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# Nondiagnostic thyroid fine needle aspiration cytology: outcome in surgical treatment

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## ABSTRACT

**Background.** Fine-Needle Aspiration (FNA) is the main screening process for distinguishing benign from malignant thyroid nodules. Despite this, by 5-29% of patients, their FNA results are not enough to confirm malign neoplasia, particularly in cases with follicular lesions. The objective of this report is to present the definitive histological results of a group of 41 patients with FNA of Thyroid nodule catalogued as "indeterminate/non diagnostic" sent for surgical treatment. **Material and methods.** A retrospective analysis was done on all of the patients who had underwent surgery for thyroid nodule, with a previous diagnosis of "indeterminate/non diagnostic" by FNA. Forty-one patients, three male (7.31%), and 38 female (92.68%), were included in the present study. **Results.** Fifteen women and one man were positive for malignancies (39.02%). The nodule was bigger than 4 cm in 23 patients in total (56.09%), and of this percentage, 6 were malignant (26.09%). According to age, 24 patients were older than 45 years (58.5%), 8 of whom showed malignant pathology (33.3%). All these variables were non significant. Fifteen of 16 patients had a definitive diagnosis of papillary carcinoma and one follicular carcinoma. **Conclusions.** The majority of patients with a diagnosis of "indeterminated/non diagnostic" had benign lesions (60.9%). The usual predictive factors for malignity such as age, sex, size of nodule, did not present a significant support in the differential diagnosis.

**Key words.** Thyroid nodule. Fine Needle Aspiration. Thyroid cancer. Thyroid surgery. Thyroid cytology. Follicular neoplasm.

*Citología por aspiración con
aguja fina de tiroides "No diagnóstica":
Resultados del tratamiento quirúrgico*

### RESUMEN

***Antecedentes.*** *La citología por aspiración con aguja fina es el procedimiento de elección en el diagnóstico preoperatorio del nódulo tiroideo. Sin embargo, a pesar de su elevada sensibilidad y especificidad, existe un buen número de casos que varían del 5-29%, donde el resultado no es útil para tomar una decisión terapéutica, particularmente en las lesiones foliculares, denominadas también "indeterminadas" o no diagnósticas.* ***Objetivo.*** *Dar a conocer los resultados de un grupo de 41 pacientes en esta categoría enviados a tratamiento quirúrgico.* ***Material y métodos.*** *Se realizó un análisis retrospectivo, en un Hospital de tercer nivel de atención, de los pacientes con citología por aspiración con aguja fina de tiroides denominada "indeterminada", evaluando el resultado histopatológico final y correlacionándolo con edad (> o< 45 años), sexo y tamaño del nódulo (> o < 4cm). En el análisis estadístico se utilizó la prueba de $\chi^2$, OR (IC 95%).* ***Resultados.*** *En 16 enfermos (39.02%) fue corroborada neoplasia maligna, 15 como carcinoma papilar y uno como carcinoma folicular, de los cuales 15 correspondieron a mujeres y sólo un varón. Las variables de edad, sexo y tamaño del nódulo, no fueron estadísticamente significativas (p 0.51, 1.00 y 0.10 respectivamente) para el diagnóstico de cáncer.* ***Conclusiones.*** *El 61% de los pacientes con nódulo tiroideo y citología por aspiración "indeterminada" tienen enfermedad benigna. No se encontraron factores predictivos significativos para determinar malignidad.*

**Palabras clave.** *Nódulo tiroideo. Aspiración con aguja fina. Cáncer de tiroides. Cirugía tiroidea. Citología de tiroides. Neoplasia folicular.*

## INTRODUCTION

Fine-Needle Aspiration (FNA) is the main screening process for distinguishing benign from malignant thyroid nodules.[1] This test also offers the best predictive value currently available to distinguish most nodular thyroid lesions: those which require surgical resection from those that do not. Despite all these advantages, in about 5-29% of patients FNA results alone are not sufficient to diagnose neoplasia, particularly in cases with follicular lesions.[2]

In follicular lesions, which include hyperplastic nodules in goiters, carcinomas, follicular variants of papillary carcinoma and follicular adenomas, it is virtually impossible to make the evaluation with light microscope.[3] The "nondiagnostic" mark remains a dilemma, where at the discretion of the physician, a thyroid surgery with high cost, and potential morbidity is required to fully make a clear pathological distinction between benign follicular adenoma and malignant follicular carcinoma in the resected specimen. Experience has shown that about 85% of the nodules surgically removed are indeed benign. Hence, a more reliable method for distinguishing the presence of thyroid cancer is needed in order to avoid unnecessary thyroid surgery.[4-6]

The aim of this study was to describe the definitive histological results from a group of 41 patients with a FNA diagnosis labelled as "indeterminate/non diagnostic" or with follicular lesions sent for surgical treatment, as well as to analyze some well known predictive factors for thyroid cancer.

## MATERIAL AND METHODS

A retrospective analysis was done on all the clinical files from the patients who had underwent surgery for thyroid nodule (TN) at the Hospital de Especialidades #25 in Monterrey, Mexico from 1997 to 2005. All included patients (n = 430) had at least one FNA before the surgical procedure and the indication for the surgery was basically made by the attending physicians (for the cytological results, rapid nodule growth, development compressive symptoms, cosmetic concerns and unknown in some patients), and completely independent of the objectives of this study.

The FNA was always performed by the endocrinologists following established standardized procedures.[2] No significant complications took place.

The results were grouped in 4 categories, according to the usual criteria[2] benign or negative; malignant or positive; insufficient to diagnose and

**Table I.** Variables and significance (N = 41).

| Variable | Cancer Yes | No | O.R | IC 95% | P - value |
|---|---|---|---|---|---|
| *Age (yrs)* | | | | | |
| > 45 | 8 | 16 | 1.77 | 0.50-6.22 | 0.51 |
| < 45 | 8 | 9 | | | |
| *Sex* | | | | | |
| Female | 15 | 23 | 1.30 | 0.15-10.72 | 1.00 |
| Male | 1 | 2 | | | |
| Tumor's size (cm) | | | | | |
| > 4 | 6 | 17 | 3.58 | 0.97-12.86 | 0.10 |
| < 4 | 10 | 8 | | | |

suspicious or "indetermínate". For the purposes of this study we only took into consideration this last category (N = 41).

In each case, demographic data was collected related to age, gender and nodule size, FNA results and the final histological diagnosis.

The results are presented in descriptive statistics and categorical variables, we used the $\chi^2$ test, OR and CI at 95%. We considered as significant values a $p < 0.05$ and OR different from 1. All statistical analyses were performed using SPSS software (Statistical Package for the Social Sciences version 10.0, SPSS Inc., Chicago, IL, USA).

## RESULTS

In table 1 the predictive characteristics of the group of patients are described, with their sex, age and tumor size. These variables were taken according to previously published classification and risk factors.[1]

From 41 patients, three were male (7.31%) and 38 were female (92.68%). 15 women and one man were positive for malignancies (39.02%). The nodule was bigger than 4 cm in 23 patients (56.09%) and in 6 were malignant (26.08%). According to age, 24 patients were older than 45 years (56.53%), 8 of whom showed malignant pathology (33.33%).

Fifteen of 16 patients had a definitive diagnosis of papillary thyroid carcinoma (93.75%) and one follicular carcinoma (6.25%).

## DISCUSSION AND CONCLUSION

TN is a very common clinical finding, with an estimated frequency based on clinical palpation that ranges from 3 to 7%.[1-4]

The widespread use of ultrasonography for the evaluation of thyroid and nonthyroid neck disease

has resulted in an increased prevalence of clinically inapparent thyroid nodules.[8]

The central role of the endocrinologist in TN evaluation and FNA biopsy is clear and recent surveys have emphasized that near 100% of endocrinologists use FNA for diagnosis of thyroid nodules. FNA is extremely useful for discerning benignity.[4,7-10]

Different studies have reported sensitivity rates ranging from 65% to 99%, with specificity rates between 72% and 100%.[1,2,8-10]

Other perspective procedures currently used include ultrasonography and scintigraphy, however it seems that FNA for diagnosis of TN is alone the most important among these choices.[1-5]

An important limitation for this procedure is, however, its inability to correct follicular neoplasms, because it is obviously not able to define the presence of capsular or vascular invasion, so it is limited to diagnose among benign or malign thyroid neoplasm, except for papillary, anaplastic and medullary carcinomas, which has a considerable higher diagnostic accuracy.[2]

Moreover, as stated before, FNA is unable to distinguish among a certain percentage of follicular lesions; there are several different studies that have reported the following:

In 20% of FNA samples a diagnosis of follicular lesion has assigned and 96 of 236 went to surgery. In most of the cases they were reported as benign lesions.[1,4-10]

A study reported by the University of Pennsylvania reported a surgical excision rate of 43% found that from the 96 samples excised surgically, 67 (70%) were benign lesions and 29 (30%) were malignant.[1]

In our study, 16 patients of 41 (39.02%) had malignant lesions, the total group reported papillary cancer, except for one case, who presented follicular cancer. This finding is similar to previous reports, where patients with FNA with a "suspicious or indeterminate" diagnosis went to surgery and a report of malign lesion showed that. The vast majorities were papillary cancer.[11]

In our study there was not difference between benign and malignant nodules accord to the age.

In the current study the male group was not significant for cancer diagnosis. In our study the nodule size was not predictive factor for malignancy. A precise pathological diagnosis is essential for the clinical and surgical planning. Patients submitted to surgery with a previous FNA diagnosis of a follicular patterned lesion may need a complete resection and even selective lymph node dissection if they present capsular and/or vascular invasion, while benign lesions may be treated with much less invasive procedures.

Many studies have tried to find clinical or morphological predictors of malignancy in thyroid nodules; however results are not fully clear. For example in our study sex, age and tumor size resulted as non significant variables for this trial. It is possible that a true difference has been overlooked. The most obvious way of increasing statistical power is to increase the number of subjects studied.

However, experts are investigating the usefulness of immunohistochemical expression and immunolocalization of some biochemical markers.[10-14] Among them are HBME-1, Cytokeratin (CK) 19 and Galectin-3, which we will integrate in a future clinical evaluation. This panel of markers is useful to differentiate the follicular patterned lesions, with special reference to the follicular variant of papillary carcinoma, expecting it will help to accurately diagnose a thyroid malignancy.

The majority of patients with an indeterminate or uncertain diagnosis had benign lesions, we found 39.02% of malignancy and the clinical features such as age, sex and size do not offer a significant contribution to the definitive diagnosis and these patients should be referred for surgical evaluation. Different authors have stated the diagnostic difficulties mainly for follicular lesions and disadvantages with FNA in this area. Up to date, there is not an established effective method for diagnosing follicular lesions preoperatively, which could clarify or discern malignant nodules; even methods such as inmunoperoxidase techniques, flow cytometry, digital image analysis and reverse transcriptase-polymerase chain reaction analysis have been equivocal.[15]

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*Reimpresos:*

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