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ORIGINAL ARTICLE

Evaluación de la eficacia del ultrasonido como indicador de malignidad o benignidad del nódulo tiroideo

Evaluation of the Efficacy of Ultrasound as an Indicator of Malignancy or Benignity of the Thyroid Nodule

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RESUMEN

Introducción: Los nódulos constituyen una las enfermedades más frecuentes de la tiroides. **Objetivo:** Determinar la eficacia del ultrasonido diagnóstico en los nódulos del tiroides. **Métodos:** Estudio descriptivo, transversal, en pacientes que acudieron a la consulta con sospecha de un nódulo del tiroides, de septiembre de 2021 a septiembre de 2022. La población en estudio fue de 413 pacientes, con diagnóstico confirmado de nódulo del tiroides. Las variables incluidas fueron: el sexo, el número de nódulos; la presencia de degeneración quística, sonografía del nódulo; presencia de halo hipoecoico, calcificaciones y resultado citohistológico. En el análisis estadístico se utilizó el cálculo de sensibilidad, especificidad; valor predictivo positivo y negativo, el índice de eficacia y la prueba de Xi cuadrado. **Resultados:** El 87.9 % pertenecieron al sexo femenino. Los nódulos únicos presentaron una mayor frecuencia de malignidad, 70.6 %, la hipoecogenicidad sonográfica; la no presencia del halo hipoecoico, de microcalcificaciones; se asoció a la malignidad con significación estadística. La presencia de degeneración quística a la benignidad en 46.2 %. De los pacientes biopsiados presentaron lesiones malignas, el 8.2 %, 21 fueron diagnosticados por ultrasonido y confirmados por citología; con una sensibilidad de 61.76 %, con una especificidad del 99.21 %; valor predictivo positivo 87.50 % e índice de eficacia del 96.13 %. **Conclusión:** Las características sonográficas sugestivas de malignidad o benignidad del nódulo de tiroides, hacen que

ABSTRACT

Introduction: Nodules constitute one of the most frequent diseases of the thyroid. **Objective:** To determine the efficacy of diagnostic ultrasound in thyroid nodules. **Methods:** Descriptive, cross-sectional study in patients with suspected thyroid nodule, who attended the clinic, from September 2021 to September 2022. The study population consisted of 413 patients with a confirmed diagnosis of thyroid nodule. Variables included: sex, number of nodules; presence of cystic degeneration, nodule sonography; presence of hypoechoic halo, calcifications, and cytohistological result. Statistical analysis used calculation of sensitivity, specificity; positive and negative predictive value, efficacy index, and Chi-square test. **Results:** 87.9 % were female. Single nodules presented a higher frequency of malignancy, 70.6 %; sonographic hypoechogenicity; absence of hypoechoic halo, presence of microcalcifications were associated with malignancy with statistical significance. The presence of cystic degeneration was associated with benignity in 46.2 %. Of the biopsied patients, 8.2 % presented malignant lesions, 21 were diagnosed by ultrasound and confirmed by cytology; with a sensitivity of 61.76 %, specificity of 99.21 %; positive predictive value of 87.50% and efficacy index of 96.13 %. **Conclusion:** The sonographic characteristics suggestive of malignancy or benignity of the thyroid nodule make diagnostic ultrasound a moderate and sensitive examination in the suspicion and detection of malignant lesions.

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el ultrasonido diagnóstico sea un examen moderado y sensible en la sospecha y detección de las lesiones malignas.

Palabras clave: nódulo de tiroides, características sonográficas, biopsia
Descriptores: nódulo tiroideo/diagnóstico/ diagnóstico por imagen; ultrasonografía; biopsia

Keywords: thyroid nodule, sonographic characteristics, biopsy
Descriptors: thyroid nodule; diagnostic/diagnostic imaging; ultrasonography; biopsy

INTRODUCTION

There are various conditions that involve the thyroid, characterized by structural and functional alterations. Thyroid nodules are one of the most frequently detected conditions, and although more than 90 % are insignificant benign lesions, thyroid nodules are important as they may represent thyroid cancer in 4.0 to 6.5% of cases in the United States.[1]

Every thyroid nodule raises suspicion of the presence of a carcinoma, although in less than 1% of them is a malignant neoplasm confirmed. In general, when there is a history of recent growth, a family member with goiter or thyroid cancer, radiation to the cervical region, or when the nodule presents as hard, accompanied by satellite lymphadenopathy, in subjects at the extremes of life (under 20 or over 60 years of age), a malignant process should be suspected.[2,3]

Thyroid cancer is the most frequent endocrinological neoplasm; however, it is difficult to accurately establish the global prevalence, especially due to the existence of the so-called "occult thyroid carcinoma" in normal glands or those with another type of lesion. "Occult" carcinomas, smaller than one cm in diameter, have been found in 4 to 35% of thyroids examined postmortem and in up to 17% of multinodular goiters.[4]

The clinical incidence of thyroid cancer, according to the American society, is of 43,800 new cases of thyroid cancer in 2022. In Brazil, there was an increase of 3.8 % in that period. In Cuba, in the same year, an incidence rate of 32 new cases per 1,000,000 inhabitants was reported, with an increase of six new cases compared to the previous five-year period and a mortality rate of 0.3 per 100,000 people per year. These data demonstrate the low malignancy of the disease; the mortality figure represents a small percentage of new cases diagnosed.[5]

Aspiration biopsy was described and evaluated in the 1930s at Memorial Hospital in New York and spread throughout Europe after being modified in Sweden with the use of fine needles. Cytology is a branch of Pathological Anatomy that studies cells that have exfoliated freely from the surface of organs or that have been obtained by brushings, washings, or Fine Needle Aspiration Biopsy (FNAB).[6,7]

Fine Needle Aspiration Cytology (FNAC) of the thyroid gland is the precise non-operator technique for diagnosing diseases of this organ. When performed by a trained cytopathologist, it is safer than clinical examination, especially when combined with other diagnostic methods such as ultrasound, scintigraphy, and sophisticated biochemical methods. The routine use of ultrasound in the clinical management of thyroid nodules considerably reduces the average number of unnecessary surgical interventions. Ultrasound-guided FNAC offers advantages over conventional FNAB, as it allows the radiologist to select the entry point and the distance to the lesion, thus guaranteeing sample collection and avoiding complications.[8,9]

In Cuba, there are few studies demonstrating that the sonographic characteristics of the thyroid nodule are related to its histological nature, an aspect that can contribute to better diagnosis and treatment for patients. The objective of this study is to determine the efficacy of diagnostic ultrasound in thyroid nodules.

METHODS

A descriptive, cross-sectional study was conducted in patients who attended the clinic with clinical suspicion of a thyroid nodule at the Calixto García Hospital, from September 2021 to September 2022. Ultrasound of the thyroid gland was performed using a Medison Sonoace 2000 device with a 7.5 MHz linear transducer, exploring the anterior and lateral region of the neck.

The study population consisted of 413 patients diagnosed with thyroid nodule who gave their consent to participate in the study. Additio-

nally, cases where cytology was reported as "non-useful" or indeterminate were excluded. The ethical principles of the Declaration of Helsinki were respected.

Variables Studied:

-Sex: According to biological sex. Male or Female.

-Number of nodules: According to the number of nodules: one nodule, two nodules, or more than two nodules.

-Presence of cystic degeneration: According to ultrasonographic description, present or absent.

-Nodule sonography: According to ultrasonographic description: hyperechoic, isoechoic, hypoechoic, and anechoic.

-Presence of hypoechoic halo: According to ultrasonographic description: present, regular and irregular, or absent.

-Presence of calcifications: According to ultrasonographic description: present, microcalcifications, coarse calcifications, or absent.

-Cytohistological result: According to the result of the cytohistological examination: Benign or Malignant.

The data obtained were stored in an Excel database and classified as positive for malignancy or benign, according to the following sonographic criteria.

Positive for malignancy were considered those nodules that the ultrasound report described as:

-Hypoechoic nodule, which may present microcalcifications and an irregular halo. The absence of these last two characteristics did not exclude the diagnosis of malignancy.

-Nodule of any sonographic intensity, with evidence of infiltration into neighboring structures and lymphadenopathy.

-Anechoic nodule with a mamillated image on any of its walls.

Benign were considered those nodules that the ultrasound report described as:

-Isoechoic nodule, with a regular hypoechoic halo, which may present calcifications and cystic degeneration. The absence of these last two characteristics did not exclude the diagnosis of benignity.

-Hyperechoic nodule, which may present any other associated ultrasonographic characteristic.

-Anechoic nodule with well-defined thin walls.

-All reports that did not correspond to those described as positive for malignancy.

The data obtained were processed, and calculations were performed for sensitivity, specificity, positive predictive value, negative predictive value, and efficacy index. Additionally, a variable association method was applied using the Chi-square test.

Sensitivity (S) S=Vp/(Vp+Fn).100
Specificity (E) E=Vn/(Vn+Fp).100
Positive predictive value
P_+=Vp/(Vp+Fp).100
Negative predictive value
P_-=Vn/(Vn+Fn).100
Efficacy index (Ei)
Ie=(Vp+Vn)/(Vp+Vn+Fp+Fn).100

RESULTS

The highest number of biopsies for thyroid nodules was in the female sex with 87.9%, of which 6.6 % were malignant lesions. The male sex exhibited a higher percentage of malignant lesions with 20 %, showing statistical significance, Table 1.

Table 1. Distribution by sex, according to type of lesion

Nature of the lesion	Male		Femal		Total	
	No.	%	No.	%	No.	%
Benign	40	80	339		379	91.8
Malignant	10	20	24	6.6	34	8.2
Total	50	100	363	100	413	100

Xi=10.40196 p < de 0.01
Source: Medical Records

Single nodules presented a higher frequency of malignancy in 70.6 %, while multiple nodules (two or more nodules) were more frequently benign (34.0 % and 40.1 %). Regarding the presence of cystic degeneration inside the thyroid nodules, its association with benignity was significant in 46.2 %, Table 2.

Table 2. Number of nodules and presence of cystic degeneration, according to type of lesión

Number of nodules	Malignant n=34		Benign n=379	
*1 nodule	24	70.6	98	25.9
2 nodules	8	23.5	129	34.0
More than 2 noduleS	2	5.9%	152	40.1%
Presence of cystic degeneration	**Malignant n=34**		**Benign n=379**	
	No	**%**	**No**	**%**
Present	6	17.6	175	46.2
^Absent	28	82.4	204	53.8
Total	34	100%	379	100

*Xi=29.92087 p < de 0.01 ^Xi=10.28877 p < de 0.01
Source: Medical Records

Sonographic hypoechogenicity of the nodules was associated with their malignancy in 52.9 %, with statistically significant differences found. Isoechogenicity of the nodules was present in 72.8 % of patients with benign nodules. Cystic lesions, however, tested positive for neoplastic cells in only 5.9 %, Table 3.

Table 3. Nodule sonography, according to type of lesión

Nodule sonography	Malignant n=34		Benigns n=379	
	No.	%	No.	%
*Hypoechoic	18	52.9	3	0.8
Isoechoic	7	20.6	276	72.8
^Hyperechoic	7	20.6	70	18.5
Anechoic	2	5.9	30	7.9
Total	34	100	379	100

* Xi= 186.6094 p < de 0.01 ^ Xi= 7.072023 p > de 0.05
~ Xi= 1.472589 p > de 0.05
Source: Medical Records

In malignant lesions, 58.8 % of the nodules were not surrounded by a hypoechoic halo, compared to an incidence of 92.1 % of hypoechoic halo in benign nodules. From a statistical point of view, significant differences were found between the presence of hypoechoic halo and malignancy. The presence of an irregular halo was a positive indicator of neoplastic cells, with p<0.01. The presence of microcalcifications in malignant nodules was significant. Of the patients with microcalcifications, 55.9 % had malignant lesions; 8.8 % of patients with thyroid carcinoma showed coarse calcifications, with no statistical significance. The absence of calcifications in benign nodules was 89.9 %, Table 4.

Table 4. Presence or absence of hypoechoic halo and calcifications in nodules, according to type of lesión

Presence of hypoechoic halo	Malignant n=34		Benign n=379	
	No.	%	No.	%
*Absent	20	58.8	30	7.9
Present	14	41.2	349	92.1
Regular	6	1	348	91.8
^Irregular	8	23.6	1	0.3
Total	34	100	379	100
Presence of calcifications	**Malignant n=34**		**Benign n=379**	
	No.	**%**	**No.**	**%**
Absent	12	35.3	337	89.9
Present	22	64.7	42	11.0
&Microcalcifications	19	55.9	24	6.3
˂Gross calcifications	3	8.8	18	4.7
Total	34	100	379	100

* Xi=106.4942 p < de 0.01 ^ Xi=179. 4625 p < de 0.01
&Xi=87.05764 p < de 0.01 < Xi=5.975803 p > de 0.05
Source: Historias Clínicas

Of the patients with thyroid nodules, 8.2 % presented malignant lesions; of these, 61.8 % were diagnosed by ultrasound as possible malignant lesions and confirmed by cytology, therefore sensitivity was 61.76 %. Specificity was high at 99.21 %, suggesting that when a nodule was presumptively considered negative for malignancy, the diagnosis was accurate in a high percentage.

The positive predictive value was acceptable at 87.5 %, indicating that most nodules presenting sonographic characteristics suggestive of malignancy were confirmed by cytology. The negative predictive value was excellent at 96.66%; only 13 patients of the total did not present sonographic characteristics suggestive of malignancy but turned out to have thyroid carcinomas, with an efficacy index of 96.13 %. The use of ultrasound and the evaluation of sonographic characteristics suggestive of malignancy, in this study, increased the efficacy index by 4.33 percentage points, Table 5.

Table 5. Cytohistological result, according to sonographic characteristics of the thyroid nodule

Ultrasound	Positive Biopsy n=34		Negative Biopsy n=379	
	No.	%	No.	%
Positivo	21	61.8	3	0.8
Negativo	13	38.2	376	99.2
Total	34	100	379	100

Legend: Negative Predictive Value: 96.66 %
Positive Predictive Value: 87.50 %
Sen : 61.76 % Specificity: 99.21 % Efficacy Index: 96.13 %
Source: Medical Records

DISCUSSION

Currently, it is considered that the female sex presents thyroid conditions more frequently due to hormonal and genetic factors linked to the X chromosome, which coincides with figures reported in some studies,[10,11] that agree that thyroid nodules are more frequent in women, with a lower percentage of malignancy compared to the male sex.

The highest presentation of malignant lesions is found in single nodules, according to observations in reviewed studies.[12] Other authors suggest (13) that there are no significant differences between patients with single nodules and those with multiple nodules; the possibility of malignancy decreases by 3 % for each increase in the number of nodules, although this is a narrow margin to consider. Currently, there is no consensus regarding patients with multiple nodular disease on whether or not to perform biopsy and, if performed, which nodules to biopsy.

Not all cystic lesions are benign, which coincides with studies[14,15] that state this, although they mention that they become suspicious if they present thickening in any of their walls, so thyroid cysts should not be considered an invariably benign condition. Currently, solid nodules are considered, on average, to have a higher risk of malignancy compared to those that are mixed or cystic; it is accepted that cystic degeneration is associated with benign nodules.

Other reviewed studies[15,16] report that hypoechoic nodules represent, in most cases, papillary carcinomas; this is one of the sonographic criteria most associated with this type of carcinoma, although it is not absolute, as not all hypoechoic nodules are neoplasms.

A complete and uniform halo around the nodule is suggestive of benignity with a specificity of 95 %. According to various authors,[16,17] most thyroid neoplasms do not present a halo or show an irregular and incomplete halo, although this is not absolute, as malignant lesions are seen in nodules with a regular halo.

Regarding microcalcifications in malignant lesions, results coincide with current studies[17,18] which report that microcalcifications are related to psammoma bodies, which are typical of papillary carcinoma. The presence of calcifications, and particularly microcalcifications, increases the risk of thyroid cancer compared to lesions that do not have them.

In the reviewed studies,[19,20] positive predictive values range between 77 and 90 %, and negative predictive values are reported between 83 and 98 %. The sensitivity of ultrasound for the diagnosis of thyroid nodules ranges between 52 and 82 %, while all exhibit high specificity values, and efficacy indices are reported between 92 and 98 %, parameters within which the values of this study fall.

It is concluded that the sonographic characteristics suggestive of malignancy or benignity of the thyroid nodule make diagnostic ultrasound a moderately sensitive examination in the suspicion and detection of malignant lesions.

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Conflict of Interest.
The authors declare that there are no conflicts of interest regarding the research presented.

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