

Trabajo Original

Employing fuzzy logic to aid in the diagnosis and malignancy assessment of thyroid nodules identified by ultrasonography

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RESUMEN

El objetivo del trabajo fue emplear la lógica Fuzzy para ayudar en el diagnóstico y el grado de malignidad de los nódulos tiroideos mediante ecografía. Se realizó un estudio transversal en el que se evaluaron 75 resultados de exámenes de pacientes con un nódulo tiroideo. Se evaluaron los siguientes hallazgos ecográficos empleando una puntuación cuantitativa: no sospechoso, poco sospechoso, moderadamente sospechoso y altamente sospechoso. Las características ecográficas evaluadas para la sospecha de malignidad se basaron en los siguientes componentes del nódulo: composición, ecogenicidad, forma, margen y focos ecogénicos, clasificados mediante el Sistema de Datos e Informes de Imágenes Tiroideas del Colegio Americano de Radiología (American College of Radiology Thyroid Imaging Data and Reporting System). Se construyó una clasificación de los nódulos tiroideos combinando la puntuación ecográfica y el Sistema Bethesda para la notificación de citopatología tiroidea mediante lógica difusa. La hipoecogenicidad y las microcalcificaciones fueron las puntuaciones que mostraron la mejor interacción con la malignidad en ecografía, mientras que la forma y el margen mostraron los menores errores de estimación en comparación con la composición. Se propuso una clasificación de los nódulos tiroideos basada en el intervalo de confianza del 95% de la hipoecogenicidad y las microcalcificaciones: no sospechoso (< 24.6); poco sospechoso (24.6 – 48.0); moderado (48.1 – 64.5); moderadamente sospechoso (64.6 – 77.0); muy sospechoso (77.1 – 92.7); y maligno (> 92.7). En conclusión, a través de la lógica Fuzzy, se construyó una clasificación para los nódulos tiroideos diagnosticados por ultrasonido basada en la ecogenicidad y las microcalcificaciones nodulares, con una aplicación práctica sencilla. Sin embargo, la clasificación de los nódulos tiroideos aún debe ser respaldada clínicamente por hallazgos anatomopatológicos.

ABSTRACT

Keywords:

Fuzzy logic

Ultrasound imaging

Thyroid nodule

The objective was to employ fuzzy logic to auxiliary in diagnosis and malignancy grade of thyroid nodules by ultrasound. A cross-sectional study evaluating 75 exams results from patients with a thyroid nodule was done. The following ultrasound findings were evaluated employing a quantitative score: not suspicious, not very suspicious, moderately suspicious, and highly suspicious. The echographic features evaluated for suspicion of malignancy were based on the following nodule components: composition, echogenicity, shape, margin, and echogenic foci, graded using the Thyroid Imaging Data and Reporting System by the American College of Radiology. By combining ultrasound scoring and the Bethesda System for Reporting Thyroid Cytopathology using fuzzy logic, a classification for thyroid nodules was constructed. Hypoechoogenicity and microcalcifications were the findings that showed the best interaction with malignancy on ultrasound, while shape and margin showed the smallest estimation errors when compared with composition. A classification for thyroid nodules was suggested based on the 95% confidence interval of hypoechoogenicity and microcalcifications: not suspicious (< 24.6); not very suspicious (24.6 - 48.0); moderate (48.1 - 64.5); moderately suspicious (64.6 - 77.0); highly suspicious (77.1 - 92.7); and malignant (> 92.7). In conclusion, a classification for ultrasound-diagnosed thyroid nodules was constructed using fuzzy logic, based on echogenicity and the presence of nodular microcalcifications. This classification has a simple and practical application. However, the classification of thyroid nodules should still be supported by clinical findings from anatomopathological examinations.

INTRODUCTION

A frequency of up to 60% of thyroid nodules detected by ultrasound has been described in the general population, reaching 68% in adults and increasing its incidence with increasing age^(1,2). Although population studies indicate an irrelevant but real increase in the incidence of thyroid cancer, this is presumably related to the environment⁽³⁾.

Ultrasound with high-frequency linear transducers is the imaging exam of first choice for morphological evaluation of the thyroid, allowing high definition images of the gland. The characterization of nodules and the estimation of malignancy risk will be based on the echographic characteristics of the nodule found, whose diagnostic sensitivity and specificity are variable, including by inter and intraobserver lability⁽⁴⁾. The high rate of thyroid nodule diagnosis by ultrasonography appears to be related to the significant increase in thyroid cancer diagnosis⁽⁵⁾.

With the exponential increase in incidental findings of thyroid nodules on ultrasound, the American College of Radiology (ACR) created committees with the goals of developing guidelines, create a standard terms for describing all thyroid nodules found on ultrasound and standardizing a risk stratification system for biopsy indication. In the ACR Thyroid

Imaging Data and Reporting System (TI-RADS), thyroid nodules are scored according to sonographic features, and are classified into four categories: benign, minimally suspicious, moderately suspicious, or highly suspicious for malignancy⁽²⁾. Thus, the total points determine the ACR TI-RADS category of the nodule that ranges from 1 to 5, with 1 being benign and 5 being highly suspicious for malignancy, and this categorization recommends follow-up with ultrasound or fine-needle aspiration (FNA) specimens.

The Bethesda System for Thyroid Cytopathology Reports has also standardized the reports for thyroid FNA, where it presents 6 categories: 1- Non-diagnostic or Unsatisfactory; 2- Benign; 3- Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance; 4- Follicular Neoplasm or Suspected Follicular Neoplasm; 5- Suspected Malignancy; and 6- Malignant. According to risk the Bethesda category is subject to clinical management guidance⁽⁶⁾.

Fuzzy logic dates back to 1965, when Lofti Zadeh, a professor at the University of California at Berkeley, who coined the term "fuzzy sets"⁽⁷⁾. Fuzzy logic an estimated logic ("almost certain"/"very unlikely"), in contrast to classical Boolean logic (true/false - yes/no), and is a multivalued logic acquired from the agreement of fuzzy group theory with human argument⁽⁸⁾,

and its methodology based on the problem management system, from the simplest to the most complex, which admits imprecision, uncertainty, vagueness, enabling an efficient response for the solution of multi-parameter divergences⁽⁹⁾. Fuzzy logic is a mathematical method for working with human uncertainty, and has been used in medicine in various diagnostic models.

The diagnosis of thyroid nodule is one of the key steps for clinical management that is usually followed by a phase of insecurity and doubts. Thus, the aim of this study was to use fuzzy logic to assist in the identification and diagnosis of the severity of thyroid nodules.

METHODS

We propose to use Fuzzy logic for the classification of thyroid nodules through a cross-sectional study, and 75 ultrasound and FNA results of individuals with thyroid nodule were evaluated. Thyroid ultrasound performed with a high-frequency linear transducer was used for detection of nodules and their classification according to the ACR TI-RADS criteria and correlated with the FNA classified according to the Bethesda System for Thyroid Cytopathology Reports.

Ultrasound evaluation

Ultrasound evaluation was performed by a single physician with gray-scale ultrasound equipment (Toshiba Aplio XG - Tokio, Japan) using a 10-12 MHz multifrequency linear probe. The scans were interpreted by B-mode per thyroid transverse and longitudinal section, and the ultrasound results were measured employing a quantitative scoring method: TI-RADS 1 = zero points; TI-RADS 2 = 2 points; TI-RADS 3 = 3 points; TI-RADS 4 = 4 to 6 points; TI-RADS 5 = 7 points. The following qualitative assessments were given to the thyroid

nodule score: 0 point = benign; 2 points = not suspicious; 3 points = not very suspicious; 4 to 6 points = moderately suspicious; and 7 points = highly suspicious.

Fine-needle aspiration specimens' thyroid nodule

The cytological examination was performed by a single pathologist, and for the cytopathological results a quantitative method was employed, categorized according to the Bethesda System for Thyroid Cytopathology Reports: 1= Non-diagnostic or Unsatisfactory; 2= Benign; 3= Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance; 4= Follicular Neoplasia or Suspected Follicular Neoplasia; 5= Suspected Malignancy; and 6= Malignant.

Study design

With the combination between ultrasound punctuation and FNA aspects through fuzzy logic, a classification for thyroid nodules has been built.

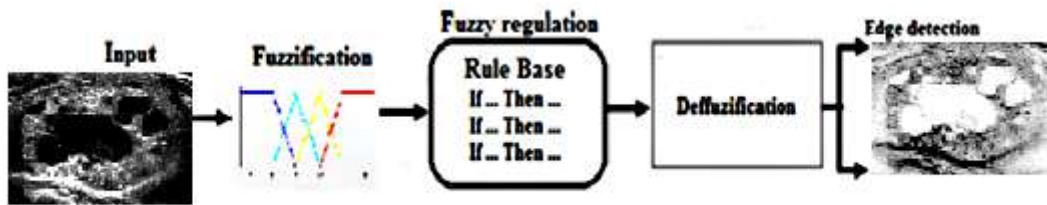
The level of statistical significance was set at p 0.05. Prism version 6.0 software free was used for data analysis (GraphPad Software Inc., La Jolla, CA, USA).

A thyroid nodule classification was performed by the sharing among ultrasonography scores and FNA scores through fuzzy logic. The fuzzy edge detection technique was grounded in a fuzzy inference system (Figure 1). The secondary alterations to thyroid nodule were identified using the fuzzy k means, and a pre-processing was performed by histogram equalization.

Source: Search result

The steps utilized in pre-processing phases consisted of RGB to Gray Scale, noise elimination, contrast upgrading, and image processing. The ultrasonography and FP input images are transformed in gray scale image, using the equation $IC = 0.333MR + 0.5 MG + 0.1666 MB$, where IY indicates magnitude of tantamount gray quality image of RGB. The noise elimination was utilized the Hard Thresholding (HT) and Soft

Figure 1. Fuzzy edge detection method



$$\text{Thresholding (ST): } HT(x) = \theta \begin{cases} 0 & \text{if } |Y| < \lambda t \text{ and } ST = \theta(y, \lambda t) = \text{sign}(Y) \cdot \lambda t \\ Y & \text{otherwise} \end{cases}$$

The λ represents universal Threshold that was evaluated using the equation:

$$\lambda_t = \sigma \sqrt{2 \log N}$$

wherein σ indicates noise difference and N the dimension of image.

The contrast enhancement was calculated with the equations:

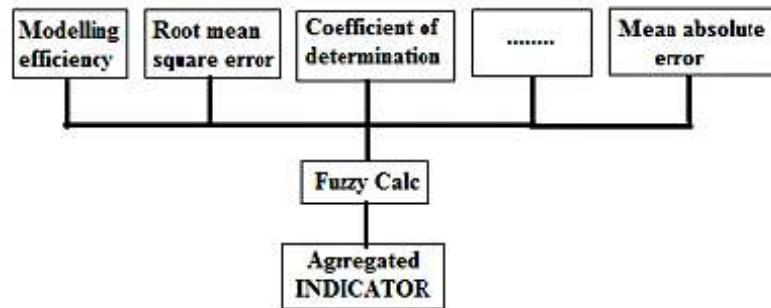
$$P_N = 255 \left[\frac{[\Phi_w(p) - \Phi_w(Min)]}{[\Phi_w(Max) - \Phi_w(Min)]} \right] \text{ and } \Phi_w = J \left[\exp \left(\frac{\mu_w - p}{\Phi_w} \right) \right]$$

Wherein min and max matches to minimum and maximum value of full image, μ_w is equivalent to local window mean, and Φ_w is equals local window standard deviation.

The image morphological processing implied equations for dilatation and erosion: Dilation: $I \oplus A_i = \{ (p+q)/p \in I, q \in A_i \}$ and Erosion: $I \ominus A_i = \{ p \in I, (p+q) \in A_i \}$. In dilatation and erosion image I is symbolized by the structuralelement A_i .

The Fuzzy-Calc (<http://fuzzy-calc.appspot.com>), an app to calculate fuzzy indicators was used with the objective to obtain a synthetic performance value for the study variables. The figure 2 demonstrates the simulation model of evaluation indexes using Fuzzy-Calc:

Figure 2. Fuzzy-Calc simulation model



Source: Search result

The segmentation of according input variables in fuzzy logic system has been divided in two pattern: 1) the ultrasonography for determine to score of ultrasound thyroid nodule characteristics (0 point = benign; 2 points = not suspicious; 3 points = not very suspicious; 4 to 6 points = moderately suspicious; and 7 points = highly suspicious), and, 2) the FNA score (1= Non-diagnostic or Unsatisfactory; 2= Benign; 3= Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance; 4= Follicular Neoplasia or Suspected Follicular Neoplasia; 5= Suspected Malignancy; and 6= Malignant).

The classification was suggested upon the estimated mean having a 95% confidence interval, based on the standard error of the mean from the Student's t test. Three decisions were considered to define the classification: the presence of at least three classes (benign, not suspicious, not very suspicious, moderately suspicious, and highly suspicious), necessity of 95% confidence intervals superposition, and minimization of estimation errors⁽¹⁰⁾.

The value T is assigned for each nodular structure was calculated with follow equations:

$$\mu = 1/9 \sum_{i=1}^n xi \text{ and } \sigma = \sqrt{1/n \sum_{i=1}^n (xi - \mu)^2}$$

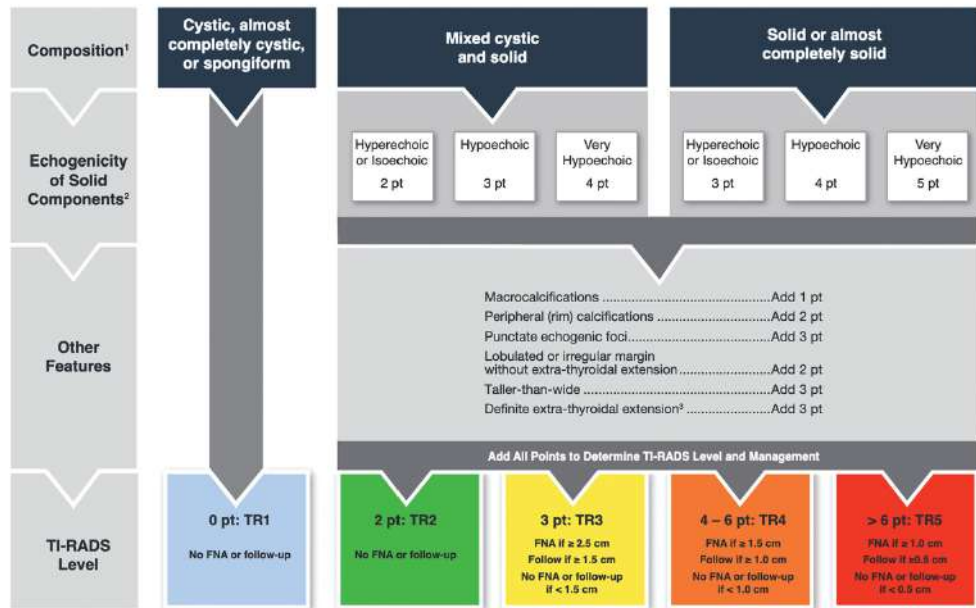
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correspond total number of pixels, xi indicate pixel values of full image.

RESULTS

The cytological variables were based on the Bethesda classification: Non-diagnostic or Unsatisfactory (Bethesda I), Benign (Bethesda II), Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance (Betheda III), Follicular Neoplasia or Suspected Follicular Neoplasia (Bethesda IV), Suspected Malignancy (Bethesda V), and Malignant (Bethesda VI). From there, we calculated the proportion of cytological changes detected in FNA in relation to the total changes in the ultrasound image. We classified these images according to the ACR TI-RADS with the following variables: benign, not suspicious, not very suspicious, moderately suspicious, and highly suspicious (Figure 3).

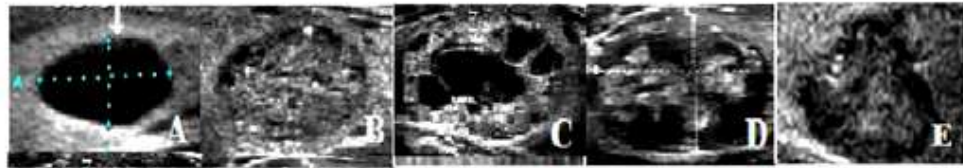
Figure 3. ACR-TIRADS classification.



¹ Classify nodule as solid if composition cannot be determined
² Classify nodule as isoechoic if echogenicity cannot be determined
³ Nodules with definite extra-thyroidal extension should be considered malignant until proven otherwise

Source: AJR Am J Roentgenol. 2021 Mar;216(3):570-578. doi: 10.2214/AJR.20.24608. Epub 2021 Jan 21.
 The ultrasonography images of thyroid nodule show the input: TI-RADS 1, TI-RADS 2, TI-RADS 3, TI-RADS 4, TI-RADS 5 (Figure 4).

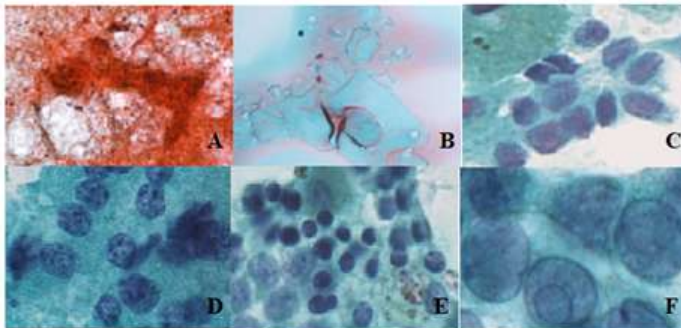
Figure 4. Thyroid nodule images.



A: TI-RADS 1 B: TI-RADS 2 C: TI-RADS 3 D: TI-RADS 4 E: TI-RADS 5

Source: Search result
 The FNA images show the input: Non-diagnostic or Unsatisfactory, Benign, Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, Follicular Neoplasia or Suspected Follicular Neoplasia, Suspected Malignancy, and Malignant (Figure 5).

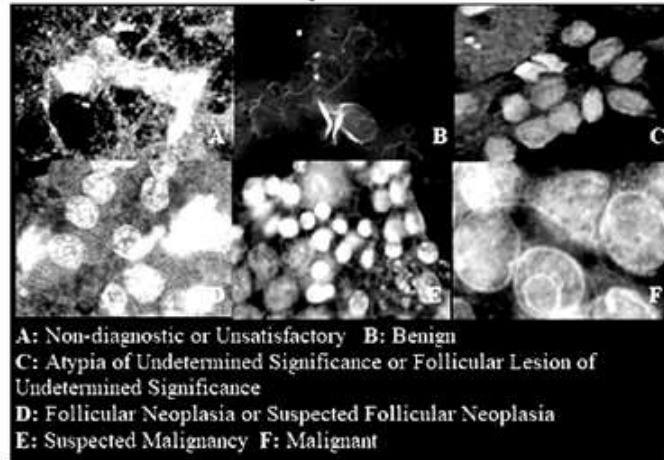
Figure 5. Fine-needle aspirations specimens.



A: Non-diagnostic or Unsatisfactory B: Benign
 C: Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance
 D: Follicular Neoplasia or Suspected Follicular Neoplasia
 E: Suspected Malignancy F: Malignant

Source: Search result
 Using MATLAB software (<https://la.mathworks.com/products/matlab.html>), automatic detection of secondary changes to FNA is quickly performed. The images were pre-processed after a contrast improvement step that consisted of resizes the images to a uniform size of 500 × 500 pixels, morphological operators and then binarization. A total of 75 fuzzy rules extracted as a rule-base based on cytopathologist and physician expert's opinion. The FNA images after pre-processing show the output: non-diagnostic or unsatisfactory, benign, atypia of undetermined significance or follicular lesion of undetermined significance, follicular neoplasia or suspected follicular neoplasia, suspected malignancy, and malignant (Figure 6).

Figure 6. Secondary changes to FNA.



Source: Search result
 The table 1 shows the classification for thyroid nodules suggested based on the 95% confidence interval of ofhypoechoogenicity and microcalcifications.

Table 1. Classification of thyroid nodule suggested based hypoechoogenicity and microcalcifications

Classification for thyroid nodule suggested	95% confidence interval
not suspicious	< 24.6
not very suspicious	24.6 - 48.0
moderate	48.1 - 64.5
moderately suspicious	64.6 - 77.0
highly suspicious	77.1 - 92.7
malignant	> 92.7

Source: Search result
 We present in table 2 the results for the detection thyroid nodule using fuzzy logic for six different ultrasound images.

Table 2. Shows the results for the detection of thyroid nodule using Fuzzy logic for six different ultrasound image

Original Image						
	Not suspicious	Not very suspicious	Moderate	Moderate suspicious	Highly suspicious	Malignant
Classification thyroid nodule using Fuzzy logic	<24.6	24.6 – 48.0	48.1 – 64.5	64.6 – 92.7	77.1 – 92.7	>92.7

Source: Search result
 We present in table 3 the results for the detection thyroid nodule using fuzzy logic for six images of cytology slides.

Table 3. Show the results for the detection of thyroid nodule using Fuzzy logic for six images of cytology slides

Original Image						
	Not suspicious	Not very suspicious	Moderate	Moderate suspicious	Highly suspicious	Malignant
Classification thyroid nodule using Fuzzy logic	<24.6	24.6 – 48.0	48.1 – 64.5	64.6 – 92.7	77.1 – 92.7	>92.7

Source: Search result
 Therefore, the proposed thyroid nodules severity classification considers the various 95% CI for the previously described classes, grounded on relationship with the found on ultrasound. The results showed that is possible to develop fuzzy systems that can thyroid nodule severity classification. Moreover, the results demonstrate that the fuzzy logic too can diagnose the various stages of thyroid nodules.

DISCUSSION

In this paper, we used the fuzzy logic with the severity classification proposal of thyroid nodules, and results found demonstrated that the technique used can classify the thyroid nodules with elevated precision. Several scientists have introduced different fuzzy logic approaches into medical diagnostics to increase confidence and reduce a classification error secondary to human error, and language strategies have been implemented in decision making with fuzzy interface⁽¹¹⁾.

The incidence of nodular goiter has increased in recent years and is believed to be related to the large scale employment of thyroid ultrasound, resulting in the diagnosis of asymptomatic nodules and thus the need to exclude a thyroid cancer that presents a frequency ranging from 7 to 15%⁽¹²⁾. Thus, current evidence demonstrates the excellent performance of thyroid ultrasound in evaluation of thyroid nodule.

The automation in evaluation of thyroid nodule has been simplified by use of combining FNA and thyroid ultrasound using high resolution equipment, associated the processing digital and analysis of images through modern computational techniques. Thus, the diagnosis by computerized systems of the thyroid nodules has been described by several authors⁽¹³⁾. In the present work we use cytopathological evaluation and morphological evaluation with FNA and ultrasound for fractionation and fuzzy logic for the identification process of features of thyroid nodules. The FNA aspects evaluated for diagnosis of thyroid nodules were the aspects benign, atypia of undetermined significance or follicular lesion of undetermined significance, follicular neoplasia or suspected follicular neoplasia, suspected malignancy, and malignant while following ultrasound findings were evaluated employing a qualitative punctuation method, measuring the aspects benign, not suspicious, not very suspicious, moderately suspicious, and highly suspicious.

Fuzzy logic was first described in 1965, it is a tool that produces a mechanism for reply to imprecise information based in qualitative language and transcribed to a numerical language. Thus, fuzzy logic has been used indeed in medicine to diagnose the diseases based clinical and imaging data⁽¹⁴⁾. The fuzzy logic has also been used in clinical research⁽¹⁵⁾. As already described above, we used the fuzzy logic with the severity classify objective of thyroid nodules.

The fuzzy logic suggested in this study was based in six FNA variables and five ultrasonography variables. The analysis exposed here demonstrated that fuzzy logic is appropriate to classify the severity of thyroid nodules.

Thyroid nodules are common and ultrasound is the main tool for evaluating nodules and should be performed when a suspicion of any thyroid nodule occurs⁽¹⁶⁾. Taking into consideration the thyroid nodule characteristics, we apply fuzzy logic to rank characteristics sonographic and FNA related to thyroid nodule. Afterwards, a transformed fuzzy neural network was produced to improve the classification precision, and lastly we extract association rules between the chosen characteristics of nodule to characterize their severity degree.

Recently, several fuzzy system free and open source software

were produced, through which simulations fuzzy logic can be performed quickly⁽¹⁷⁾. In this work the evaluations were performed with Fuzzy-Calc, and the MATLAB package, the first an app was used calculate fuzzy indicators with the objective to obtain a synthetic performance value for the study variables, and MATLAB fuzzy logic toolbox was used for comparative study between FNA and ultrasound. The MATLAB software offer several tools and module used in this work was the Image Processing Toolbox⁽¹⁸⁾.

The medical diagnostic depend upon practice and expertise of medical practitioner. Fuzzy logic is a technique to establish what accuracy what is imprecise in medicine, and has been playing a considerable role in the diagnosis and treatment of diseases⁽¹⁹⁾. Several researches employing models identification and image manipulation techniques to diagnose of diseases have been developed⁽²⁰⁾. Our study as compared to the other studies was more embracing, because as it involved the use of FNA and ultrasonography in different stages of the thyroid nodules using fuzzy logic, and classifying the thyroid nodules with high precision.

Thus, by the fuzzy logic, a classification of thyroid nodules based on FNA and ultrasound was constructed with a simple practical application. The fuzzy logic technique has been applied in many areas of knowledge, and in medicine it has been used for diagnosis, classification of diseases, and optimization of medical treatments.

CONCLUSION

A classification for ultrasound-diagnosed thyroid nodules was constructed using fuzzy logic, based on echogenicity and the presence of nodular microcalcifications. This classification has a simple and practical application. However, the classification of thyroid nodules should still be supported by clinical findings from anatomopathological examinations.

Disclosure of potential conflicts of interest:

None of the authors have any potential conflicts of interest to disclose.

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