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A clinic evaluation of novel nomenclature

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Bilal Arslan*, Ahmet Dağ*, Fadime Eda Gökalp Satıcı**, Rabia Bozdoğan Arpacı**, Asena Ayça Özdemir***

**Department of Surgery, Division of Surgical Oncology, Mersin University School of Medicine, Mersin, Turkey*
***Department of Pathology, Mersin University School of Medicine, Mersin, Turkey*
****Department of Biostatistics, Mersin University School of Medicine, Mersin, Turkey*

Non invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P). A clinic evaluation of novel nomenclature

AIM: *We aimed to find out unnecessarily overdiagnosed and overtreated patients, their preventable morbidities, expenditures which might not have occurred in the last decade concerning newly proposed nomenclature*
MATERIAL AND METHODS: *Among 1553 patients operated between 2010-2019, 197 were recorded. Pathology specimens were re-evaluated by two experienced pathologists to reveal those patients who could have diagnosed as NIFT-P.*
RESULTS: *According to the changes first suggested by Nikiforov in 2016 and partially revised in 2018; 55 of 197 patients were diagnosed with NIFT-P. Four (7.2%) patients had NIFT-P (operated after 2016), 14 patients (25.5%) had follicular adenoma, 13 patients (23.6%) had unknown malign potential, five patients (9.1%) had papillary microcarcinoma, two patients (3.6%) had papillary microcarcinoma encapsulated, five patients (9.1%) had papillary carcinoma follicular and two patients (3.6%) had papillary carcinoma encapsulated. 40 patients (72.7%) underwent thyroidectomy (bilateral total), 12 patients (21.8%) thyroidectomy (lobectomy, unilateral), two patients (3.6%) thyroidectomy (completion, total) and one patient (1.8%) neck dissection + thyroidectomy (bilateral, total).*
DISCUSSION: *The follicular variant of the papillary thyroid carcinoma was re-defined with a novel nomenclature as a noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P) according to its indolent behavior that did not require aggressive treatment,so lobectomy is sufficient, was suggested in 2016.*
CONCLUSIONS: *We found out that if we hadn't applied thyroidectomy (total or completion) to those 43 patients concerning new nomenclature, we could have prevented complications (2 patients, %3,6) and cut down the expenses caused by overtreatment in the last decade. NIFT-P has an excellent prognosis for its low locoregional or distant recurrence, so lobectomy is sufficient.*

KEY WORDS: Bethesda, NIFT-P, Total Thyroidectomy, Complication

Introduction

The incidence of thyroid cancer is increasing worldwide [1,2]. This trend is arguably related to the increase in the frequency of screening with USG in the asymptomatic healthy population. Increased diagnosis frequency of papillary thyroid carcinoma encapsulated follicular variant (FVPTC) is also suggested to contribute as well [3,4]. Accurate diagnosis of the FVPTC in the absence of a universal common definition is challenging and puts both surgeons and pathologists in a difficult situation [5]. Inconsistencies are common even between the pathologists working in the same clinic. Noninvasive FVPTC differs from infiltrative FVPTC since it is less aggressive and has an indolent behavior. Many health systems in the world recommend a conservative approach for noninvasive FVPTC [6,7].
However, it is still traditionally treated with total thy-

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Correspondence to: Bilal Arslan, Division of Surgical Oncology, Department of Surgery, Mersin University, Çiftlikköy Campus, 33343 Yenişehir, Mersin, Turkey (e-mail: bilalarslan84@hotmail.com; bilalarslan@mersin.edu.tr)

ABBREVIATIONS

NIFT-P: Noninvasive follicular thyroid neoplasm with papillary-like nuclear features

FVPTC: Papillary thyroid carcinoma encapsulated follicular variant

PTC: Papillary thyroid carcinoma

FNA: Fine needle aspiration

RAI: Radioactive iodine

roidectomy like PTC. In addition to a cancer diagnosis and traditional PTC-like treatment, patients and doctors have to cope with the risk of postoperative complications such as hoarseness due to recurrent laryngeal nerve damage and hypoparathyroidism. The increase in expenditures due to post-operative RAI therapy and the obligation to use L-thyroxine for life are other undesirable effects. In many aspects, it has seemed to be an overdiagnose caused to overtreatment which led to many problems in healthcare delivery for years.

All the controversy, contradictions and confusions affirmed that a new nomenclature was imperative. The non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P) definition first emerged in 2016, based on the criteria that Nikiforov suggested and was partially revised in 2018. It has been suggested that this non-aggressive tumor group does not require total thyroid excision, as opposed to PTC, RAI therapy doesn't require. It has been shown that lobectomy is sufficient and surveillance can be safely performed with USG and thyroglobulin [8]. We aimed to find out overdiagnosed and overtreated patients unnecessarily, their preventable morbidities, and expenditures concerning newly proposed nomenclature by evaluating patients' pathology specimens who undergone thyroidectomy (total or completion) instead of lobectomy in the past decade which might not have occurred.

Matherial and Methods

This study was approved by the Board of Ethics of the Mersin University on date 18/12/2019 with record 2019/563. The files of 2088 patients operated by the same team between 2010-2019 were analyzed retrospectively. Among 1553 patients diagnosed with well-differentiated thyroid carcinoma; 208 patients who were operated due to FVPTC, follicular adenoma, follicular carcinoma, a follicular lesion with unknown malignancy potential, well-differentiated tumor with uncertain malignancy potential, NIFT-P or postoperative diagnosis were re-evaluated. 11 patients, whose pathology slides could not be retrieved were excluded from the study. 197 patients were included in the study. All histological pathology slides were reexamined independently under a microscope by 2 experienced pathologists who were specialized at thyroid gland pathologies to reveal those patients who could have diagnosed as NIFT-P.

The patients were selected according to the criteria in the article "papillary thyroid carcinoma encapsulated follicular variant nomenclature revision" published in 2016, which was presented as a consensus. The major diagnostic criteria for papillary thyroid carcinoma encapsulated follicular variant are (1) partial or complete encapsulation and separation with a clean demarcation line from adjacent non-tumor tissue, (2) absence of invasion, (3) follicular growth pattern (4), nuclear properties of papillary thyroid carcinoma. The exclusion criteria are that; the entire tumoral tissue cannot be examined microscopically, there is another tumoral focus larger than 1 cm, presence of undifferentiated component, presence of necrosis, presence of papillary structure, presence of psammoma body, number of mitotic figures is 3 or above at 10x magnification or diagnosis of a different subtype of the papillary thyroid carcinoma. Lesions with no capsule and vascular invasion, no necrosis, mitosis, papillary structure, no solid/trabecular growth pattern, and specimens that scored about 2-3 points in nucleus evaluation were diagnosed as NIFT-P.

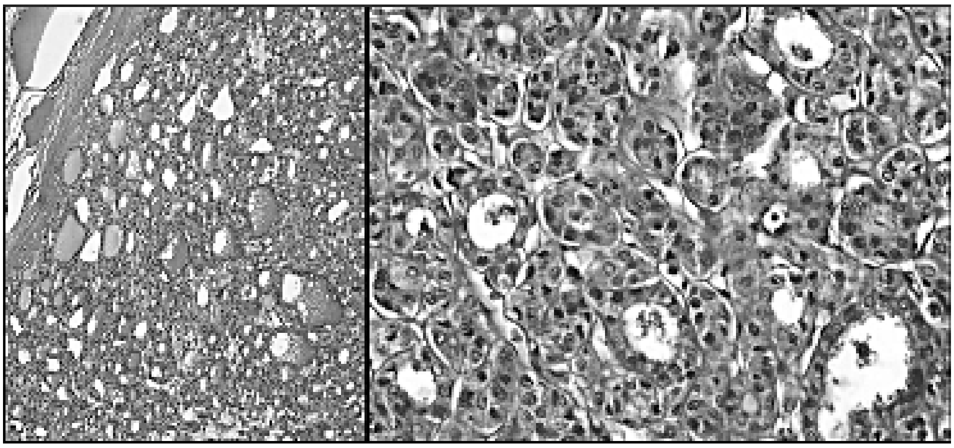
PTC is divided into two subtypes according to the presence of capsular and vascular invasion: non-invasive FVPTC and infiltrative FVPTC. The non-invasive FVPTC is closer to the NIFT-P definition. Although the presence of less than one papillary structure was considered as a diagnostic criterion in 2016, this is further reduced to the total absence of papillary structures in the 2018 revision. In this study, we considered the absence of papillary structure as the NIFT-P diagnostic criteria. Pathology slides and specimens of 197 patients were examined with these criteria according to the new classification and 55 patients were diagnosed as NIFT-P. Demographics, preoperative Bethesda classifications, types of surgery, postoperative pathological examinations, histological subtypes, morbidity, and mortality were evaluated.

Statistics

Analyses were carried out by Medicres 'www.e-picos.com'. Descriptive statistics thereof were represented as frequency and percentage. Continuous parameters were represented by the average and standard deviation.

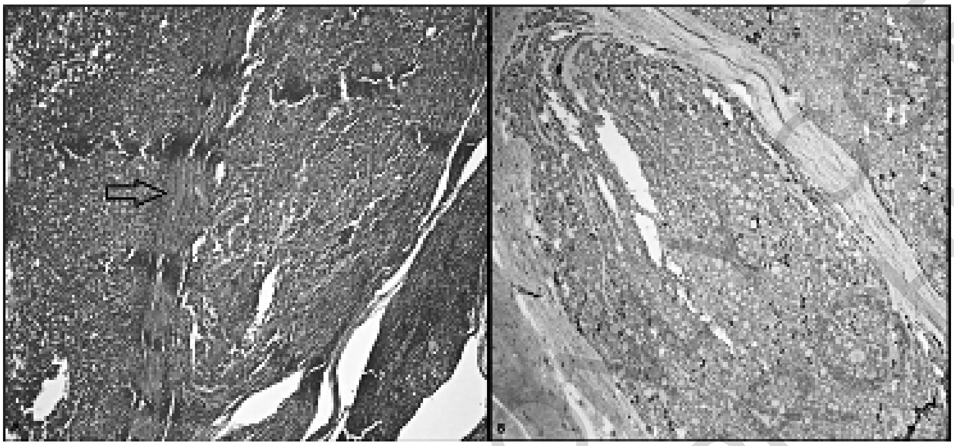
Results

According to Nikiforov's article published in 2016 and according to 2018 partially revised criteria, 55 of 197



A B

Fig. 1: A) NIFT-P case with intact capsule (H&E, x100); B) Papillary thyroid carcinoma like nucleus properties are exhibited with more magnification in the same case. Nuclear groove and transparency in chromatin are prominent (H&E, x400).



A B

Fig. 2: A) Capsule invasion of papillary carcinoma with encapsulated growth pattern (arrow) (H&E, x40); B)Prominent, cytoplasmic and diffuse CK19 expression in the invading tumor cells (H&E, x40).

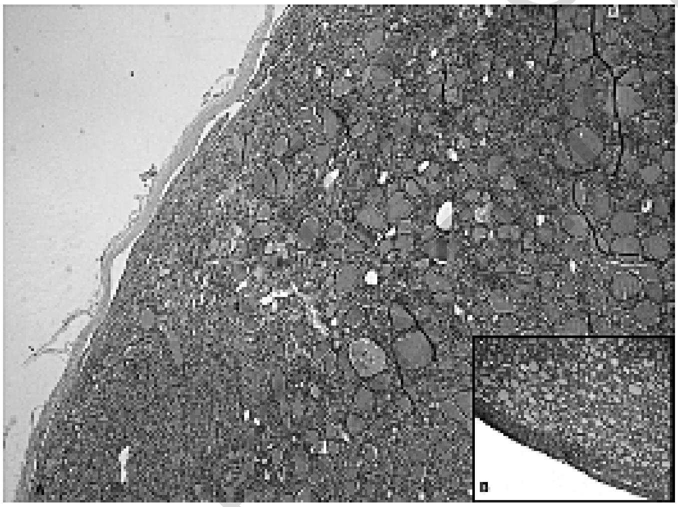


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Fig. 3: A) Non-invasive encapsulated papillary thyroid carcinoma (H&E, x100); B) Intact capsule is outlined with trichrome stain. (H&E, x100).

patients were diagnosed as NIFT-P (Figs. 1, 2, 3). The average age of patients was 48.6 (21-79). 42 of the patients were female and 13 were male. The mean follow-up period was 56 (2-125) months. The average nodule size was four cm (0.4cm-7cm). Preoperative evaluation of FNA results of these NIFT-P patients according to the Bethesda classification system was displayed (Table I). Distribution of the procedures applied to patients was as follows; 40 patients (72.7%) underwent thyroidectomy (bilateral total), 12 patients (21.8%) underwent thyroidectomy (total unilateral), two patients (3.6%) who underwent thyroidectomy (completion, total), 1 patient (1.8%) underwent neck dissection + thyroidectomy (bilateral, total). Distribution of surgical procedures and corresponding Bethesda classification were displayed (Table II).

The applied surgical procedure and histopathological results were displayed (Table III). Two patients (100%)

Table I - *Bethesda Classification-Histological Type*

		NIFT-P	Unknown Malign Potential Follicular type	Papillary Microcarcinoma Follicular Type	Papillary Microcarcinoma Encapsulated	Papillary Carcinoma Follicular Type	Papillary carcinoma Encapsulated	Follicular Adenoma	Follicular Carcinoma	Well D Tumor Unknown Malign Potential	Well D Tumor Unknown Malign Potential	Total
B- 2	B- 1	0	0	0	0	0	0	0	0	0	0	0
	n	2	7	1	2	1	2	9	0	0	1	25
	%	50,0%	53,8%	20,0%	100,0%	20,0%	100,0%	64,3%	0,0%	0,0%	25,0%	45,5%
B-3	n	0	1	1	0	1	0	0	0	2	0	5
	%	0,0%	7,7%	20,0%	0,0%	20,0%	0,0%	0,0%	0,0%	100,0%	0,0%	9,1%
B- 4	n	2	4	0	0	2	0	3	3	0	1	15
	%	50,0%	30,8%	0,0%	0,0%	40,0%	0,0%	21,4%	75,0%	0,0%	25,0%	27,3%
B- 5	n	0	1	0	0	0	0	1	0	0	1	3
	%	0,0%	7,7%	0,0%	0,0%	0,0%	0,0%	7,1%	0,0%	0,0%	25,0%	5,5%
B- 6	n	0	0	3	0	1	0	1	1	0	1	7
	%	0,0%	0,0%	60,0%	0,0%	20,0%	0,0%	7,1%	25,0%	0,0%	25,0%	12,7%
Total	n	4	13	5	2	5	2	14	4	2	4	55
	100	100	100	100	100	100	100	100	100	100	100	

Table II - *Surgical Procedure-Bethesda Classification*

			Surgical Procedure				Total
			Neck dissection, radical or functional (unilateral), Thyroidectomy (bilateral, total)	Thyroidectomy (bilateral, total)	Thyroidectomy (completion, total)	Thyroidectomy (unilateral, total)	
Bethesda	2	n	0	21	0	4	25
		%	0,0%	52,5%	0,0%	33,3%	45,5%
	3	n	0	1	2	2	5
		%	0,0%	2,5%	100,0%	16,7%	9,1%
	4	n	0	9	0	6	15
		%	0,0%	22,5%	0,0%	50,0%	27,3%
	5	n	0	3	0	0	3
		%	0,0%	7,5%	0,0%	0,0%	5,5%
	6	n	1	6	0	0	7
		%	100,0%	15,0%	0,0%	0,0%	12,7%
Total		n	1	40	2	12	55
%		100,0%	100,0%	100,0%	100,0%	100,0%	

who underwent completion thyroidectomy were Bethesda-3. Four of 12 patients (33.3%) who underwent thyroid lobectomy were Bethesda-2, two patients (16.7%) were Bethesda-3, six patients (50%) were Bethesda-4 (Table-II). Examinations of the pathology specimens of the operated patients yielded the following primary diagnoses; four (7,2%) patients had NIFT-P (operated after 2016), 14 patients (25.5%) had follicular adenoma, 13 patients (23.6%) had an unknown malign potential follicular type, five patients (9.1%) had papillary microcarcinoma follicular type, two patients (3.6%) had papillary microcarcinoma encapsulated, five patients (9.1%) had papillary carcinoma follicular type and 2 patients (3.6%) had papillary carcinoma encapsulated. Bethesda classification and histopathological subtype comparisons were displayed (Table IV). 21 Bethesda-2 and one Bethesda-3 (total 22) patients undergone total thyroidectomy instead of unilateral lobectomy as they mostly admitted to the hospital with a severe enlargement of a thyroid nodule, tracheal pressure, or

Table III - *Surgical Procedure-Histological Type*

		NIFT-P	Unknown Malign Potential Follicular Type	Papillary Microcarcinoma Follicular Type	Papillary Microcarcinoma Encapsulated	Papillary Carcinoma Follicular Type	Total	Follicular Adenoma	Follicular Carcinoma	Well D Tumor Unknown Malign Potential	Undetermined	
Neck dissection, Thyroidectomy (bilateral, total)	n	0	0	0				0	0	0	1	1
	%	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%	25,0%	1,8%
Thyroidectomy (bilateral, total)	n	2	8	4	2	4	1	12	4	1	2	40
	%	50,0%	61,5%	80,0%	100%	80,0%	50,0%	85,7%	100,0%	50,0%	50,0%	72,7%
Thyroidectomy (completion, total)	n	0	0	1	0	0	0	0	0	1	0	2
	%	0,0%	0,0%	20,0%	0,0%	0,0%	0,0%	0,0%	0,0%	50,0%	0,0%	3,6%
Thyroidectomy (unilateral, total)	n	2	5	0	0	1	1	2	0	0	1	12
	%	50,0%	38,5%	0,0%	0,0%	20,0%	50,0%	14,3%	0,0%	0,0%	25,0%	21,8%
Total	n	4	13	5	2	5	2	14	4	2	4	55
	100	100	100	100	100	100	100	100	100	100	100	

Table IV - *The Bethesda System for Reporting Thyroid Cytopathology: implied risk of malignancy and recommended clinical management in 2009 (before NIFTP) and in 2018 (after NIFTP)*

Diagnostic category	Risk of malignancy (1st edition 2009)	Risk of malignancy without NIFTP (2nd edition 2018)	Risk of malignancy with NIFTP (2nd edition 2018)	Usual management (1st edition 2009)	Usual management (2nd edition 2018)
Non-diagnostic or unsatisfactory	Not assessed	5–10%	No significant changes	Repeat FNA with ultrasound guidance	No significant changes
Benign	0–3%	No significant changes	No significant changes	Clinical and sonographic follow-up	No significant changes
Atypia of undetermined significance or follicular lesion of undetermined significance	5–15%	10–30%	6–18%	Repeat FNA with ultrasound guidance	Repeat FNA, molecular testing, or lobectomy*
Follicular neoplasm or suspicious for a follicular neoplasm	15–30%	25–40%	10–40%	Lobectomy	Molecular testing, lobectomy**
Suspicious for malignancy	60–75%	50–75%	45–60%	Near-total thyroidectomy or lobectomy	Near-total thyroidectomy or lobectomy***
Malignant	97–99%	No significant changes	94–96%	Near-total thyroidectomy	Near-total thyroidectomy or lobectomy*

cosmetic complaints. The fact that goiter is considered to be endemic in Turkey and 4-5 times more common in women than men. The total or completion thyroidectomy procedure unnecessarily applied to 20 patients. Two patients underwent completion thyroidectomy by evaluating pathology unknown malign potential follicular type. Of these 18 patients undergone total thyroidectomy, nine patients were evaluated as follicular neoplasia, three patients were evaluated as suspicious for malignancy and six patients were evaluated as malignant unnecessarily. Of 40 patients undergone thyroidectomy (bilateral, total) one had temporary recurrent nerve damage. Of two patients (3.6%) who undergone thyroidectomy (completion, total) one had temporary hypoparathyroidism. One patient (1.8%) who undergone neck dissection + thyroidectomy (bilateral, total) had no

complication. If we had evaluated all patients according to new nomenclature as NIFT-P before surgery, we wouldn't have overdiagnosed and overtreated these patients, so we would have faced many complications mentioned above less frequently.

Discussion

Although the incidence of thyroid cancer has nearly tripled worldwide in recent years, there has been no significant change in its mortality [9,10]. The frequency of FVPTC is between 9-22% among PTC. FVPTC prognosis is studied under two different subtypes depending on molecular properties as infiltrative and non-invasive encapsulated types.

The incidence of NIFT-P among PTC is estimated to be 18% in North America and Europe. When the first definition emerged, it was considerably lower than the commonly suggested rate [8]. Its frequency varies between less than 1% and 28% in different regions around the world [10]. Especially in the Asian population, the rate is lower than in other parts of the world. The same study reports the rate of 2% in the Korean peninsula. Possible causes of this wide variation are; possible different interpretations even among very specialized pathologists due to the presence of a wide variety of histological diagnostic criteria, geographic and genetic differences, different molecular mechanisms and mutation profiles, different criteria employed in different series studies and different managements of indeterminate thyroid nodules in the west and Asia [11,12].

In our study, this 3% rate (55/1553) was found to be lower than Europe and the USA and was rather compatible with the Korean peninsula. Some reasons for this difference can be the entire evaluation of the tumoral tissue capsule and having an absence of papillary structures as a criterion in our study, following the Korean study and other possible unknown environmental, ethnic factors.

Since it was first defined in 2007, Bethesda classification has been widely used all over the world. It was revised in 2017 after the NIFT-P classification. In a large-scale multicenter study involving 6943 patients by W.C.W.L. Faquin et al. suggested that the novel emerged NIFT-P definition had significant effects on the assessment of malignancy risks on the Bethesda classification [9]. Decrements were seen in AUS/FLUS category (Bethesda-3) by 5.2%-13.6%, FN category (Bethesda-4) by 9.9%-15.1%, SM category (Bethesda-5) by 17.6%- 23.4% ($p<0.05$). In the Benign (Bethesda-1) and malignant (Bethesda-6) categories, decreases by 0.3-3.5% and 2.5-3.5% were detected, respectively. In a multicentered Asian study involving 2044 patients, 2.9% (59 cases) of the patients had NIFT-P diagnosis. The preoperative FNA results of the patients were; 10.2% non-diagnostic, 18.6% benign, 22.0% AUS/FLUS, 32.2% FN/SFN, 11.9% SM, and 5.1% malignant. A 20% reduction in the risk of malignancy in the FN/SFN category was observed in this study [13]. In another study, the risk of malignancy was unchanged in the non-diagnostic category, benign 5.5% to 2.5%, AUS/FLUS, 42.3% to 22.3%, FN/SFN from 48.7% to 17.9%, SFM, 93.6% to 61.7% and finally, the diagnosis of malignancy decreased from 100% to 97% [14,15,16]. In the study of Cibas and Ali, there was no significant change in the non-diagnostic and benign categories in the Bethesda 2017 malignancy risk classification after the emergence of the NIFT-P definition. However, AUS/FLUS from 10-30% to 6-8%, FN/SFN from 25-40% to 10-40%, SM 50-75% to 45-60%, malignant category decreased from 97-99% to 94-96% [16] (Table IV). Accordingly, the majority of patients diagnosed with histological NIFT-P are in the preoperative Bethesda-3,4,5 category. The recommended procedure for categories 4 and 5 is lobectomy or total thyroidectomy. In category three, the decision to repeat surgery or FNA can be made by evaluating the cytomorphological, sonographic, molecular findings of the nodule [17].

There was no Bethesda-1 patient in patients diagnosed with NIFT-P in our study. Contrary to the literature, in this re-examination, the majority of these diagnoses fell into the Bethesda-2 classification with 25 patients (45.5%). Even the total of all Bethesda-3,4,5 patient groups which accounted for 23 patients (43%), was not as much as the Bethesda-2 patients. In our clinic, the majority of the patients with a diagnosis of NIFT-P in a re-evaluation of the nodules were classified as Bethesda-2, which is a major difference in comparison to the previous studies in the literature.

According to the 2018 Bethesda classification of indeterminate thyroid nodules; malignancy risks of Bethesda-2,3,4 are 3%, 6-18%, 10-40% respectively. The type of management recommended is a follow-up in Bethesda-2, and usually one-sided lobectomy in Bethesda-3 and 4 (Table IV). In our study, 21 patients underwent a total thyroidectomy due to Bethesda-2, and four patients who underwent unilateral lobectomy. Follicular adenoma, Hashimoto thyroiditis, granulomatous thyroiditis are included in this group. Many reasons can be proposed for the high rate of thyroidectomy procedure in our study for the patient group that should have been followed-up. The fact that goiter is considered to be endemic in Turkey and 4-5 times more common in women than men. The frequency of goiter in Turkey ranges between 5-56%, more frequent in areas with iodine deficiency (endemic goiter) [18]. The majority of our patients admitted to the hospital with a severe enlargement of a thyroid nodule, shortness of breath, and cosmetic complaints. Although the FNA results are benign as Bethesda -2; for such reasons usually, the lobectomy procedure is not sufficient and total thyroidectomy is applied. Although we could not find any other study with this argument in the literature, we consider this as an accu-

rate reflection of the situation in Turkish society. However, it should be remembered that endemic goiter due to iodine deficiency is a preventable condition. Morbidity and mortality may occur in these patients as a complication of a surgery that they do not require because of an FNA proven malignancy but because of pressure symptoms and cosmetic complaints. Additionally, these patients are dependent on L-thyroxine treatment for lifelong. It is a problem for the Turkish healthcare system.

Although in the experienced hands, thyroid surgery has a very low level of morbidity and mortality all over the world, undesired complications may occur occasionally. General complications such as bleeding, seroma, infection, and pain can be observed in the early postoperative period. Additionally, recurrent laryngeal nerve injury specific to thyroid surgery is one of the most feared complications. Other undesirable complications of superior laryngeal nerve injury are deepened voice, persistent hypocalcemia, permanent hypoparathyroidism, esophagus, and tracheal injury[18]. It is suggested that performing central neck dissection increases the risk of nerve injury. So a minimally invasive approach should be considered in thyroid gland pathologies. It is the best option to apply the only lobectomy rather than total thyroidectomy or central neck dissection if it is adequate. The novel nomenclature NIFT-P came to the rescue of both physicians and patients dealing with this tough situation. It eased and brightened surgeons at this issue which dragged to make their minds up with a minimally invasive approach. This minimally invasive approach would prevent many complications anticipated, gives both patients and surgeons confidence, and reduce the healthcare expenditures.

In our patient group seroma, bleeding and infection did not occur. Of 40 patients undergone thyroidectomy (bilateral, total) one (1.8%) had temporary recurrent nerve damage. Of two patients (3.6%) who undergone thyroidectomy (completion, total) one (%1,8) had temporary hypoparathyroidism. One patient (1.8%) who undergone neck dissection + thyroidectomy (bilateral, total) had no complication. The patient developed hoarseness due to temporary recurrent nerve damage; it resolved within six weeks. Although hoarseness is not persistent, such conditions affect the psychological state of the patients and the motivation of the physicians. The other patient who underwent completion thyroidectomy had hypocalcemia due to temporary hypoparathyroidism. Although calcium values returned to normal in less than six months, this also led to a deterioration in the physiological states and quality of life of patients. This also led to a deterioration in the physiological states and quality of life of patients. If these total two patients were previously diagnosed with NIFT-P and had lobectomy instead, the incidence of these complications could be further reduced. It is obvious that applying overtreatment to the patients following overdiagnosis causes needless complications. Therefore, the recognition of NIFT-P has the potential to reduce complications, lifelong use of L-thyroxine, unnecessary RAI related complications, and healthcare expenditures. In the USA, it is suggested that saving between 5000 and 8000 USD per patient is possible only by not applying RAI treatment [19]. In total, approximately 45000 patients are estimated to be affected by this definition worldwide every year. The magnitude of the numbers indicates that the NIFT-P definition should be considered [8].

In a study by Uijo Cho et al., 6269 patients who were operated for thyroid papillary carcinoma with routine central neck dissection were re-examined according to the NIFT-P definition in the new nomenclature. In the study, lymph node positivity and presence of genetic mutation were also evaluated. 152 patients matching the NIFT-P definition were revealed. These patients were re-examined according to the absence of papillary structures or the presence of less than 1% papillary structures. When evaluated according to this rigid criterion, 140 patients were observed to comply with the NIFT-P definition. When the presence of 1% papillary structures was taken as cut-off value; lymph node metastasis rate and BRAFV600E mutation rates were 3% and 10%, respectively in noninvasive tumors, and 9% and 4% respectively in invasive tumors. When the absence of papillary structures was taken as the rigid criterion, the BRAFV600E mutation was not seen in any patient, but in noninvasive tumors, micrometastasis was observed in the central region at the rate of 3%. Non- BRAFV600E and RAS mutations in non-invasive tumors were observed as 4% and 47%, respectively [20]. Based on these findings, it was argued that NIFT-P should not be evaluated as a benign thyroid neoplasm, micrometastatic lymph node metastases were possible and the diagnosis cannot be appropriate in the presence of papillary structures [21]. In our study, we could not perform the BRAFV600E and RAS mutation analyses due to technical insufficiencies. However, in the presence of suspicious LAP, we performed central or lateral neck dissection. One patient (1.8%) underwent central + lateral neck dissection along with total thyroidectomy due to lymph node involvement. No hematoma, lymphatic fistula, or other complications developed. The pathology report indicated papillary microcarcinoma metastasis was present in two lymph nodes. During the follow-up period that went on for 120 months, we have not faced with a relapse or metastasis in our patients, and all turned back into their normal daily life.

The previous series in the literature reported that patients diagnosed with NIFT-P (based on 0% papillary structure) did not develop locoregional recurrence and distant metastasis; in the study mentioned above, there may be micrometastases to central lymph nodes. Since central lymph node dissection is not routinely performed for such patients worldwide, it is not possible to detect micrometastases. It should be remembered that these

patients may have metastases to the lymph nodes even if they are diagnosed with NIFT-P, which is indicated by our study as well. Evaluation of all findings and data led to the suggestion in the ATA guidelines that NIFT-P can be considered as a papillary thyroid carcinoma with low recurrence (1-2%). Besides, although micrometastases can be seen in the central region, it is safe to assume that NIFT-P and noninvasive FVPTC are associated with low-risk thyroid papillary non-aggressive carcinoma. Thus, aggressive treatments such as completion thyroidectomy and RAI may be redundant. Patients in this group are still in the evaluation phase and large-centered long-term series are needed [22,23].

Evaluating the results of Nikiforov's study together with previous observations yields, patients diagnosed with NIFT-P after detailed histopathological examination have a recurrence risk of less than 1% within 15 years. On the contrary, well-differentiated thyroid cancers may show distant metastasis and recurrence after many years and often tend to recur within the first 10 years. In the same study by Nikiforov et al, patients diagnosed with NIFT-P underwent lobectomy and did not receive RAI treatment. This indicates that patients who have been operated for NIFT-P do not need completion thyroidectomy and followingly RAI. Besides, the psychological effect of having a disease with a "cancer reminding name" (carcinoma) will disappear, as well as reduce the complication rates associated with completion thyroidectomy and the risk of secondary tumor development due to RAI [20].

Considering the data in the literature and the findings in our study, we think that NIFT-P is not a benign tumor, it has a low risk of malignancy, and it should be kept in mind that the exact diagnosis can be made after microscopic examination after surgical excision. While the unilateral lobectomy operation may be sufficient for these patients; because of the malignant tumor in the definition of the disease, the total thyroidectomy operation has been performed all over the world for years. This increases the risk of postoperative complications such as hoarseness due to recurrent laryngeal nerve damage or hypoparathyroidism. Post-operative RAI therapy and the obligation to use L-thyroxine for life are other undesirable effects. RAI therapy and completion thyroidectomy are unnecessary in these patients. Thyroglobulin and neck USG is sufficient for follow-up. As a result of this approach, morbidity, mortality, and healthcare expenditures will decrease worldwide, and patients will not be crushed under the heavy psychological burden of "cancer reminding name".

Conclusion

NIFT-P is a well-defined encapsulated tumor with a predominant follicular form or small nuclear properties of PTC. It has an excellent prognosis due to its low locoregional or distant recurrence. We know that due to the non-aggressive, indolent behavior of the disease, unilateral lobectomy operation is sufficient. RAI therapy and completion thyroidectomy are unnecessary in these patients and seems to be overtreatment. Thyroglobulin and neck USG is sufficient for follow-up.

Notwithstanding, concerning new proposed nomenclature NIFT-P some diagnoses (follicular carcinoma, etc.) and aggressive surgical treatments which we used in the past might transform into a conservative minimal invasive approach. The importance of this is naming the disease as a low-risk neoplasm with a non-aggressive behavior as opposed to previous malignant definition has had significant effects on patients' surgical procedure, healthcare planning, and psychological status, and also significantly reduce hospital costs and it might prevent postoperative complications.

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Commento e Commentary

Prof. Matteo Angelo Cannizzaro
già Ordinario di Endocrinochirurgia
Università degli Studi di Catania

Negli ultimi anni è stata sperimentata una nuova classificazione di numerosi casi di FVPTC in NIFPT. La NIFPT è una neoplasia non invasiva originata da tireociti, mostra le caratteristiche nucleari del cancro papillare ed è caratterizzato da una malignità molto bassa.
L'esame istologico postoperatorio è fondamentale per la diagnosi definitiva di NIFPT. Per decidere di procedere con una lobectomia o una tiroidectomia totale sono utili le seguenti caratteristiche fisiche ed ecografiche, caratteristiche molecolari. Un'attenta valutazione della lobectomia dovrebbe includere anche una valutazione del lobo controlaterale per evitare di perdere la coesistenza di lesione maligna.

* * *

On the last years a new classification of numerous cases of FVPTC in to NIFT-P has been experienced. NIFT-P is a non invasive neoplasm originated from thyrocytes. It shows nuclear features of papillary cancer and it is characterized by a very low malignancy.
Postoperative histological examination is fundamental for definitive diagnosis of NIFT-P. In order to decide to proceed with a lobectomy or a total thyroidectomy the following physical and ultrasound features, molecular characteristics are usefull. A carefull assessment of the lobectomy should as well include an evaluation of the contralateral lobe to avoid missing the coexistence of malignant lesion.