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Research Article

Value of Thyroid Imaging Reporting and Data System in Initial Bethesda Category III Thyroid Nodules

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Background. To evaluate the role of Thyroid Imaging Reporting and Data System (TI-RADS) in predicting malignancy for cytological Bethesda system III nodules. *Method*. The study included 188 thyroid nodules with first Bethesda system III cytology on surgery or repeat FNA. Patients' clinicopathologic parameters and ultrasonographic (US) nodule characteristics were evaluated according to benignity and malignancy. Using the TI-RADS classification system, thyroid nodules were categorized. *Results*. The size of malignant nodules was significantly lower than that of benign nodules ($P < 0.001$). Thyroid nodules associated with concomitant thyroid carcinoma had a significantly increased risk of malignancy ($P < 0.001$). Univariate analysis indicated that there were significant differences in the images of benign and malignant nodules in terms of solid composition, hypoechogenicity or marked hypoechogenicity, a taller-than-wide or irregular shape, ill-defined margins, and microcalcifications presence ($P < 0.05$). TI-RADS categories 4c (OR = 8.3, 95% CI 3.8–18.1; $P = 0.043$) and 5 (OR = 9.4; 95% CI 1.2–74.2; $P = 0.026$) were predictive for malignancy. *Conclusions*. The TI-RADS US evaluation may assist the physician in deciding whether to proceed with follow-up, repeating FNA, or surgical intervention.

1. Introduction

Ultrasound-guided fine-needle aspiration (US-FNA) is a precise and cost-effective procedure for diagnosing thyroid nodules [1–3]. Since Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was published [4], several studies have shown varied rates of category III Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS) and variable cancer risk [5–7]. The varied malignant rates make management decisions difficult. The TBSRTC recommends clinical correlation and repeated fine-needle aspiration (FNA) at an appropriate interval for nodules having an initial AUS/FLUS diagnosis [4]. Hence, a repeated effort to acquire diagnostic cytologic material is required in nodules initially diagnosed as AUS/FLUS. Numerous research studies showed that core-needle biopsy used in place of repeat FNA in such individuals results in high rates of conclusive and accurate diagnoses [8, 9]. However, the decision to use core need biopsy takes into consideration patient safety and incidence of complications which may prohibit its widespread use. Other studies have focused on suspicious ultrasound features that suggest malignancy in AUS/FLUS nodules; however, the criteria have varied widely.

Horvath et al. [10] introduced the Thyroid Imaging Reporting and Data System (TI-RADS) for facilitating the interaction between radiologists and physicians via the use of a standardised reporting format. This system evolved from the Breast Imaging Reporting and Data System (BIRADS). Numerous forms of TI-RADS have been identified since its introduction [11, 12]. Kwak et al. [12] demonstrated that the TI-RADS, which depends on the number of suspicious ultrasound characteristics of taller-than-wide shape, microcalcifications, microlobulated or irregular margins,

hypoechogenicity, or marked hypoechogenicity, and solidity is precise for stratifying risk, despite the fact that each ultrasound characteristic is assigned the same weight without regard for the probability of malignancy associated with each ultrasound characteristic, and this version of TI-RADS is extremely simple for usage. It has been well suggested that TI-RADS is an excellent tool for predicting the thyroid nodules' malignant potential and is helpful in making clinical management [13, 14]. However, only a few studies have investigated the value of TI-RADS for initial Bethesda III nodules [15, 16].

Therefore, we analyzed the feasibility of using TI-RADS in predicting malignancy for thyroid nodules having AUS/FLUS as an initial FNA diagnosis. Also, we explored the management strategies for these nodules.

2. Materials and Methods

2.1. Study Population. The present retrospective study was approved by our Institutional Review Board. Prior to enrollment in the study, each patient provided written informed consent.

From July 2015 to July 2020, our institution performed ultrasound-guided FNA on 7,385 thyroid nodules in 6,849 individuals. US-FNAs were conducted on all thyroid nodules ($N = 6{,}378$) that exhibited one or more of the suspicious US characteristics. FNAs were done on each nodule in each lobe when thyroid nodules exhibiting suspicious US characteristics were bilateral.

On cytology, a total of 1077 thyroid nodules (14.3%) were categorized as Bethesda category III (AUS/FLUS). Owing to an absence of additional investigation such as repeat FNA or surgery, 903 of these nodules were excluded. The study comprised a total of 188 thyroid nodules in 174 individuals with follow-up data. We evaluated these individuals' clinical information, ultrasound results, and pathologic data.

Our standard protocol for a Bethesda grade III cytology result included repeating FNA. Patients with repeated Bethesda category III or higher findings are encouraged to have a surgical resection. Follow-up with repeated ultrasound every six months was done for those who had a benign diagnosis (Bethesda category II) on repeating FNA. Individual cases, however, were managed differently depending on an overall clinical feature evaluation.

Surgery was performed on 179 nodules (95.2%) with or without repeat FNA for the following reasons: Bethesda category IV or higher on repeat FNA ($n = 15$), suspicious US features with nodule sizes less than 1 cm ($n = 71$), the presence of concurrent thyroid malignancy (known papillary thyroid carcinoma (PTC) in the same contralateral gland) ($n = 29$), history of neck irradiation ($n = 24$), family history of thyroid carcinoma ($n = 19$), and when nodular size is relatively large (greater than 4 cm in the longest diameter) ($n = 21$).

2.2. US Examination and TI-RADS Category. For conventional US, we utilised a MyLab90 X-vision (Esaote, Italy) machine fitted with an L523 (413 MHz) linear array transducer. The ultrasound assessments were conducted by one of eight radiologists with between five and twenty-five years of experience performing thyroid radiology.

According to the largest diameter on US, nodule size was defined. US thyroid nodules features were recorded as follows: component (cystic, solid, or mixed), margin (well-defined or ill-defined), echogenicity (hyperechoic, isoechoic, hypoechoic, or marked hypoechoic), calcifications (no calcification, microcalcification, large and dense calcification, and rim calcification), shape (taller than wide, irregular, and ovoid to round). The term "marked hypoechogenicity" referred to a level of echogenicity that is lower than that of the cervical strap muscles. Ill-defined margins were described as those that were microlobulated, spiculated, or otherwise ill-defined, such that the tumour could not be distinguished from healthy parenchyma. Hyperechoic foci with a diameter of less than 1 mm were described as microcalcification.

In TI-RADS, solid components, marked hypoechogenicity, ill-defined margins, higher-than-wide or irregular shape, and microcalcifications are considered as suspicious malignant US features (Figure 1). Nodules were categorized, using the TI-RADS system, as follows [12]: no suspicious ultrasound characteristics are categorized as category 3; one suspicious ultrasound characteristic is categorized as category 4a; two suspicious ultrasound characteristics are categorized as category 4b; three or four suspicious ultrasound characteristics are categorized as category 4c; and five suspicious ultrasound features are categorized as category 5.

2.3. US-Guided FNA and Cytological Analysis. FNA was performed manually with a 23-gauge needle under US guidance. Each lesion was aspirated at least twice without suction, and the aspirated materials were expelled onto a glass slide and immediately placed in 95% ethanol for Papanicolaou staining. The remaining material was rinsed with saline and processed for formalin-fixed paraffin-embedded cell blocks.

The cytological results were reported according to the Bethesda classification, which has been applied at our institution since 2010 [4]. Cytologic diagnoses were made as follows: (1) nondiagnostic or unsatisfactory (Bethesda category I), (2) benign (Bethesda category II), (3) AUS/FLUS (Bethesda category III), (4) follicular neoplasm or suspicious for a follicular neoplasm (Bethesda category IV), (5) suspicious for malignancy (Bethesda category V), and (6) malignant (Bethesda category VI).

2.4. Data and Statistical Analysis. As a standard reference, postsurgical histopathology or repeated FNA cytology with follow-up ultrasound results was employed. Thyroid nodules that were not surgically removed, without change or regression on follow-up ultrasound for at least one year following benign findings on repeat US-FNA cytology, were eventually categorized as benign.

On the basis of the following parameters, the comparison between the benign and malignant groups was done: clinical characteristics (age, gender, and concomitant thyroid

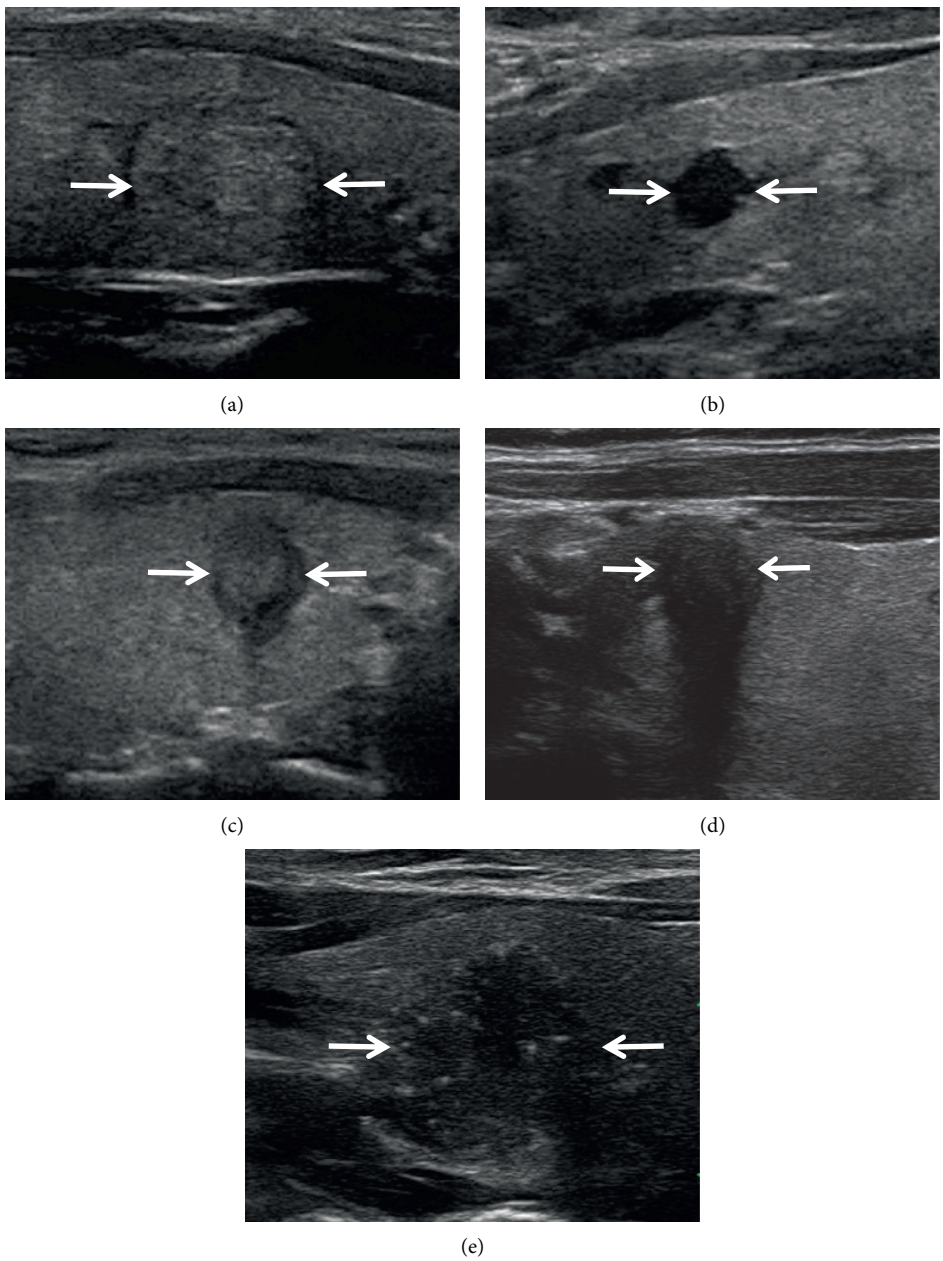

Figure 1: Thyroid Imaging Reporting and Data System: (a) category 3, no suspicious ultrasound characteristics; (b) category 4a, one suspicious ultrasound characteristic (marked hypoechogenicity); (c) category 4b, two suspicious ultrasound characteristics (ill-defined margins and higher-than-wide); (d) category 4c, four suspicious ultrasound characteristics (solid components, marked hypoechogenicity, ill-defined margins, and higher-than-wide); (e) category 5, five suspicious ultrasound characteristics.

cancer) and ultrasound features (lesion size, margin, calcification, echogenicity, composition, form, and TI-RADS evaluation). Continuous variables were represented as mean ± standard deviations, while categorical variables were represented as counts and percentages. The independent two-sample *t*-test and chi-square test were used to compare continuous and categorical variables. The area under the curve (AUC) was determined for the diagnostic performance of the TI-RADS assessment.

Using statistical software programs (SPSS statistical software, version 16.0), statistical analyses were carried out. At <0.05, differences were considered statistically significant.

3. Results

3.1. Patient Statistics. The present study included 174 patients, and 139 (79.9%) of them were females, with 46.9 (range: 23–73) years as mean age. On ultrasonography, the thyroid nodules' mean size was 10.4 mm (range: 5–55 mm), with 126 (67%) measuring less than 10 mm. Among benign and malignant nodules, gender and age did not differ significantly ($P = 0.91$; 0.83). The size of malignant nodules was significantly smaller than the size of benign nodules ($P < 0.001$). Thyroid nodules associated with concomitant thyroid carcinoma had a significantly increased malignancy

risk ($P < 0.05$). Table 1 summarises the patients' characteristics.

4. Pathologic Results

As regards the 188 thyroid nodules categorized as Bethesda category III on initial FNA (Figure 2), 106 (56.3%) were malignant, and 82 (43.7%) were benign. Twenty-four (12.8%) nodules underwent repeat FNA. Nine (37.5%) were benign (Bethesda category II), four (16.7%) were suspected to be malignant (Bethesda category V), and five (20.8%) were malignant (Bethesda category VI). Repeat FNA revealed a second Bethesda category III result in six cases (25%). All nine nodules with benign cytology on repeat FNA had more than a year of follow-up ultrasound assessment. Thyroid nodules having a Bethesda category more than III or with a second Bethesda category III result on repeating FNA were surgically resected. A total of 179 nodules (95.2%) were surgically confirmed, either with or without repeating FNA. Of these nodules, 106 were diagnosed as malignant (59.2%), with 102 cases of classic PTC (including 71 papillary thyroid microcarcinoma (PTMC) and 3 follicular variant PTC cases, in addition to one PTC case of Hürthle cell variant). Seventy-three nodules were diagnosed as benign (13 adenomatous nodules, 12 Hashimoto thyroiditis, 2 subacute thyroiditis, and 46 colloid nodules) (Table 2).

4.1. Diagnostic Value of TI-RADS Category. Table 3 details the cancer risk associated with each ultrasound feature. Solid composition, ill-defined margins, microcalcifications presence, marked hypoechogenicity, and higher-than-wide or irregular shape showed a high malignancy risk ($P < 0.05$). The TI-RADS US classification revealed a statistically significant difference in malignancy risk ($P < 0.001$). The AUC was 0.71 (95% confidence interval (CI) 0.64–0.79; Figure 3) at a cutoff value of category 4c. As regards malignancy evaluation, the sensitivity and specificity were 100% and 15.9%, respectively, in cases of category 4b, 90.6% and 46.3%, respectively, in cases of category 4c, and 10.3% and 98.8%, respectively, in cases of category 5. Categories 4c (OR = 8.3; 95% CI 3.8–18.1; $P < 0.001$) and 5 (OR = 9.4; 95% CI 1.2–74.2; $P = 0.011$), respectively, were predictive for malignancy (Table 4).

5. Discussion

US and FNA are the mainstays of clinical assessment of thyroid nodules. As regards thyroid nodules that had Bethesda III cytology as their initial diagnosis, the total malignancy risk was relatively high (58.8%), which exceeded the recommended 5–15% risk range by the Bethesda system [4]. However, because surgical criteria and treatment options for thyroid nodules vary significantly between institutions and surgeons, the malignant rate varies greatly among studies, ranging from 5% to 55.5% [17, 18]. US-FNAs were conducted at our institution on nodules that exhibited one or more of the suspicious US features, which created a bias. Moreover, the present study only comprised 17.4% (188/1077) of nodules whose initial diagnosis was AUS/FLUS and underwent further evaluation, and this led to difficulty in evaluating the accurate malignant risk.

Table 1: Clinical characteristics in 174 patients with initial Bethesda system III cytology.

Clinical features	Benign ($n = 78$)	Malignant ($n = 96$)	P value
Age, years	49.6 ± 10.95	44.78 ± 10.3	0.829
Gender (F/M)	62/16	77/19	0.906
Nodule size, mm	1.39 ± 1.06	0.77 ± 0.48	0.001
Concurrent cancer, n (%)	7 (9.0)	22 (22.9)	0.014

F, female; M, male.

Similar to most studies [15, 19, 20], sex or age was not a predictor of carcinoma in cases with AUS/FLUS cytology. In contrast, we found that nodule size or concurrent thyroid cancer in these nodules significantly increased the malignancy risk. In addition, for overcoming the diagnostic limitations of cytology in Bethesda III nodules, several studies evaluated the ultrasound value in malignancy prediction for these nodules to make proper management strategy [18, 19]. According to Rosario, the US is helpful for identifying malignancy in category nodules, with 79.4% sensitivity, 90.5% specificity, positive predictive values of 71%, and negative predictive values of 93.75% [21]. Several other studies also reported that suspicious US features were important malignancy predictive factors in category III nodules [6, 18]. Our results showed that solid components, taller-than-wide or irregular shape, marked hypoechogenicity, ill-defined margins, and microcalcifications had a significant association with malignancy. Therefore, these risk factors, such as nodule size, concurrent thyroid cancers, and suspicious US features, may help to identify those who have a higher malignant rate.

Horvath et al. [10] established the TI-RADS application for thyroid nodule assessment based on ultrasound characteristics. The systems by Horvath et al. and Park et al. were both complicated and difficult to implement in the clinical setting [10, 11]. Kwak's version [12], which we utilised in this study, is straightforward, practical, and accurate, and it does an excellent job of stratifying malignancy risk. In the current study, the risk of malignancy associated with nodules with TI-RADS category 4a was 0%, 4b was 28.6%, 4c was 66.4%, and 5 was 91.7%. The odds ratios of malignancy in nodules with three or more suspicious US findings were 8.3 (95% CI 3.8–18.1) and 9.4 (95% CI 1.2–74.2). Thus, US follow-ups are considered appropriate for nodules with one suspicious US finding. Repeat FNA or surgery should be recommended for category 4b, 4c, and 5 nodules. However, 43 category 4c nodules have benign results in the current study. Among them, 10 were Hashimoto thyroiditis, and 1 was subacute thyroiditis. Several previous studies have reported that the sonographic features of focal Hashimoto's thyroiditis (FHT) is extremely variable, making it difficult to distinguish FHTs from other thyroid nodules, particularly malignancies [22–24]. In this study, the majority of FHT

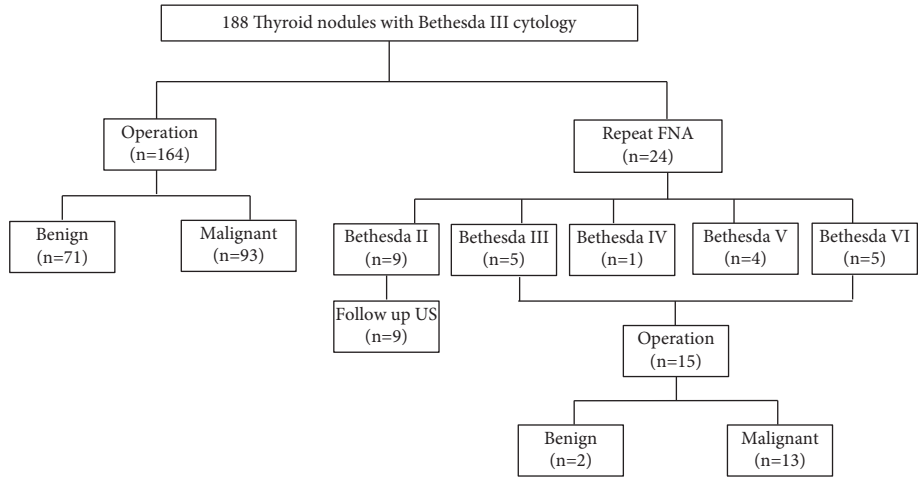

Figure 2: Flowchart. FNA, fine-needle aspiration.

Table 2: Pathological findings.

Pathological findings	No. of nodules
Malignant	106
Papillary carcinoma, classical (PTMC)	102 (71)
Papillary carcinoma, follicular variant	3
Papillary carcinoma, Hürthle cell variant	1
Benign	82
Colloid nodules	46
Adenomatous nodules	13
Hashimoto thyroiditis	12
Subacute thyroiditis	2
Bethesda category II cytology on repeat FNA with US follow-up	9

PTMC, papillary thyroid microcarcinoma; No., number; FNA, fine-needle aspiration.

Table 3: Ultrasonographic characteristics and rates of malignancy of the 188 nodules with initial Bethesda system III cytology.

US features	Total ($n = 188$)	Benign ($n = 82$)	Malignant ($n = 106$)	Chi-square value	P value
Composition*				4.81	0.028
Solid	180	75	105		
Mixed	8	7	1		
Echogenicity				86.97	<0.001
Hypoechoic	95	71	24		
Isoechoic	2	2	0		
Hyperechoic	4	3	1		
Marked hypoechoic	87	6	81		
Margin				8.74	0.003
Ill-defined	68	20	48		
Well-defined	120	62	58		
Calcifications				9.35	0.009
Microcalcification	51	14	37		
Macrocalcification	43	18	25		
Absent	93	50	43		
Shape				25.43	<0.001
Taller than wide	56	15	41		
Irregular	31	6	25		
Ovoid to round	101	61	40		
TI-RADS#				21.69	<0.001
Category 4b	35	25	10		
Category 4c	128	43	85		
Category 5	12	1	11		

*No cyst nodules on Bethesda system III cytology. #Each of the 13 nodules classified as TI-RADS category 4a was benign. US, ultrasound; TI-RADS, Thyroid Imaging Reporting and Data System.

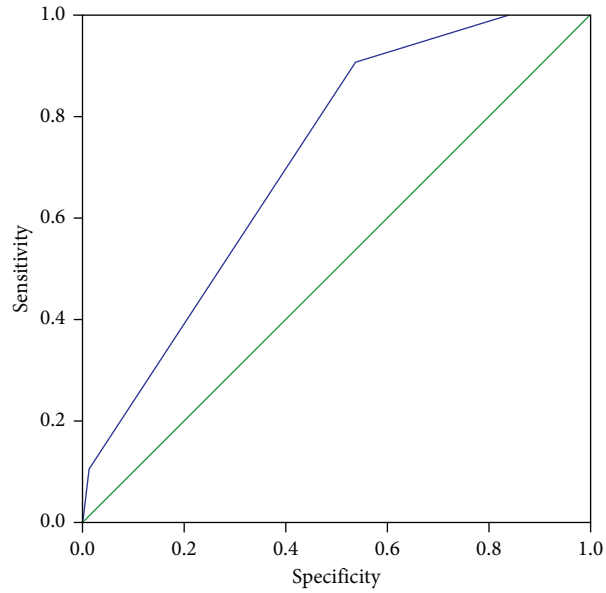

Figure 3: Receiver operating characteristic curve of TI-RADS for Bethesda III nodules.

Table 4: Diagnostic values of TI-RADS for the 188 nodules with initial Bethesda system III cytology.

TI-RADS assessment	Total	Benign	Malignant	Sensitivity (%)	Specificity (%)	Accuracy (%)	OR (95% CI)
Category 4a	13	13	0				
Category 4b	35	25	10	100	15.9	62.8	
Category 4c	128	43	85	90.6	46.3	69.7	8.3 (3.8–18.1)
Category 5	12	1	11	10.3	98.8	48.9	9.4 (1.2–74.2)
Total	188	82	106				

OR, odds ratios; CI, confidence interval; TI-RADS, Thyroid Imaging Reporting and Data System.

nodules (83.3%) were classified as TI-RADS category 4c, which was suspicious for malignancy. Therefore, repeated FNA should be recommended for category 4c nodules with a background of HT to spare patients from unnecessary surgery.

Of the 10 false-negative US final assessments with borderline category 4c classification, one nodule was diagnosed as a Hürthle cell variant of PTC, and the other 9 were confirmed as PTMC. Our previous study showed that nodule size impacted the predictive values of suspicious US features and microcalcifications were less frequent in small malignant nodules (5–10 mm) than in large malignant nodules (>10 mm) [25]. Wang et al. reported, in their study of 113 consecutive PTMC nodules with histopathologic correlation, that half had a well-defined capsule, which correlated with well-defined margins seen on US [26].

Several limitations existed in our study. First, there is a possibility of selection bias since we eliminated 83.8% (903/1077) of patients initially classified as Bethesda category III owing to the absence of additional examination. Furthermore, nine thyroid nodules were not surgically excised. On repeat FNA, these nodules were identified as benign and did not alter in size or shape during follow-up US examination. But, in these nine nodules, the follicular neoplasm possibility cannot be excluded because most follicular neoplasms have a relatively benign US appearance [27].

6. Conclusions

In initial Bethesda III nodules, a TI-RADS US evaluation may assist the physician in deciding between follow-up and repeat FNA or surgery. When thyroid nodules were classified as category 4c on a background of HT, repeat FNA should be recommended to spare patients from unnecessary surgery. US follow-ups are considered appropriate for nodules with one suspicious US finding. Repeat FNA or surgery should be recommended for category 4b, 4c, and 5 nodules.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

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References

[1] D. Danese, S. Sciacchitano, A. Farsetti, M. Andreoli, and A. Pontecorvi, "Diagnostic accuracy of conventional versus sonography-guided fine-needle aspiration biopsy of thyroid nodules," *Thyroid*, vol. 8, no. 1, pp. 15–21, Article ID 9492148, 1998.

[2] M. E. O'Malley, M. M. Weir, P. F. Hahn, J. Misdraji, B. J. Wood, and P. R. Mueller, "US-guided fine-needle aspiration biopsy of thyroid nodules: adequacy of cytologic material and procedure time with and without immediate cytologic analysis," *Radiology*, vol. 222, no. 2, pp. 383–387, Article ID 11818603, 2002.

[3] B. R. Haugen, E. K. Alexander, and K. C. Bible, "2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer," *Thyroid*, vol. 26, no. 1, pp. 1–133, Article ID 26462967, 2016.

[4] E. S. Cibas and S. Z. Ali, "The Bethesda System for reporting thyroid cytopathology," *American Journal of Clinical Pathology*, vol. 132, no. 5, pp. 658–665, Article ID 19846805, 2009.

[5] V. Y. Jo, E. B. Stelow, S. M. Dustin, and K. Z. Hanley, "Malignancy risk for fine-needle aspiration of thyroid lesions according to the Bethesda System for Reporting Thyroid Cytopathology," *American Journal of Clinical Pathology*, vol. 134, no. 3, pp. 450–456, Article ID 20716802, 2010.

[6] D. W. Kim, E. J. Lee, S. J. Jung et al., "Role of sonographic diagnosis in managing Bethesda class III nodules," *AJNR Am J Neuroradiol*, vol. 32, no. 11, pp. 2136–2141, Article ID 21920860, 2011.

[7] M. Rossi, S. Lupo, R. Rossi et al., "Proposal for a novel management of indeterminate thyroid nodules on the basis of cytopathological subclasses," *Endocrine*, vol. 57, no. 1, pp. 98–107, Article ID 27623969, 2017.

[8] K. T. Park, S. H. Ahn, J. H. Mo et al., "Role of core needle biopsy and ultrasonographic finding in management of indeterminate thyroid nodules," *Head & Neck*, vol. 33, no. 2, pp. 160–165, Article ID 20848434, 2011.

[9] D. G. Na, J. H. Kim, J. Y. Sung et al., "Core-needle biopsy is more useful than repeat fine-needle aspiration in thyroid nodules read as nondiagnostic or atypia of undetermined significance by the Bethesda system for reporting thyroid cytopathology," *Thyroid*, vol. 22, no. 5, pp. 468–475, Article ID 22304417, 2011.

[10] E. Horvath, S. Majlis, R. Rossi et al., "An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management," *The Journal of Cinical Endocrinology and Metabolism*, vol. 94, no. 5, pp. 1748–1751, Article ID 19276237, 2009.

[11] J. Y. Park, H. J. Lee, H. W. Jang et al., "A proposal for a thyroid imaging reporting and data system for ultrasound features of thyroid carcinoma," *Thyroid*, vol. 19, no. 11, pp. 1257–1264, Article ID 19754280, 2009.

[12] J. Y. Kwak, K. H. Han, and J. H. Yoon, "Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk," *Radiology*, vol. 260, no. 3, pp. 892–899, Article ID 21771959, 2011.

[13] H. J. Moon, E. K. Kim, and J. Y. Kwak, "Malignancy risk stratification in thyroid nodules with benign results on cytology: combination of thyroid imaging reporting and data system and Bethesda system," *Annals of Surgical Oncology*, vol. 21, no. 6, pp. 1898–1903, Article ID 24558069, 2014.

[14] J. H. Yoon, H. S. Lee, E. K. Kim, H. J. Moon, and J. Y. Kwak, "Thyroid nodules: nondiagnostic cytologic results according to thyroid imaging reporting and data system before and after application of the Bethesda system," *Radiology*, vol. 276, no. 2, pp. 579–587, Article ID 25848904, 2015.

[15] V. Y. Park, E. K. Kim, J. Y. Kwak, J. H. Yoon, and H. J. Moon, "Malignancy risk and characteristics of thyroid nodules with two consecutive results of atypia of undetermined significance or follicular lesion of undetermined significance on cytology," *European Radiology*, vol. 25, no. 9, pp. 2601–2607, Article ID 25740802, 2015.

[16] J. H. Yoon, H. J. Kwon, E. K. Kim, H. J. Moon, and J. Y. Kwak, "Subcategorization of atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS): a study applying Thyroid Imaging Reporting and Data System (TIRADS)," *Clinical Endocrinology*, vol. 85, no. 2, pp. 275–282, Article ID 26639612, 2016.

[17] L. Estrada Muñoz, C. Díaz Del Arco, L. Ortega Medina, and M. J. Fernández Aceñero, "Thyroid atypia/follicular lesion of undetermined significance: attitudes towards the diagnosis of Bethesda system III nodules," *Acta Cytologica*, vol. 61, no. 1, pp. 21–26, Article ID 27852075, 2017.

[18] H. M. Gweon, E. J. Son, J. H. Youk, and J.-A. Kim, "Thyroid nodules with Bethesda system III cytology: can ultrasonography guide the next step?" *Annals of Surgical Oncology*, vol. 20, no. 9, pp. 3083–3088, Article ID 23700214, 2013.

[19] W. S. Yoo, H. S. Choi, and S. W. Cho, "The role of ultrasound findings in the management of thyroid nodules with atypia or follicular lesions of undetermined significance," *Clinical Endocrinology*, vol. 80, no. 5, pp. 735–742, Article ID 24117478, 2014.

[20] R. Carr, B. Ustun, and D. Chhieng, "Radiologic and clinical predictors of malignancy in the follicular lesion of undetermined significance of the thyroid," *Endocrine Pathology*, vol. 24, no. 2, pp. 62–68, Article ID 23595630, 2013.

[21] P. W. Rosario, "Thyroid nodules with atypia or follicular lesions of undetermined significance (Bethesda Category III): importance of ultrasonography and cytological subcategory," *Thyroid*, vol. 24, no. 7, pp. 1115–1120, Article ID 24684285, 2014.

[22] X. Fu, L. Guo, and H. Zhang, "x201C;Focal thyroid infernox201D; on color Doppler ultrasonography: a specific feature of focal Hashimoto's thyroiditis," *European Journal of Radiology*, vol. 81, no. 11, pp. 3319–3325, Article ID 22608398, 2012.

[23] W. J. Moon, S. L. Jung, and J. H. Lee, "Benign and malignant thyroid nodules: US differentiation--multicenter retrospective study," *Radiology*, vol. 247, no. 3, pp. 762–770, Article ID 18403624, 2008.

[24] J. D. Iannuccilli, J. J. Cronan, and J. M. Monchik, "Risk for malignancy of thyroid nodules as assessed by sonographic criteria: the need for biopsy," *Journal of Ultrasound in Medicine*, vol. 23, no. 11, pp. 1455–1464, Article ID 15498910, 2004.

[25] Y. R. Hong, Y. L. Wu, Z. Y. Luo, N. B. Wu, and X.-M. Liu, "Impact of nodular size on the predictive values of gray-scale, color-Doppler ultrasound, and sonoelastography for assessment of thyroid nodules," *Journal of Zhejiang University - Science B*, vol. 13, no. 9, pp. 707–716, Article ID 22949361, 2012.

[26] Y. Wang, L. Li, and Y. X. Wang, "Ultrasound findings of papillary thyroid microcarcinoma: a review of 113 consecutive cases with histopathologic correlation," *Ultrasound in Medicine and Biology*, vol. 38, no. 10, pp. 1681–1688, Article ID 22920548, 2012.

[27] S. J. Rhee, S. Y. Hahn, E. S. Ko, J. W. Ryu, E. Y. Ko, and J. H. Shin, "Follicular variant of papillary thyroid carcinoma: distinct biologic behavior based on ultrasonographic features," *Thyroid*, vol. 24, no. 4, pp. 683–688, Article ID 24341498, 2014.