

Pathological and Clinical Correlation European Union-Thyroid Imaging Reporting and Data System (EU-TIRADS) Classification of Thyroid Nodules in Two University Hospitals in Cotonou

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Abstract

Introduction: Since its creation in 2017 by the European community, the EU-TIRADS classification has enjoyed an excellent reputation in several countries around the world. Indeed, several studies conducted in these countries testify to the effectiveness of this tool for the management of nodular thyroid pathology. However, in Benin, the contribution of this classification has not yet been evaluated. It is therefore to overcome this inadequacy that we undertook this study. **Objective:** Participate in improving the diagnostic and therapeutic management of thyroid nodules at the CNHU HKM in Cotonou and at the CHUZ in Suru-Léré. **Methods:** This is a cross-sectional study with retrospective data collection spread over a period of 3 years 5 months, from January 2019 to May 2022 and carried out jointly in the Endocrinology Metabolism Nutrition and ORL-CCF departments of the CNHU HKM of Cotonou and in the ORL-CCF department of the CHUZ of Suru-Léré. The study population consisted of patients who consulted the University Clinic of Endocrinology Metabolism Nutrition, the University Clinic of ORL-CCF of the CNHU-HKM and the University Clinic of ORL-CCF of the CHUZ of Suru-Léré for thyroid nodule and who have had surgery. The study data was collected from patients hospitalization records using a survey form. **Results:** On ultrasound, according to the EU-TIRADS classification, 56.8% of nodules presented a low risk of malignancy (EU-TIRADS 3) compared to respectively 19.8%; 23% and 2.5% of nodules with zero (EU-TIRADS 2), intermediate (EU-TIRADS 4) and high (EU-TIRADS 5) risk of malignancy. Regarding the performance of this classification, it is sensitive in 37.5% of cases and has a specificity of 78.5% with a PPV (Positive Predictive Value) and a NPV (Negative Predictive Value)

respectively of 6.6 % and 91.6%. Furthermore, the bivariate correlations revealed that the size of the nodule was significantly associated with the malignancy of the nodule ($p = 0.014$) and the calculated value of the Yule's Q coefficient (0.375) reflects a moderate intensity of the connection between the EU-TIRADS and histology. Conclusion: the EU-TIRADS classification, due to its excellent NPV, is of great interest for the management of thyroid nodules at the CNHU-HKM of Cotonou and at the CHUZ of Suru-Léré. In view of this, particular emphasis must be placed on its regular and rigorous use.

Keywords

Thyroid Nodules, EU-TIRADS Classification, Malignancy

1. Introduction

The thyroid nodule is an abnormality of the endocrine system characterized by the development of a mass within the thyroid gland. It is one of the most common endocrine pathologies and the nature of these nodules can be benign or malignant. Although most often benign, these nodules can also take on a malignant character which turns out to be the dread in terms of thyroid pathology.

Cervical ultrasound, which constitutes a key examination in the management of these nodules, is not sufficient on its own to effectively assess the risk of malignancy of these nodules given its operator-dependent nature. It is to compensate for this insufficiency that a new tool has emerged: the Thyroid Imaging Reporting and Data System classification (TIRADS). This system makes it possible to define benign nodules and those at risk of low, intermediate and high malignancy, as well as indications for FNA. EU-TIRADS aims to serve doctors in their practice, to improve the inter observer reproducibility and to simplify the communication of results [1]. A thyroid carcinoma is the most common type of nodule worrying, and although not common, it has therapeutic implications problematic. The endocrinologist and surgeon caring for a patient with a nodule thyroid must take into account two main clinical problems: the possibility of hormonal excess or insufficiency resulting from this lesion and the risk of malignancy [2]. These questions guide the patient's care, which can vary from simple monitoring to surgical resection

Since its creation, the TIRADS classification has been widely used throughout the world with some variations depending on the scientific societies, thus giving rise to several classification models including the EU-TIRADS classification. The latter (2017 version) has been used in Benin for almost 5 years and has not yet been evaluated unlike European countries. In view of these elements, we understand the relevance of this study.

2. Method

This was a cross-sectional study with retrospective data collection spread over a

period of 3 years 5 months, from January 2019 to May 2022. The study population consists of patients who consulted in the Endocrinology Metabolism university clinic. Nutrition then secondarily to the ENT-CCF university clinic of the CNHU-HKM and/or to the ENT-CCF university clinic of the CHUZ of Suruléré for thyroid nodules and who were operated on.

The inclusion criteria were files with a thyroid ultrasound an EU-TIRADS classification and definitive pathological examination.

In the case of multinodular goiter, only one nodule will be included in the study (the most dominant nodule, *i.e.* which has more malignancy criteria). Incomplete files are excluded (the TIRADS score does not appear in the ultrasound report) and patients without histological proof.

The variables studied were: socio-demographic, personal medical, medication, surgical and family history, results of the clinical examination, thyroid assessment, cervical ultrasound data plus EU-TIRADS classification, type of thyroidectomy and the results of anatomopathology.

The questionnaire is digitized on KoBo Toolbox and KoboCollect then the data analysis is carried out with R Project 4.2.0 software.

3. Results

3.1. Sociodemographic Characteristics of Patients

Age (**Figure 1**):

The average age was 44.4 ± 11.8 years. The age extremes were 16 and 75 years. The 41 - 50 age group was the most represented with 30%.

The average age of patients with a benign nodule was 44.2 ± 12.3 years.

The average age of patients with a malignant nodule was 44.6 ± 10.6 years.

Sex of 81 patients, 75 (92.6%) were female compared to 6 (7.4%) male, *i.e.* a male/female sex ratio of 0.08.

3.2. Interview Data

The majority of patients had no personal or family history of thyroid disease.

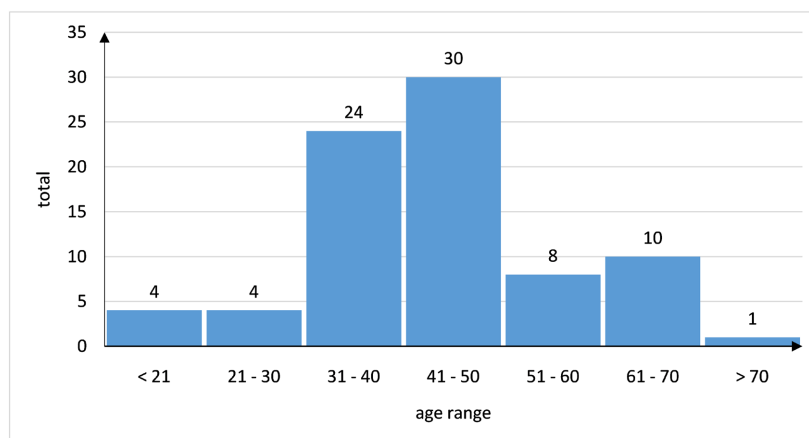


Figure 1. Distribution of patients according to age range.

Signs of loco-regional compression were absent in 81.5%. Among those who had it, dyspnea was predominantly present (8.6%).

Patients had no signs of hyperthyroidism (65.4%) and hypothyroidism (87.2%).

3.3. Physical Signs

The thyroid nodules were predominantly firm in consistency (84.0%), all mobile when swallowed, non-painful (97.5%), without cervical lymphadenopathy and varying in size between 1 and 4 cm.

3.4. Paraclinical Data

Ultrasound

The size of the nodules was mainly between 2 and 4 cm 40.7%. The nodules were mainly hyperechoic 28.4%. The nodules were multiple in 87.7% (**Table 1**).

The nodules had a regular outline in 54.3% of patients. Microcalcification was found in 6.2% and macrocalcification in 16%.

The vascularization was not specified in 58.0% of patients. It was peripheral in 21.0%. Cervical lymphadenopathy was not present in the majority of patients (80.2%).

EU-TIRADS score (**Table 2**)

Thyroid nodules were classified EU-TIRADS 3 in the majority of patients (55.6%).

Pathological anatomy

Benign nodules were predominant (86.4%) in the patients. As for malignant nodules, the majority type was papillary carcinoma, *i.e.* 6 out of 8 patients. Corrélation entre EU TIRADS et l'examen anatomo-pathologique (**Table 3**).

The EU-TIRADS classification on ultrasound allowed us to identify 73 benign thyroid nodules out of the 81. One (1) nodule classified benign on ultrasound was confirmed malignant by pathology. The 7 nodules classified as malignant by EU-TIRADS were confirmed by pathology.

Correlation between EU-TIRADS score and histological nature (**Figure 2**)

The sensitivity of the EU-TIRADS score was 87.5%. The specificity was 21.4%. The positive predictive value was 11.2%. The negative predictive value was 98.7%. Yule's Q coefficient is 0.3125 reflecting a moderate intensity of the connection between EU-TIRADS and histology

Factors associated with malignancy (**Table 4**)

Nodule size was significantly associated with nodule malignancy ($p = 0.014$). Another hand, multiplicity of nodule, the site of nodule, the shape of nodule, the echogenicity, the echostructure, the microcalcification and vascularisation didn't be associated with malignancy.

4. Discussion

Our study noted a strong female predominance with a sex ratio (male/female) of

Table 1. Ultrasound characteristics of nodules.

	Total	Percentage (%)
Nodule size		
2 - 4 cm	33	40.7
>4 cm	26	32.1
1 - 2 cm	15	18.5
<1 cm	1	1.2
Unspecified	6	7.4
Nodule echogenicity		
Hyper echogenic	23	28.4
Iso echogenic	17	21.0
Hypo echogenic	13	16.0
Anechoic	2	2.5
Unspecified	26	32.1
If hypoechogenic, specify		
Moderately	12	92.3
Strongly	0	0.0
Unspecified	1	7.7
Nodule contour		
Regular	44	54.3
Irregular	6	7.4
Unspecified	31	38.3
Microcalcification		
Yes	5	6.2
No	44	54.3
Unspecified	32	39.5
Macrocalcification		
Yes	13	16.0
No	33	40.7
Unspecified	35	43.2
Vascularisation		
Peripheral	17	21.0
Mixed	10	12.3
Central	1	1.2
Absence	6	7.4
Unspecified	47	58.0
Cervical adenopathy		
Yes	14	17.3
No	65	80.2
Unspecified	2	2.5

Table 2. Distribution of patients according to EU-TIRADS classification.

	Signification	Total	Percentage (%)
Classification EU-TIRADS			
2	Benign	17	21.0
3	Low risk	45	55.6
4	Intermediate risk	17	21.0
5	High risk	2	2.5

Table 3. Diagnostic value of EU-TIRADS versus histology in the diagnosis of thyroid nodule malignancy.

		Anatomopathology		
		Malignant	Benign	Total
EU-TIRADS	Malignant (3, 4 and 5)	7	57	64
	Benign (2)	1	16	17
	Total	8	73	81

Table 4. Distribution of patients according to ultrasound findings and malignancy of nodules on histology.

		N = 81		
		Benign N = 73	Malignant N = 8	p-value
Nodule				
	Multiple	73 (90.1%)	7 (87.5%)	0.6
	Unique	8 (9.9%)	1 (12.5%)	
Site of nodule				
	Right	32 (39.6%)	5 (62.5%)	0.4
	Left	43 (53.1%)	3 (37.5%)	
	Isthmus	5 (6.1%)	0 (0.0%)	
	Unspecified	1 (1.2%)	0 (0.0%)	
Nodule size				0.014
	<1 cm	0 (0.0%)	1 (12.5%)	
	>4 cm	21 (30.0%)	5 (62.5%)	
	1 - 2 cm	18 (20.0%)	0 (0.0%)	
	2 - 4 cm	38 (44.3%)	1 (12.5%)	
	Unspecified	4 (5.7%)	1 (12.5%)	
Nodule shape				0.2
	Oval	36 (44.4%)	5 (62.5%)	
	Round	5 (6.2%)	0 (0.0%)	
	Irregular	3 (3.7%)	1 (12.5%)	
	Unspecified	37 (45.7%)	2 (25.0%)	

Continued

Echostructure of nodules			0.4
Spongiform	18 (22.2%)	0 (0.0%)	
Mixed	16 (19.8%)	3 (37.5%)	
Solid	13 (16.0%)	2 (25.0%)	
Cystic	9 (11.1%)	1 (12.5%)	
Unspecified	25 (30.9%)	2 (25.0%)	
Nodule echogenicity			0.8
Anechoic	2 (2.9%)	0 (0.0%)	
Hyper echogenic	23 (32.9%)	4 (50.0%)	
Hypo echogenic	13 (18.5%)	2 (25.0%)	
Iso echogenic	17 (24.3%)	1 (12.5%)	
Unspecified	26 (21.4%)	1 (12.5%)	
If hypo echogenic, specify strongly	0 (0.0%)	1 (50.0%)	0.1
Moderately	12 (92.3%)	1 (50.0%)	
Unspecified	1 (07.7%)	0 (0.0%)	
Nodule contour			0.2
Regular	44 (54.3%)	4 (50.0%)	
Irregular	6 (7.4%)	2 (25.0%)	
Unspecified	31 (38.3%)	2 (25.0%)	
Microcalcification			0.079
Yes	5 (6.2%)	2 (25.0%)	
No	44 (54.3%)	3 (37.5%)	
Unspecified	32 (39.5%)	3 (37.5%)	
Macrocalcification			0.7
Yes	13 (16.0%)	0 (0.0%)	
No	33 (40.7%)	4 (50.0%)	
Unspecified	35 (43.3%)	4 (50.0%)	
Vascularisation			0.076
Peripheral	17 (21.0%)	2 (25.0%)	
Mixed	10 (12.3%)	2 (25.0%)	
Absence	6 (7.5%)	0 (0.0%)	
Central	1 (1.2%)	1 (12.5%)	
Unspecified	47 (58.0%)	3 (37.5%)	
Cervical adenopathy			>0.9
Yes	14 (17.3%)	1 (12.5%)	
No	65 (80.2%)	7 (87.5%)	
Unspecified	2 (2.5%)	0 (0.0%)	

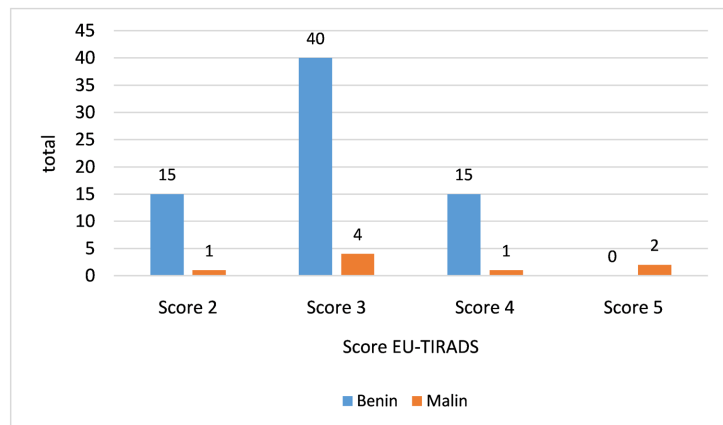


Figure 2. Correlation between EU-TIRADS score and histological nature.

0.08, *i.e.* 6 men for 75 women. This trend had been reported in other studies in Europe as well as in Africa and Asia [3] [4] [5] [6]. Indeed, female sex would constitute one of the risk factors for the occurrence of thyropathies in general.

The average age of the patients was 44.4 ± 11.8 years. Our results were similar to those reported in Western literature which showed an average age varying between 50 and 60 years [7] [8].

The EU-TIRADS classification of thyroid nodules on cervical ultrasound in our study found 21%; 55.6%; 21.6% and 2.5% corresponding respectively to a zero risk of malignancy (EU-TIRADS 2); low (EU-TIRADS 3); intermediate (EU-TIRADS 4) and high (EU-TIRADS 5). These results are similar to those obtained by several studies [7] [8]. Indeed, in Poland Skowrońska *et al.* [9] 4.3%; 65.7%; 24.3% and 5.7% for respectively EU-TIRADS 2, EU-TIRADS 3, EU-TIRADS 4 and EU-TIRADS 5. Kovatcheva *et al.* [10] found 4.8% of nodules classified EU-TIRADS 2; 37.4% of nodules classified EU-TIRADS 3; 25.2% of nodules classified EU-TIRADS 4 and 32.6% of nodules classified EU-TIRADS 5. In Italy, Magri *et al.* [11] found in their study that 0.7% of nodules corresponded to stage 2; 55.6% at stage 3; 22% at stage 4 and 21.7% at stage 5 of the EU-TIRADS classification. For their part, Trimboli *et al.* [12], nodules were classified as EU-TIRADS 2, 3, 4, and 5 in 6.7%; 46.4%; 26.2% and 20.7%, of cases respectively. A Moroccan study carried out by Hamza AZAL [5] also found a predominance of nodules classified EU-TIRADS 3, *i.e.* 53.44% compared to 7.75% of nodules classified EU-TIRADS 2; 29.3% of nodules classified EU-TIRADS 4 and 9.48% of nodules classified EU-TIRADS 5. On the other hand, our results are different from those of Yeste Fernández *et al.* [13] in Spain who noted instead a predominance of nodules corresponding to Stage 4 of the EU-TIRADS classification, *i.e.* 51.6% versus respectively 6.4%; 22.6% and 16.1% for stages 2, 3 and 5. This difference could be explained by the fact that Yeste Fernández *et al.* [13] worked with a population of children in whom thyroid nodules (TN) have a higher risk of malignancy. Likewise, the investigation carried out by Dobruch-Sobczak *et al.* [14] differ from the results of our study. Indeed, in this Polish study, the dominant stage of the EU-TIRADS classification is

stage 5, *i.e.* 43% compared to respectively 18.29%; 11.04% and 12.23% of cases for stages 2, 3 and 4. The reason for this difference could be due to the fact that when recruiting study subjects, those with symptomatic purely cystic lesions were excluded from this study. However, cystic lesions are almost benign nodules. We could therefore think that this exclusion criterion favored a greater number of malignant nodules in the study by Dobruch-Sobczak *et al.* [14].

Several authors have been interested in the most significant ultrasound characteristics for predicting the risk of malignancy. With regard to our study, the bivariate correlation between the ultrasound characteristics of the nodules and the pathology results made it possible to identify the size of the nodules as being a factor significantly associated with the risk of malignancy of the Thyroid nodule ($p = 0.014$). This result contrasts with that of Skowrońska and col in Poland [9] for whom solid composition, hypoechogenicity, microcalcifications, “higher than wide”, irregular shape and uncircumcised margins were the most common ultrasound characteristics reliable in predicting the malignancy of a nodule on ultrasound rather than the size of the nodules for which they found no significant link. Dobruch-Sobczak *et al.* [14] found no significant difference between benign and malignant nodules regarding their size. Their observation differs from ours. Indeed, Dobruch-Sobczak *et al.* [14]. Identifies the presence of irregular margins (OR = 13.82), solid or almost solid composition (OR = 9.82), hypoechoic echogenicity (OR = 5.75), shape that is taller than wide (OR = 4.86), markedly hypoechoic microcalcifications (OR = 3.65) and macrocalcifications (OR = 1.60) as the ultrasound features most significantly associated with malignancy. This can also be explained by the fact that ultrasound is operator dependent.

In Morocco, the study carried out by Hamza AZAL [5] made it possible to isolate the form which is thicker than long, the central vascularization and microcalcifications as reliable ultrasound criteria of malignancy.

A correlation between the data from the anatomic-pathological examination and the EU-TIRADS classification made it possible to evaluate the performance of the EU-TIRADS classification in our study. It was therefore a question of determining the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) relating to this classification.

Our study revealed a sensitivity of 87.5% for EU-TIRADS. This rate is close to that found by Magri *et al.* in Italy [9] (83.2%) from Trimboli *et al.* in Europe [12], Hamza AZAL in Morocco [5] and Yeste Fernández *et al.* in Spain [13] who found 93% and 92.3% and 100% respectively. Regarding the specificity of EU-TIRADS, it was 21.4%. This value is very close to that found by Yeste Fernández *et al.* in Spain [13], *i.e.* 25%. As for them, Magri *et al.* [11], Trimboli *et al.* [12] and Hamza AZAL [5] found 74.5% respectively; 67.5% and 68.62% for the specificity of this classification. These values are much higher than those found in our survey.

Regarding the positive predictive value (PPV), the values vary depending on the stage of classification. Thus for EU-TIRADS 3, it was equal to 9% which is

significantly lower than the 33.3% determined by Dobruch-Sobczak *et al.* [14] and the 55.6% of Skowrońska *et al.* As for EU-TIRADS 4, our study revealed a PPV of 6.25%. The latter is 6 times smaller than in the study carried out by Dobruch-Sobczak *et al.* [14] who determined a value of 38%. As for EU-TIRADS 5, the PPV was 100% in our study. This value is more than 3 times higher than that found by Kovacheva *et al.* in Bulgaria [10] where the PPV was 30.6%. This could be explained by the enormous difference in study sample size between the 2 studies (1000 nodules in the Bulgarian study versus 81 in our study).

Concerning the NPV, our study reveals a rate of 94.1%. This result is similar to those of Magri *et al.* in Italy [11] which found a rate equal to 90.6%. For their part, Trimboli *et al.* [12] and Hamza AZAL [5] found 74% and 73% respectively. These figures are lower than ours probably because of the size of the population which is larger in these 2 studies than in our study. On the other hand, the NPV that we determined is lower than that determined by Yeste Fernández *et al.* in Spain [13] this could be linked to the very small sample size of the Spanish study, either 24 subjects compared to 81 patients in our study.

5. Conclusion

Cervical ultrasound, due to its simplicity, availability, performance and non-invasive nature remains the examination of choice. This study showed that the EU-TIRADS classification, due to its excellent NPV, is of great interest for the management of thyroid nodules at the CNHU-HKM of Cotonou and at the CHUZ of Suru-Léré. By correlating the results of the ultrasound with those of the definitive pathological examination, this study showed that the EU-TIRADS classification is an examination allowing the selection of nodules at risk of malignancy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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