

# Risk of Malignancy in Thyroid Nodules Using the American College of Radiology Thyroid Imaging Reporting and Data System in the NIFTP Era

## Authors

Pedro Wesley Rosario, Alexandre Lemos da Silva, Maurício Buzelin Nunes, Michelle Aparecida Ribeiro Borges

## Affiliation

Santa Casa de Belo Horizonte, Minas Gerais, Brazil

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## Correspondence

P. W. Rosario, MD

Instituto de Ensino e Pesquisa da Santa Casa de Belo Horizonte

Rua Domingos Vieira, 590

Santa Efigênia CEP 30150-240

Belo Horizonte MG

Brazil

Tel.: +55/31/32388 819, Fax: +55/31/32388 980

[pedrowsrosario@gmail.com](mailto:pedrowsrosario@gmail.com)

## ABSTRACT

Recently, the American College of Radiology (ACR) proposed a Thyroid Imaging Reporting and Data System (TI-RADS) for thyroid nodules based on ultrasonographic features. It is important to validate this classification in different centres. The present study evaluated the risk of malignancy in solid nodules > 1 cm using ACR TI-RADS. The risk of malignancy was defined including noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) and after its exclusion from malignant tumours. For the present study, the original images were revised, and each nodule was assigned to one of the TI-RADS levels proposed for solid nodules: TR3, TR4, or TR5. This risk of malignancy was significantly different for the three levels: 1.7%, 11.2%, and 60.6% for TR3, TR4, and TR5, respectively, when NIFTP was included, and 0.6%, 7.9%, and 60.2% for TR3, TR4, and TR5, respectively, when NIFTP was excluded from malignant tumours. The nodules corresponding to NIFTP were classified according to ACR as TR3 in 28.5% of cases, TR4 in 67.8%, and TR5 in only 3.5%. The nodules corresponding to cancer were classified according to ACR as TR3 in only 2.3% of cases, TR4 in 27%, and TR5 in 70.5%. In conclusion, this study shows the validity of the ACR TI-RADS for solid thyroid nodules, even after the exclusion of NIFTP from malignant tumours.

## Introduction

Recently, the American College of Radiology (ACR) proposed a Thyroid Imaging Reporting and Data System (TI-RADS) for thyroid nodules based on ultrasonographic features that consists of five levels [1]. Different from the classification of the American Thyroid Association (ATA) [2] in which some nodules may not meet the criteria for any of the categories [3–5], the TI-RADS permits to classify all nodules. However, it is important to validate this classification in different centres. Diagnostic fine-needle aspiration (FNA) is not recommended for TR1 (benign) and TR2 (not suspicious) nodules [1]. Thus, greater interest exists in the risk of malignancy of TR3 (mildly suspicious), TR4 (moderately suspicious), and TR5 (highly suspicious) nodules.

In the 4th edition of the World Health Organization classification of tumours of endocrine organs, the noninvasive encapsulat-

ed follicular variant of papillary thyroid carcinoma (EFVPTC) is no longer considered “cancer” [6]. These tumours are now called “noninvasive follicular thyroid neoplasm with papillary-like nuclear features” (NIFTP) [6]. However, few studies have re-evaluated the risk of malignancy according to the ultrasonographic appearance of the nodule after the exclusion of NIFTP [7, 8].

We previously evaluated the risk of malignancy in thyroid nodules > 1 cm using the ultrasonographic classification of ATA [3, 7]. The risk of malignancy was defined including NIFTP [3] and after its exclusion from malignant tumours [7]. The present study evaluated the risk of malignancy of these nodules using the ACR TI-RADS [1].

## Patients and Methods

This study is derived from a prospective study [3, 7] that evaluated the ultrasonographic features of 1502 nodules > 1 cm. These nod-

ules were solid or predominantly solid and nontoxic in 1106 patients, all of them submitted to ultrasonography (US)-guided FNA and the results of cytology classified using the Bethesda system [2]. As reported previously [3, 7], there were 1005 nodules with benign cytology (on two occasions in the case of nodules with highly suspicious US findings) and 497 with nonbenign cytology, with histology being obtained from 485/497 (97.6%).

For the present study, the original images were revised separately by two professionals experienced in thyroid imaging and each nodule was assigned to one of the TI-RADS levels proposed for solid nodules [1]: TR3, TR4, or TR5. Despite disagreement on the sum of points in 20 nodules (difference of only 1 point), there was agreement between the two examiners on TI-RADS level in all nodules.

Fisher's exact test or the  $\chi^2$  test was used to detect differences in the proportion of cases. A p-value < 0.05 was considered to be significant.

## Results

The risk of malignancy of each TI-RADS level is reported in ► **Table 1**. This risk was significantly different for the three levels to which solid nodules can be assigned: 1.7%, 11.2%, and 60.6% for TR3, TR4, and TR5 ( $p < 0.0001$ ), respectively, when NIFTP was included, and 0.6%, 7.9%, and 60.2% for TR3, TR4, and TR5 ( $p < 0.001$ ), respectively, when NIFTP was excluded from malignant tumours.

The nodules corresponding to NIFTP ( $n = 28$ ) were classified according to ACR as TR3 in 28.5% of cases, TR4 in 67.8%, and TR5 in only 3.5%. Much differently, the nodules corresponding to cancer ( $n = 170$ ) were classified according to ACR as TR3 in only 2.3% of cases, TR4 in 27%, and TR5 in 70.5%.

## Discussion

Our results favour the use of the ACR TI-RADS classification [1]. First, in contrast to the ATA classification [2] in which 4% of the nodules did not meet the criteria for any of the categories and had a risk of malignancy of 16% [3], in the present series all nodules could be classified using the ACR TI-RADS. In two other studies, 5% [5] and 14% [4] of the nodules were not defined using the ATA classification, with

malignancy in 15% [5] and 10% [4], respectively. Second, since the sum of points ranges from 4 to 6 for level TR3 and is 7 or higher for level TR5, the small difference (1 point) in the sum of points observed for few nodules did not change the TI-RADS level, with 100% agreement between the two examiners. This excellent agreement was obtained with only two examiners who work in the same research centre and have large experience with thyroid US. It should be noted that significant disagreement may be observed when many professionals with variable experience who work in different places (research institutions or private companies) are involved [9]. Third, a large difference in the risk of malignancy was observed between the three TI-RADS levels to which solid nodules can be assigned [1]. The finding that calls attention is the very low risk of malignancy observed for TR3 nodules ( $\leq 3\%$ ) and, conversely, the high risk found for TR5 nodules ( $\geq 50\%$ ). Some comparative studies suggested superior performance of ACR TI-RADS over the ATA classification [4, 5].

An important issue addressed in this study was the impact of non-invasive EFVPTC on the risk of malignancy. Until now, in the series that evaluated the risk of malignancy according to the ultrasonographic features of the nodules, these tumours were considered malignant [4, 5, 10], including the multicentre study validating the ACR TI-RADS in the United States [10]. With the recent change that no longer considers these tumours to be malignant [6], the originally reported malignancy rates might be lower, at least for some TI-RADS levels, since the distribution of NIFTP is not uniform at the different levels. When we recalculated the risk of malignancy after excluding NIFTP, this rate was 0.6% for TR3 nodules and 8% for TR4 nodules, while no change was observed for TR5 nodules. Thus, a reduction in the risk of malignancy is possible in the case of TR3 and TR4 nodules but does not appear to occur in TR5 nodules. Only two studies have evaluated the impact of excluding NIFTP on the risk of malignancy estimated by US but did not use ACR TI-RADS. In the first study using the ATA classification, we showed a reduction in the risk of malignancy for low- and intermediate-suspicion nodules [7]. In the second study, Chaigneau et al. [8], using the French TIRADS for nodules with indeterminate cytology, demonstrated a reduction in the risk of malignancy mainly for TIRADS 4A nodules. Like in the present study, in these two, the risk of malignancy in more suspicious nodules (high suspicion by ATA [7] and French TIRADS 4B or 5 [8]) did not change after the exclusion of NIFTP.

Our study is also the first to evaluate ACR TI-RADS in NIFTP. We showed that TR4 was the most frequent, TR5 was uncommon (3.5%), and TR3 was common in this neoplasm, in contrast to carcinomas in which TR5 corresponded to 70% of cases and TR3 was rare ( $< 3\%$ ).

In conclusion, this study confirms the validity of the ACR TI-RADS [1] for solid thyroid nodules, even after the exclusion of NIFTP from malignant tumours [4], and shows the ultrasonographic appearance of this neoplasm using ACR TI-RADS.

## Compliance with Ethical Standards

The study was approved by the Research Ethics Committee of our institution. Informed consent was obtained from all individual participants included in the study.

► **Table 1** Risk of malignancy in solid thyroid nodules > 1 cm according to the TI-RADS of the American College of Radiology [1].

TI-RADS [1] (number of nodules)	Risk of malignancy (95% confidence interval)	
	Malignant NIFTP	Non-malignant NIFTP
TI-RADS 3 (n = 694)	1.7% (0.96–3%)	0.6% (0.17–1.5%)
TI-RADS 4 (n = 580)	11.2% (8.9–14%)	7.9% (6–10.4%)
TI-RADS 5 (n = 216)	56% (49.3–62.5%)	55.5% (49–62%)

TI-RADS: Thyroid Imaging Reporting and Data System; NIFTP: Noninvasive Follicular Thyroid Neoplasm with Papillary-like nuclear features.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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