lesions. Accurate diagnosis of benign pathology avoids unnecessary breast surgery. The accurate percutaneous diagnosis of breast cancer can facilitate preoperative planning, thus enabling surgical treatment of breast cancer in one operation. Fine needle aspiration (FNA) has been shown to have a high sensitivity and specificity in male. Two studies demonstrated that FNA had sensitivity and specificity that approached 100% [7, 14]. This is comparable with large studies in female disease in which sensitivity and specificity were reported as 97.1% and

Table 2 Comparisons of core needle biopsy and excisional biopsy results

Core biopsy	No. of lesion	No. of lesions upstaged with excision	Underestimation rate (%)
DCIS	6	4 IDC	66.7
High-risk lesions (ADH, papilloma with atypia)	8	3 DCIS and 1 IDC	50

ADH atypical ductal hyperplasia, *DCIS* ductal carcinoma in situ, *IDC* invasive ductal carcinoma

Table 3 Diagnostic performance of core needle biopsy of breast lesions in men

Result	Value (%)
Sensitivity	98.9
Specificity	100
Positive predictive value	100
Negative predictive value	99.3
False positive	0
False negative	1.1
Accuracy	99.6

99.1%, respectively [15]. However, FNA has a high rate of unsatisfactory specimens, as suggested in two male lesion studies. Westenend et al. analyzed a series of 153 FNAs of male breast masses, finding an inadequate rate of 13% [9]. Siddiqui et al. studied the largest series of 614 FNAs of male breast masses, reporting similar result with an inadequate rate of 15.3% [8]. However, FNA still remains as a primary diagnostic tool in male breast lesion diagnosis. Other studies also found CNB to be more reliable in collecting samples and identifying lesion in men, as compared to FNA [11, 12]. Thus, CNB seems to be quite an accurate diagnostic method if compared with published studies concerning FNA as a primary diagnostic tool in male. Previous reports of image-guided CNB in female, have shown that the procedure's accuracy is similar to that of surgical excision [16]. It's is consistent with current findings in male.

Our study also demonstrate the diagnostic value of CNB in male breast lesions regarding sensitivity, specificity, and other parameters that are comparable with the finding on the results that have been reported with CNB in the female [17, 18]. To our knowledge, only a limited number of articles have examined the value of CNB in the evaluation of breast masses found in male [10–13]. Because the results of CNB in these studies were reported in different ways, we have summarized these findings so that we were able to make a comparison (Table 4).

Pathological underestimation is an important concern on the CNB of the breast. Although the use of CNB in male breast lesions has been reported, there is no enough data to assess the underestimation due to fewer than ten breast cancer cases in those studies [10, 12, 13]. The larger number of cases was the study of Bichhierai et al. [11]. Six cases of undefined lesions were found in the CNB. The pathological result of one case was invasive carcinoma after surgical biopsy. Unfortunately, there are no specific pathological descriptions for the six undetermined lesions of the CNB in their study. In the current study, sufficient breast cancer cases enable to analyze the pathological underestimation of male breast masses. Two different types of underestimation emerged as we compared preoperative and postoperative pathological outcomes. Four of six cases, which were initially diagnosed as DCIS by CNB, were later found to be invasive carcinoma. In addition, one case was upgraded from high-risk ADH to DCIS. This may be due to insufficient materials collected by 14-gauge CNB. The other type of underestimation could be attributed to the heterogeneity of the lesion itself, such as papillary lesions. In our study, three cases of papillary lesions with atypia were pathologically underestimated. Postoperative pathology confirmed two cases of intracystic (encapsulated) papillary carcinoma, another case is invasive papillary carcinoma. As a result, a relative high underestimation rate of 57.1% (8/14) by 14-gauge CNB suggests the necessity of combining multiple assessment tools. The conserving surgery is probably optimal treatment when dealing with high-risk cases.

This study also measures the false-negative rate of CNB. This is another important issue that needs attention during clinical practice. In our study, for patients with CNB benign breast lesions, we adhere to the principles of triple tests (clinical, imaging and pathological). On the other hand, we try to avoid missing diagnosis and delaying the detection of early breast cancer through long-term follow-ups. CNB results indicated that 137 cases were benign lesions. However, 1 in 58 cases was found to be DCIS after open biopsy. We then re-analyzed data of this patient and found the inconsistency between imaging and pathological findings. Regardless of a low rate of 1.7%, the occurrence of false negative in CNB results reminds clinicians the importance of triple tests when assessing male breast lesions. Therefore, the principle of triple test is also subject to follow in the management of male breast lesions. To minimize underestimation and false negativity, we provide the diagnostic recommendations for management of breast lesions in men detected by core needle biopsy in clinical practice (Table 5).

In conclusion, our study confirms that ultrasound-guided CNB is an accurate diagnostic tool for assessing male breast lesions that require tissue sampling. The diagnostic sensitivity of ultrasound-guided CNB for breast malignancies reaches 98.9%, making this method the preferred choice for diagnosing breast carcinoma in man breast lesions that are

Table 4 Comparison of findings in core needle biopsy of breast lesions in men with those results published in the previous literature

Author	Country	Lesions	CNB malignancy	CNB benign	Undetermined	Re-biopsy	Follow-up	G	Cores
Westend (2003)	Netherlands	26	6	20	–	3 (3 benign)	5–94 months	–	–
Janes (2006)	UK	113	3 (2 MBC)	110	–	–	–	14	2–3
Bazzocchi (2010)	Italy	31	7	24	–	–	Mean 31 months	14	3.5 (2–5)
Bichhierai (2017)	Italy	131	32 (27 MBC)	93	6	6 (1 MBC, 5 benign)	9.2 years (0.6–18)	14	3–7
Yang, current study	China	234	89 (86 MBC)	137	8	66 (5 MBC, 61 benign)	4.2 years (2–9.6)	14	4 (2–7)

MBC male breast cancer, *G* gauge cutting needle

Table 5 The diagnostic pathway for breast lesions in men by core needle biopsy

CNB results of breast lesions in men	Management recommendation
High-risk lesions (ADH and papilloma with atypia etc.)	Surgical excision
DCIS	Surgical excision
Benign	Observation with clinical or imaging follow up or surgical excision

CNB core needle biopsy, *ADH* atypical ductal hyperplasia, *DCIS* ductal carcinoma in situ, *IDC* invasive ductal carcinoma

visible sonographically. Triple test and careful follow-up of nonspecific benign lesions are the cornerstones of successful management in male breast lesions.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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