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ORIGINAL ARTICLE

Incidence of noninvasive follicular thyroid neoplasm with papillary-like nuclear features and change in risk of malignancy for "The Bethesda System for Reporting Thyroid Cytology"

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Introduction The second edition of *The Bethesda System for Reporting Thyroid Cytopathology* has incorporated the recent change in nomenclature, noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), with an anticipated change in the risk of malignancy (ROM). We examined our institutional experience in the incidence of NIFTP and the change in the ROM in *The Bethesda System for Reporting Thyroid Cytopathology*.
Materials and methods A computerized search was performed from January 2013 to August 2017 for all thyroid fine needle aspirations (FNAs), the corresponding surgical resection specimens, and clinical follow-up data. All thyroid specimens reported as follicular variant of papillary thyroid carcinoma were reviewed and reclassified, and all NIFTP diagnoses from April 2016 to August 2017 were identified. The ROM for each category was calculated before and after the change and analyzed for significance.
Results A total of 4500 thyroid FNA cases were collected. Of these, 479 cases had surgical resection specimens available and 36 cases had been diagnosed as NIFTP. Of these, 22 had been previously diagnosed as FVPT. Of 27 cases of NIFTP, 14 and 13 were atypia of undetermined significance/follicular lesion of

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undetermined significance and follicular neoplasm/suspicious for follicular neoplasm, respectively. A reduction in the ROM was observed in these 2 categories ($P = 0.03$ and $P = 0.04$, respectively).

Conclusions In our institution, NIFTP has accounted for 13% of all malignant thyroid neoplasms since the change in nomenclature. Although the ROM was decreased in the affected categories, with absolute statistically significant decreases in ROM of 15% and 16.2% for category III and IV, respectively, the overall ROM change was marginal.

Introduction

The introduction of *The Bethesda System for Reporting Thyroid Cytopathology* (TBSRTC) almost 1 decade ago had a significant effect on the management of thyroid nodules.[1] It has established a standard reporting terminology for o fine needle aspiration (FNA) for thyroid nodules into 6 distinct categories: nondiagnostic (ND), benign (B), atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm/suspicious for follicular neoplasm (FN/SFN), suspicious for malignancy (SM), and malignancy (M). Each reporting category has defined and reproducible diagnostic criteria, with a suggested risk of malignancy (ROM) associated with each category to guide patient treatment.[2,3] This unified reporting format has made TBSRTC popular and widely accepted by clinicians and pathologists, making it one of the most commonly used reporting system for thyroid FNA. The end result has been an overall reduction in unnecessary thyroid resections.[4-7]

The introduction of a new diagnostic entity, noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), has modified the traditional understanding of thyroid neoplasms.[8] Papillary thyroid carcinoma (PTC), the most common carcinoma of the thyroid, has been defined by its distinct nuclear features. All variants of PTC have previously been classified as a malignant tumor that will require total thyroidectomy in most cases. However, the nomenclature change has recategorized a subset of these tumors with PTC nuclear features (ie, NIFTP) as a potentially indolent neoplasm with biologic behavior similar to that of follicular adenoma. Many PTCs previously categorized as a follicular variant (FVPTC) could possibly be reclassified as NIFTP.

The effect of reclassification of a malignant lesion to an indolent one would change the ROM in TBSRTC.[9-11] The second edition of TBSRTC has proposed changes in the implied ROM for the indeterminate categories, with a ROM of 6%-18% for AUS/FLUS, 10%-40% for FN/SFN, and 45%-60% for SM.[12] Various institutions have performed retrospective analyses and recalculations of the ROM. In these studies, most NIFTP lesions found on FNA were classified as AUS/FLUS, FN/SFN, and SM. The reported frequency of NIFTP has been highly variable, ranging from 1.3% to 33% of malignant neoplasms.[9,11,13-15] The reported decrease in ROM has also ranged widely, from 8% to 48%, in the affected categories.[9,11,14-16] The difference in the frequency of NIFTP and change in ROM has likely resulted from institutional population variability, the poor interobserver reproducibility classifying NIFTP, and the TBSRTC indeterminate categories. Most previous studies analyzed retrospective reviews of thyroid resections before the nomenclature change. The diagnostic criteria for NIFTP have also been revised to exclude any papillary structures, require examination of sufficient sections, and exclude BRAF mutations.[17] In the present study, we aimed to determine the incidence of NIFTP and the change in ROM in TBSRTC categories using combined data from before and after the nomenclature revision in our single-institution experience.

Materials and methods

We performed a retrospective search of all thyroid resection and thyroid FNA specimens from January 2013 to August 2017. All FNA samples were categorized according to TBSRTC as ND, B, AUS/FLUS, FN/SFN, SM, or M. Relevant patient history and clinical data were collected, and all follow-up thyroid surgical pathologic diagnoses were matched to the corresponding nodule sampled by FNA. Our institution routinely performs Diff-Quik and Papanicolaou stains for cytology smears with additional material collected for ThinPrep with rapid on-site assessment. We also receive air-dried smear slides and/or FNA passes collected in Cytolyt solution from several outpatient clinics. All thyroid FNA samples were matched to the surgical pathology resection specimens by reviewing the size and location on ultrasound imaging and thyroidectomy samples. Cytologic−histologic correlation was performed to ensure the FNA specimen represented the diagnostic nodule on the surgical resection. All noncorresponding nodules, including incidental papillary thyroid microcarcinoma (<1 cm), were excluded from our cohort.

All thyroid surgical pathology diagnoses of FVPTC before the NIFTP revision (from January 2013 to March 2016) were reviewed by 2 pathologists with anatomic pathology and cytopathology board certifications. These diagnoses of FVPTC were recategorized to NIFTP if they met the original strict criteria for NIFTP reported by Nikiforov et al[8] and the revised current recommendations.[17] Tumors with the following were not considered NIFTP: capsular invasion or infiltration; vascular invasion; any papillary architecture; extrathyroidal extension; overt nuclear features of PTC; solid/trabecular or insular growth >30%; all cell, columnar, or cribriform morular morphology; necrosis; mitosis >3 per 10 consecutive high power fields; or metastasis. For thyroid resection specimens after the implementation of the NIFTP diagnosis at our institution (April 2016 to August 2017), all surgical pathology diagnoses were reviewed for a diagnosis of NIFTP and the corresponding thyroid FNA cases were studied.

The ROM for each TBSRTC category was calculated by dividing the total number of FNA specimens that proved to be malignant on resection by the total number of surgical resections in each category. We also studied the overall ROM (OROM), which was calculated by dividing the total number of FNA samples that proved to be malignant on follow-up by the total number of FNA samples in each category. The ROM and OROM were calculated before and after the NIFTP reclassification. In addition, the decrease in the ROM and OROM were calculated and analyzed for statistical significance using the Z test.

The institutional review board approved the present retrospective study, which was conducted in accordance with the institutional review board guidelines.

Results

A total of 4500 thyroid FNA samples were identified from 3352 patients. Of the 3352 patients, 2932 were female (87%) and 421 were male (13%). Their age ranged from 8 to 94 years (average age, 55 years; median age, 57 years). The overall rate of TBSRTC diagnostic categories were as follows: ND, 9.4%; benign, 72.2%; AUS/FLUS, 9.7%; FN/SFN, 4.0%; SM, 1.2%; and M, 3.4%. A total of 2612 thyroid resection cases were identified for the same search period, and the corresponding follow-up surgical pathology results were available for 479 FNA samples (Table 1). The interval from FNA to surgery ranged from 2 weeks to 18 months. Of the 479 FNA samples, the follow-up surgical resection diagnosis was a benign thyroid lesion for 269, a malignant lesion for 174, and NIFTP for 36. The most common malignant neoplasm was PTC (154; 89%). Of these, 24 (16%) were FVPTC, including 9 with a predominant follicular pattern with some papillae, 6 encapsulated with invasion, 8 nonencapsulated/infiltrative, and 1 encapsulated, noninvasive with psammoma bodies. Of the benign lesions, 72 (27%) were follicular adenomas (Table 2).

Before the change in nomenclature, 42 thyroid resection specimens with previous FNA workup had been diagnosed as FVPTC. The slide review and application of the strict criteria for an NIFTP diagnosis, 22 FVPTC cases (52%) were reclassified as NIFTP. The proportion of FVPTC cases (excluding those reclassified as NIFTP) of all PTC cases with a previous FNA evaluation was 22% (20 FVPTC of 89 PTC cases).

Since the introduction of the NIFTP terminology, 14 cases of NIFTP had been diagnosed and had corresponding FNA results. After the nomenclature change, of all thyroid resection specimens, a total of 13 FVPTC cases had been diagnosed and had previous FNA results available. The proportion of FVPTC cases among all PTC cases with previous FNA data available was 17% (11 FVPTC of 63 PTC cases).

A total of 36 NIFTP cases with corresponding FNA data available were identified for the present study. All 36 NIFTP cases had had the entire capsule submitted for evaluation, and the 22 NIFTP nodules had been submitted in their entirety. Before the nomenclature change, the rate of NIFTP

Table 1 Risk classification for thyroid lesions and change in ROM.

Sample	Nondiagnostic	Benign	AUS/FLUS	FN/SFN	Suspicious	Malignant	Total
Total FNA (n; %)	426 (9.4)	3249 (72.1)	435 (9.7)	182 (4.2)	54 (1.2)	154 (3.4)	4500 (100)
FNA with follow-up (n)	38	151	93	86	25	86	479
Benign	31	133	57	47	1	0	269
Malignant	7	14	22	26	22	83	174
NIFTP	0	4	14	13	2	3	36
ROM (%)	18.4	11.9	38.7	45.3	96	100	
ROM/NIFTP (%)	18.4	9.9	23.7	30.2	88	96.5	
OROM (%)	1.6	0.55	8.2	21.4	44.4	55.8	
OROM/NIFTP (%)	1.6	0.43	5.1	14.3	40.7	54	
Absolute decrease in ROM (%)	0 (P = 1.00)	2 (P = 0.5)	15 (P = 0.03)	15.1 (P = 0.04)	8 (P = 0.3)	3.5 (P = 0.08)	
Relative decrease in ROM (%)	0	16.8	38.8	34.0	8.3	4.1	
Absolute decrease in OROM (%)	0 (P = 1.00)	0.12 (P = 0.5)	3.1 (P = 0.06)	7.1 (P = 0.08)	3.7 (P = 0.8)	1.8 (P = 0.8)	
Relative decrease in ROM (%)	0	21	37.8	33.2	8.3	3.2	

Abbreviations: ROM, risk of malignancy; AUS/FLUS, atypia of undetermined significance/follicular lesion of undetermined significance; FN/SFN, follicular neoplasm/suspicious for follicular neoplasm; FNA, fine needle aspiration; NIFTP, OROM, overall risk of malignancy.

Table 2 Thyroid lesion diagnosis and subtype proportion.

Diagnosis	Specimens (n)
Resection total	479
PTC	154
% of all thyroid neoplasms	55
% of all malignant thyroid neoplasms	89
FVPTC	24 (16% of PTC)
Encapsulated, noninvasive	1 (1 case with psammoma bodies)
Encapsulated, invasive	6
Nonencapsulated/Infiltrative	8
Predominant follicular architecture	9
NIFTP	36 (13% of all thyroid neoplasms)
Follicular/Hurthle cell carcinoma	11 (4)
Medullary carcinoma	6 (12)
Poorly differentiated carcinoma	1 (0.4)
Anaplastic carcinoma	0 (0)
Metastatic carcinoma	2 (0.7)
Follicular adenoma	72 (26)
Benign (other)	197

Abbreviations: FVPTC, follicular variant of papillary thyroid carcinoma; NIFTP, noninvasive follicular thyroid neoplasm with papillary-like nuclear features; PTC, papillary thyroid carcinoma.

diagnoses among the PTC cases with previous FNA data available was 25% (22 NIFTP of 89 PTC cases). After the nomenclature change, the rate was 22% (14 NIFTP of 3 PTC cases). An initial total thyroidectomy and hemithyroidectomy had been performed in 27 and 11 patients, respectively. Before the nomenclature change, 6 patients had undergone hemithyroidectomy. Of these 6 patients, 3 had undergone completion thyroidectomy, 2 had been scheduled for completion thyroidectomy but had been lost to follow-up, and 1 was monitored clinically. After the nomenclature change, 7 patients had undergone hemithyroidectomy, none of whom had received completion thyroidectomy.

The 38 patients with an NIFTP diagnosis ranged in age from 21 to 73 years (average, 49 years; median, 47 years), and 32 were female and 6 were male. The size of the nodules ranged from 0.6 to 5.0 cm, and most patients had presented with a single nodule. The commonly described radiologic features were of a solid, well-circumscribed hypoechoic nodule with hypervascularity. The gross appearance of the nodules was firm, tan, and well-circumscribed. Of the 38 NIFTP cases, 24 had presented as a single nodule or single nodule with benign cystic lesions. Multinodular goiter was the most common background thyroid change. Three cases had presented with $\geq$2 NIFTPs, all on the ipsilateral thyroid. The most common neoplastic lesion associated with NIFTP was papillary thyroid microcarcinoma (mPTC) on the ipsilateral or contralateral thyroid. Five NIFTP cases had mPTC, some with $\leq$5 mPTCs. One case had follicular carcinoma and classic PTC found on the contralateral thyroid. Two cases had an invasive follicular variant of PTC on the ipsilateral thyroid. A total of 11 NIFTP cases had undergone a molecular analysis; 6 cases had a *RAS* mutation and 5 cases had no known mutations.

The ROM and OROM were calculated for each TBSRTC category. A decrease in ROM and OROM was noted for most categories, except for the ND category. Most NIFTPs were interpreted on the FNA samples as AUS/FLUS or FN/SFN. The rate of NIFTP in these indeterminate categories was 15% each. The ROM decreased from 38.7% to 23.7% for those with AUS/FLUS and from 45.3% to 30.2% for those with FN/SFN. The corresponding absolute decreases in the ROM were 15% and 15.1%, and the differences were statistically significant ($P = 0.03$ and $P = 0.04$, respectively). The relative decreases in the ROM were 38.8% and 34.0% for the AUS/FLUS and FN/SFN categories, respectively. The reduction in the OROM was not significant for these 2 categories. Smaller changes in the ROM and OROM were observed in the B, SM, and M categories (Table 1). For the remaining categories of ND, B, S, and M, the decrease in the ROM and OROM were 0%, 2%, 8%, and 3.5% and 0%, 0.12%, 3.7%, and 1.8%, respectively.

Discussion

Reclassification of NIFTP as an indolent entity has been expected to have a significant effect on the ROM in the TBSRTC. Many studies have reported on the change in the ROM in TBSRTC even before the introduction of the terminology. Most reported data have noted a change in the indeterminate categories; however, the findings and the significance of the change have varied widely among the studies. The reported decrease in the ROM has ranged from 5.2% to 61% for AUS/FLUS, 3.1% to 20.6% for FN/SFN, and 0% to 41.5% for SM.[9-11,13-16,18-20] The most dramatic differences were noted in the AUS/FLUS and SM categories. Our study, and the study by Ohori et al,[19] did not find a significant decrease in the SM category, because not many NIFTPs were found in the SM category. In our experience, most of the cases diagnosed as SM by FNA were found to be PTC on surgical resection. Also, a recent study by Li et al[16] reported only small decrease in the proportion of ROM in the affected categories. Our findings and those from previous studies have been summarized in Table 3. Although a recent meta-analysis by Layfield et al[21] found that the recategorization reduced the ROM in most categories, our results showed that the significant reductions were in the AUS/FLUS and FN/SFN categories.

We have reported on 2 measures of the malignancy rate: ROM and OROM. The surgical follow-up rate was 47% for the FN/SFN diagnosis and 21% for the AUS/FLUS diagnosis. The data from patients who had undergone surgery at outside institutions were not available for evaluation. The true ROM for these 2 indeterminate categories is probably somewhere between the ROM and OROM (5.1%-23.7% for

Table 3 Percentage of decrease in the ROM in TBSRTC: review of reported data.

Study	ND	Benign	AUS/FLUS	FN/SFN	SM	M
Present study	0	3.3	15	16.2	8	3.5
Li et al,[16] 2018	0	1.2	3.3	5.9	2.3	0.6
Layfield et al,[21] 2017	0	3.6	2.3	2.5	17.0	12.8
Zhou et al,[15] 2018	0	1.1	9.2	7.1	11.5	7.8
Faquin et al,[11] 2016	1.4	3.5	13.6	15.1	23.4	3.3
Canberk et al,[20] 2016	6.5	1.0	15	20	24	11
Strickland et al,[9] 2015	1.9	7.8	17.6	8.0	41.5	5.1

Abbreviations: AUS/FLUS, atypia of undetermined significance/follicular lesion of undetermined significance; FN/SFN, follicular neoplasm/suspicious for follicular neoplasm; M, malignancy; ND, nondiagnostic; SM, suspicious for malignancy.

AUS/FLUS and 13.7%-29.1% for FN/SFN). The original suggested ROM in the TBSRTC was ∼4%, 0% to 3%, 5% to 15%, 15% to 30%, 60% to 75%, and 97% to 99% for ND, B, AUS/FLUS, FN/SFN, SM, and M.[22] Our study found that the change in ROM for FN/SFN is within the currently recommended ROM. Also, the true ROM for the AUS/FLUS category in our study would most likely be within the 5% to 15% range.

The multi-institutional studies by Zhou et al[15] and Faquin et al[11] noted a wide variability in the rate of NIFTP diagnoses and differences in the distribution of NIFTP in the TBSRTC categories. This has been attributed to institutional differences in diagnostic thresholds, patient treatment, patient demographic data, and many other factors that could influence the ultimate diagnosis. Perhaps the most important factor is the NIFTP diagnosis rate, which has also varied widely in the reported data. Our rate of NIFTP diagnosis since the introduction of the new terminology was ∼13% of all PTC cases. The reported range of an NIFTP diagnosis among PTC cases has been 3%-27.5%.[9,10,15,16,20] Although the NIFTP diagnosis criteria have been strictly defined, recognizing such lesions can be challenging and likely have poor interobserver variability. The true incidence of NIFTP is not yet known; however, it would be prudent to perform future studies for validation of the true ROM in TBSRTC.

As more studies report on the incidence of NIFTP and the corresponding FNA diagnosis, the ROM for TBSRTC will be able to be fine-tuned to reflect the true predictive value of TBSRTC. However, regardless of the change in the ROM, the effect of the NIFTP reclassification is significant for patients. The psychological, emotional, and financial implication of the consequences of an FNA diagnosis could potentially have great effects. Defining the cytomorphologic features of NIFTP is crucial to supplement TBSRTC. A few studies have attempted to define these features and have suggested features such as the degree of microfollicular pattern, pseudoinclusions, nuclear elongations, grooves, nuclear size, and nuclear clearing.[23-26] However, more studies are needed to confirm and further define definitive criteria. Similar to the studies by Strickland et al[26] and Bizzarro et al,[27] we noted that the diagnostic nuclear features of PTC are not very prominent in FNA samples of NIFTP. NIFTP will lack prominent pseudoinclusions, nuclear grooves, papillary architecture, and psammoma bodies. Our observations, however, revealed a mixture of 2-cell populations within a cluster of neoplastic cells in cases of NIFTP (Fig. 1A). In contrast, the FVPTC cases showed the typical nuclear features of PTC, with prominent nuclear pseudoinclusions without papillary architecture (Fig. 1B). The histologic features of the NIFTP are shown in Fig. 1C, D. Both NIFTPs and FVPTCs have a predominant follicular pattern with microfollicular architecture and lacked papillary architecture and/or psammoma bodies. Two-cell populations within a cluster of neoplastic cells were also observed in 3 of 5 FVPTC cases. However, our study was limited by the low number of FVPTC cases available for review. A recently reported study by Alves et al[17] noted that most NIFTPs will not show the florid nuclear features of PTC and that additional evaluation is necessary to determine whether papillae or invasion are present. Their data also suggested excluding cases with any true papillary structures from the diagnosis of NIFTP.[17] Caution should also be used for FNA cytopathology findings when overt PTC nuclear features are seen in cases with predominant microfollicles. In our institution, a disclaimer has been added when NIFTP is suspected or cannot be ruled out in the final diagnosis report. The disclaimer helps clinician in determining the necessity for additional studies or in planning the appropriate operative plan.

Although NIFTP can be histologically confirmed by resection, the effect on patient care will dramatically improve if the cytology findings can suggest an indolent rather than a malignant lesion in the FNA diagnosis, significantly reducing avoidable and potentially damaging overtreatment. The findings from molecular studies can also aid in patient treatment. With the recent advances in molecular pathologic evaluation and its increasing use as a screening tool, mutation profiles are already being used. It was previously established that NIFTP is more likely to be associated with the *RAS* mutation and that classic PTC cases will have BRAF V600E.[28,29] Our limited data showed that 6 of 11 cases (55%) analyzed for mutation had a *RAS* mutation. NIFTP also does not harbor *TERT*, *RET*, or *NTRK* fusion mutations.[29] The *RAS* gene is a part of the GTPase signaling pathway, resulting in cell division and growth. The 3 *RAS* genes (*HRAS*, *KRAS*, and *NRAS*) are the most common oncogenes in human cancer.[30] In NIFTP, mutation in the *RAS* gene occurs with a frequency of 30% to 54% (*NRAS* > *HRAS* >> *KRAS*).[8,28,31] *RAS* mutations, however, have also been found in cases of invasive FVPTC and follicular adenoma; thus, the presence of a RAS mutation

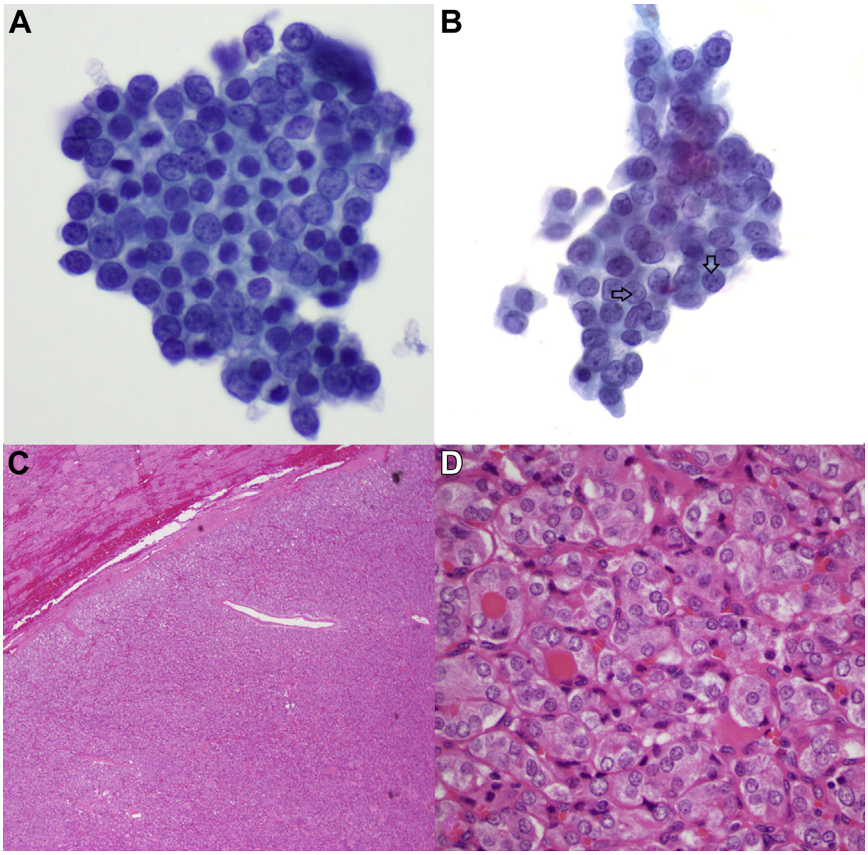

Figure 1 A, Papanicolaou-stained ThinPrep image of noninvasive follicular thyroid neoplasm with papillary-like nuclear features from fine needle aspiration sample showing tumor cells with pale chromatin and some nuclear membrane irregularities. Also seen are darker, normal-appearing follicular cells seen within the aggregate of tumor cells, demonstrating a 2-cell population within a cluster of neoplastic cells. B, Fine needle aspiration of follicular variant papillary thyroid carcinoma (PTC) showing more prominent PTC nuclear features, with prominent nuclear pseudoinclusions (arrows). Images of corresponding surgical resection specimen of noninvasive follicular thyroid neoplasm with papillary-like nuclear features showing encapsulated tumor cells in follicular architecture at C, low power and D, higher power showing tumor cells with PTC nuclear features.

will not be helpful for the differentiation of NIFTP versus malignant neoplasm versus benign lesion.[32] Other driver mutations found in NIFTP include *PAX8-PARG*, *THADA* fusions, and *BRAF* K601E.[8,31] Although no pathognomonic mutation has been found for NIFTP, the presence of *RAS*, *PAX-9PARG*, *THADA* fusion and *BRAF* K601E and the absence of mutations commonly seen in malignant thyroid cancers can help when NIFTP is suspected. When NIFTP cases were shifted from the malignant to nonmalignant category, the positive predictive values of "positive" molecular test results decreased significantly.[33,34] Thus, in the era of NIFTP, a "positive" molecular test result should be interpreted within the patient's clinical context and should not exclude conservative surgical management. Future studies aimed at determining the distinctive molecular profile of NIFTP would be very useful to improve the risk stratification for the cytologically indeterminate thyroid nodules, offering a more personalized, risk-based approach to the diagnosis and management of thyroid nodules.

Recently, the American Head and Neck Society endocrine section consensus reported practice guidelines for surgical recommendations to reflect the effect of NIFTP on clinical management.[35] The multidisciplinary study proposed a quality-driven, cost-effective, safe, and effective management plan aimed at reducing treatment variations and improving overall quality for patients. It summarizes the current understanding of NIFTP for the cytopathologic, histologic, and molecular aspects and the limited clinical follow-up data reported in making their recommendations. In their summary of the findings, the cytopathologic features supportive of NIFTP in the indeterminate Bethesda categories of III, IV, and V included the presence of a follicular pattern, hypercellularity, microfollicular architecture, and sheet-like architecture and the absence of papillae, psammomatous calcifications, prominent nuclear pseudoinclusions, prominent nuclear grooves, and necrosis or mitoses. However, the study noted the limitations in the preoperative evaluation of NIFTPs. Also, although classic PTC can be distinguished from NIFTP, the cytomorphologic features of invasive FVPTC versus NIFTP can overlap. Similarly, no distinct molecular mutation has been determined for NIFTP. According to the American Head and Neck Society guidelines, NIFTP is considered a precancerous lesion and an appropriate surgical target. Furthermore, total thyroidectomy is a valid, acceptable, and, potentially, preferable option. The decision should ultimately be determined from the preoperative clinical features, such as the presence of significant contralateral lobe nodules, lymph node metastasis, tumor fixation, vocal cord paralysis or voice change, posterior capsule tumor abutment on imaging studies, or radiologic evidence of extrathyroidal extension. Other factors to consider include the possibility of a second surgery and multidisciplinary discussion for a more conservative approach. NIFTP does not recur and patients will require less active follow-up after surgery.

Conclusions

The change in terminology has resulted in a vast interest among clinicians and pathologists alike with anticipation of a change in the ROM. Although it has been mostly agreed that a decrease in the ROM will result, it is not yet certain what the true percentage of decrease will be and which category will be most affected. Most reported studies have been retrospective analyses of reclassifying FVPTC to NIFTP. Future prospective studies with data collected after the nomenclature change would be helpful in confirming or clarifying the changes in the ROM.

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