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Ultrasound-guided fine-needle aspiration cytology: Diagnostic value in breast solid masses.

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Abstract

Objective: To evaluate the efficacy of ultrasound-guided fine-needle aspiration cytology for the diagnosis of breast solid masses.

Materials and method: It is a retrospective study with 705 patients carrying a solid breast mass who underwent ultrasound-guided fine-needle aspiration cytology for the diagnosis. The fine needle aspiration cytology (FNAC) was performed with ultrasound guidance and a 21 G gauge needle was used. The cytological results were classified as benign, suspicious, malignant or insufficient. The benign results were considered negative for malignancy and the malignant and suspect results were considered positive for malignancy. Insufficient results were not included in analysis of the accuracy of the study.

In all cases the histological result of the masses was obtained and it was taken as reference test. The ultrasound-guided FNAC accuracy was evaluated for all cases and then specifically for the masses classified in the categories 3, 4 and 5 of BI-RADS.

Results: When all cases were included the results were the following: sensitivity 96%, specificity 92%, positive predictive value 97%, negative predictive value 89%, false positives 3%, false negatives 11% and overall accuracy 95%. For the BI-RADS category 3 the results were the following: sensitivity 100%, specificity 98%, positive predictive value 90%, negative predictive value 100%, false positives 10%, there were no false negatives and overall accuracy 98%.

For the BI-RADS category 4 the results were the following: sensitivity 92%, specificity 85%, positive predictive value 95%, negative predictive value 78%, false positives 5 %, false negatives 21% and overall accuracy 91%. For the BI-RADS category 5 the results were the following: sensitivity 99%, specificity 75%, positive predictive value 99.6%, negative predictive value 40%, false positives 0.4%, false negatives 60% and overall accuracy 99%.

Conclusion: Ultrasound-guided FNAC is a valuable diagnostic technique for breast solid masses. In the probably benign masses (BI-RADS 3) its objective is to rule out malignancy for safely avoid biopsy and planning an imaging follow-up. In the suspicious and highly suggestive of malignancy masses (BI-RADS 4 and 5) the objective is to confirm malignancy prior to definitive treatment, when neoadjuvant chemotherapy is not needed.

Keywords: Breast, Fine-needle, Aspiration, Cytology, Cancer.

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Introduction

Fine-needle aspiration cytology (FNAC) is a minimally invasive diagnostic procedure that can be used in palpable and non-palpable breast lesions. In case of non-palpable breast lesions, the procedure is done under stereotactic or ultrasound guidance. The diagnosis is based on the analysis of the characteristics of single cells contained in the samples of the lesion.

The role of FNAC has been challenged with the development of percutaneous techniques of histological diagnosis (core biopsy and vacuum-assisted biopsy). These techniques yield higher volume samples, preserving tissue structure of the lesion and are processed and analyzed as a histological sample. The diagnostic accuracy is higher and it is possible to analyze the molecular profiling of cancers diagnosed. For these reasons, many institutions have abandoned the

use of FNAC in breast lesions, and currently are using percutaneous techniques of histological diagnosis.

However, FNAC remains as a reliable diagnostic method, if it is done with rigorous quality conditions in obtaining the sample and if there is a highly trained medical cytologist in the institution [1]. The method is cheaper than the histological diagnosis techniques and is accessible by institutions without a high technological development. Is a less traumatic procedure for the patient and the results may be available in less time.

FNAC and percutaneous techniques of histological diagnosis can coexist if there are protocols with the adequate indications of each technique. FNAC has its applications in the evacuation of cystic breast lesions, the diagnosis of breast masses, and the preoperative evaluation of suspicious axillary lymph nodes in patients with breast cancer already known.

We believe that in case of breast masses the objectives, reliability and usefulness of the FNAC are linked to the imaging features of the lesion. The aim of this work is to evaluate the efficacy of ultrasound-guided FNAC for the diagnosis of breast solid masses. The results also were correlated with the likelihood of malignancy of the lesions according to their imaging features.

Materials and Methods

It is a retrospective study where 705 consecutive patients carrying a solid breast mass were included. The work was done at the Breast Center for Diagnosis and Treatment (CENDYTMA) of the Spanish Association (Montevideo, Uruguay).

All patients were studied with mammography and breast ultrasound. Palpable and non-palpable masses were included in the analysis. The cystic masses were not included. The imaging features of the masses were analyzed and classified according to the BI-RADS categories (Breast Imaging Reporting and Data Base; American College of Radiology) [2]. The ultrasound equipment was a General Electric, Logiq P5 model, with a 10MHz linear transducer.

The fine needle aspiration cytology (FNAC) was performed with ultrasound guidance and a 21 G gauge needle was used. The procedure was made with the patient's consent and in most cases the medical cytologist was present. Several passes were made through the lesion, with permanent aspiration. In all cases the sample was spread on a glass slide and allowed to air dry. May Grünwald Giemsa staining technique was used.

The cytological results were classified as benign, suspicious, malignant or insufficient. When the medical cytologist was present, a proof of sufficiency of the sample was performed. In cases with insufficient samples, the procedure was repeated at the time. When a diagnostic sample could not be obtained, the final result remained insufficient. For the purposes of the calculations, the benign results were considered negative for malignancy and the malignant and suspect results were considered positive for malignancy. Insufficient results were not included in analysis of the accuracy of the study.

In all cases the histological result of the masses was obtained, and it was taken as reference test. The ultrasound-guided FNAC accuracy was evaluated for all cases and then specifically for the masses classified in the categories 3, 4 and 5 of BI-RADS. Oval masses, with larger diameter parallel to the skin and circumscribed margins were classified as BI-RADS 2 (benign) if they had no changes in relation to previous studies and as BI-RADS 3 (probably benign) if we had no previous studies to compare.

Masses with not circumscribed margins (undefined, microlobulated or angular) or with suspicious microcalcifications inside, were classified as BI-RADS 4 (suspicious). Nodules with irregular morphology and spiculated margins were classified as BI-RADS 5 (highly suggestive of malignancy). For the calculations the SPSS version 12.0 software was used.

Results

The average age of patients studied was 60 years (19-92 years). 2 nodules were classified as BI-RADS 2 (0.3%), 111 were classified as BI-RADS 3 (16%), 317 were classified as BI-RADS 4 (45%) and 275 were classified BI-RADS 5 (39%). In 177 cases (25%) the cytological result was negative for malignancy and in 505 cases (72%) was positive for malignancy. The sample was insufficient in 23 cases (3%) of which 17 were categorized as BI-RADS 4 and the other 6 as BI-RADS 5.

The final histological result obtained by percutaneous biopsy or surgical biopsy was benign in 179 cases (25%) and malignant in 526 cases (75%). The average size of diagnosed malignant tumors was 18 mm (1 to100). Table 1 is the list of diagnosed benign lesions and their frequency.

Table 2 is the list of diagnosed malignant lesions and their frequency. In the 23 cases with insufficient sample, the

Table 1. *Benign lesions (final histological results)*

Histology	Nº	%
Fibroadenoma	88	49
Hamartoma	10	6
Papiloma	7	4
Complex sclerosing lesion	6	3
Benign T Phillodes	4	2
Adenosis	3	2
Miofibroblastoma	2	1
Fat necrosis	1	0.6
Lymph node	1	0.6
Lipoma	1	0.6
Adenoma	1	0.6
Mastitis linfocitaria	1	0.6
Benign nonespecific	54	30

histological result was benign in 7 (30%) and malignant in 16 (70%).

Table 3 shows the correlation between the cytological findings and histological results after discarded the cases with insufficient sample. Considering all cases, regardless of the BI-RADS classification, analysis of the effectiveness of FNAC gave the following results: sensitivity 96%, specificity 92%, positive predictive value 97%, negative predictive value 89%, false positives 3%, false negatives 11% and overall accuracy 95%.

Table 4 shows the correlation between the cytological findings and histological results for masses classified as BI-RADS 3 (n=111). The analysis of the effectiveness of FNAC for BI-RADS 3 masses gave the following results: sensitivity 100%, specificity 98%, positive predictive value 90%, negative predictive value 100%, false positives 10 %, there were no false negatives and overall accuracy 98%.

Table 5 shows the correlation between the cytological findings and histological results for nodules classified as BI-RADS 4 (n=300). 17 suspicious nodules with insufficient sample were not included. The analysis of the effectiveness of FNAC for BI-RADS 4 masses gave the following results: sensitivity 92%, specificity 85%, positive predictive value 95%, negative predictive value 78%, false positives 5%, false negatives 21% and overall accuracy 91%.

Table 2. *Malignant lesions (final histological result)*

Histology	**Nº**	**%**
IDC	231	44
IDC/DCIS	197	37
ILC	65	12
DCIS	28	5
IDC/ILC	3	0.6
Others	2	0.4

Note: IDC=Invasive Ductal Carcinoma; DCIS=Ductal Carcinoma *In Situ*; ILC=Invasive Lobular Carcinoma

Table 3. *Correlation between cytological results and the final histology*

		Histology		**Total**
		M	**B**	
Cytology	**P**	491	14	505
	N	19	158	177
Total		510	172	682

Note: M=Malignant; B=Benign; P=Positive; N=Negative

Table 4. *Correlation between cytological results and the final histology for BI-RADS 3 masses*

		Histology		Total
		M	B	
Cytology	P	18	2	20
	N	0	91	91
Total		18	93	111

Note: M=Malignant; B=Benign; P=Positive; N=Negative

Table 5. *Correlation between cytological results and the final histology for BI-RADS 4 masses*

		Histology		**Total**
		M	**B**	
Cytology	**P**	210	11	221
	N	17	62	79
Total		227	73	300

Note: M=Malignant; B=Benign; P=Positive; N=Negative

Table 6. *Correlation between cytological results and the final histology for BI-RADS 5 masses*

		Histology		**Total**
		M	**B**	
Cytology	**P**	263	1	264
	N	2	3	5
Total		265	4	269

Note: M=Malignant; B=Benign; P=Positive; N=Negative

Table 6 shows the correlation between the cytological findings and histological results for nodules classified as BI-RADS 5 (n=269). 6 highly suggestive of malignancy masses with insufficient sample were not included. The analysis of the effectiveness of FNAC for BI-RADS 5 masses gave the following results: sensitivity 99%, specificity 75%, positive predictive value 99.6%, negative predictive value 40%, false positives 0.4 %, false negatives 60% and overall accuracy 99%.

Discussion

After a time of high widespread of the FNAC for the diagnosis of breast lesions, now is entering into disuse due to the development of percutaneous techniques of histological diagnosis (core biopsy and vacuum-assisted biopsy).

However, we believe that the technique still has its place in the strategy for the diagnosis of breast masses, if it is done with strict quality control and if there is a trained medical cytologist in the institution. In the scientific literature there is a wide variability in the evaluation of the diagnostic value of FNAC. Yu and colleagues [1] conducted a meta-analysis of 46 studies including 16,642 patients with breast lesions in which FNAC was used. The sensitivity was 92.7% (95% confidence interval, 92.1-93.3) and the specificity was 94.8% (95% confidence interval, 94.3-95.2).

Wesola et al. [3] conducted a literature review and found sensitivity values of ultrasound-guided FNAC between 25% and 95%; specificity values ranged from 97% to100% false positives were between 1.4% and 1.6% false negatives were between 6% and 11%. He et al. [4] gather 1238 patients with FNAC. The sensitivity was 87.7%, specificity 99.4%, false positives 0.6%, false negatives 2.3% and overall accuracy 99.4%.

Aker et al. [5] in a series of 733 cases of ultrasound-guided FNAC published the following results: sensitivity 98%, specificity 90%, overall accuracy 96%, and positive

predictive value 96%, negative predictive value 94%, false positive 2.6%, and false negative 1.4%.

The Japanese Society of Clinical Cytology published an evaluation of the results of FNAC in breast lesions in Japan [6]. 10890 patients who underwent a FNAC for a breast lesion were included. The results were the following: sensitivity 96.7%, specificity 84.3%, positive predictive value 92.4%, false negatives 3.3%, false positives 0.25% overall accuracy 88%, and insufficient samples 17.7%. The FNAC false positives are reported between 0.3% and 11% [7], while the false negatives between 6% and 11% [8,9].

Leconte et al. [10] presented a series of 427 masses with the diagnosis of fibroadenoma after FNAC. No cancer was detected in this group, by biopsy or by follow up. The conclusion is that masses with cytological diagnosis of fibroadenoma do not require short-term follow up. Routinary follow-up is sufficient for these lesions.

Gordon et al. [11] published a study of 1070 breast masses with the cytological diagnosis of fibroadenoma. After a 3 year follow-up no cancer was diagnosed in this population. In 194 cases there was a growth of the lesion during the follow-up period (average of 20% in 6 months). The conclusion was that solid masses with benign cytological diagnosis can be followed safely and there is an acceptable growth rate of 20% for an interval of 6 months.

The wide variability of the results may be due to differences in the study design. In some of them, palpable and non-palpable lesions are included, while in others only palpable lesions; when no palpable lesions are included, in some studies stereotactic guidance is used, while in others ultrasound guidance is used or both techniques are used; in some works the cystic lesions are excluded and not in others; some studies excluded the insufficient samples from the analysis and in others they are included.

Several studies included in the analysis the cases with insufficient samples. Yu et al. [1], in their meta-analysis analyzed the effectiveness of FNAC in 11 of these studies involving insufficient samples as positive for malignancy. The results were as follows: sensitivity 92.5% (95% confidence interval, 90.6-93.3), specificity 76.8% (95% confidence interval, 75.1-78.4).

Our study is the evaluation of ultrasound-guided FNA in solid breast masses. Insufficient samples were excluded. The results are within the range of the above-mentioned results in the international literature. If we consider all the cases, the results were: sensitivity 96%, specificity 92%, positive predictive value 97%, negative predictive value 89% false positive rate 3% false negative rate 11%, overall accuracy 95% . We did not find articles with a correlation between the cytological results and the likelihood of malignancy of the lesion according to its imaging features.

We believe that this exercise is relevant as it helps to make decisions in different clinical scenarios. To determine the likelihood of malignancy of each lesion we turn to the BI-RADS categorization. Under this system, in the category 3 (probably benign), the likelihood of malignancy is less than or equal to 2%, in the category 4 (suspicious) the likelihood is higher than 2% but less than 95% and in the category 5 (highly suggestive of malignancy) the likelihood is equal or higher than 95%.

In category 3 the main objective of FNAC should be safely rule out malignancy. According to our data this objective was met because there were no false negatives and the negative predictive value was 100%. There are several situations in which the FNAC is useful in this category as an alternative to imaging follow-up: requirements of the own patient due to the anxiety for the resolution of the case, in patients with increased risk, in patients who are pregnant or are planning a pregnancy during the follow-up, when there are doubts regarding compliance of imaging follow-up, or in patients already diagnosed with another concurrent malignancy.

A benign result in this category and in these situations, avoids percutaneous biopsy or surgical biopsy and an imaging follow-up could be safely planned. In categories 4 and 5, the main objective of FNAC should be safely confirming malignancy to plan appropriate treatment. According to our data the goal was met because the positive predictive value for the category 4 was 95% and for the category 5 was 99.6%. When neoadjuvant chemotherapy is required, FNAC cannot replace percutaneous biopsy, as the assessment of the complete molecular profile of the tumor is necessary.

According to our data, a benign outcome in the latter categories is not acceptable since the rate of false negatives is high (21% in category 4 and 60% in category 5). In these situations the histological diagnosis of the lesion is required. Another important finding of our research is the high percentage of cancers diagnosed in the group of patients with insufficient FNAC samples (70%). This shows the need for a histological diagnosis when cytological sample is insufficient.

A limitation of our study is that the effectiveness of the FNAC was not evaluated in terms of age groups, lesion size or patient's risk profile. In conclusion, our research indicates that ultrasound-guided FNAC retains its value in the strategy for the diagnosis of breast solid masses. In the probably benign masses (BI-RADS 3) its objective is to rule out malignancy for safely avoid biopsy and planning an imaging follow-up strategy. In the suspicious and highly suggestive of malignancy masses (BI-RADS 4 and 5) the objective is to confirm malignancy prior to definitive treatment, when neoadjuvant chemotherapy is not needed. A benign result in the BI-RADS 4 and 5 categories is not acceptable and a histological diagnosis is needed, as in cases with insufficient cytological samples.

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