THE RISK OF THYROID MALIGNANCY IN PATIENTS WITH SOLITARY THYROID NODULE *VERSUS* PATIENTS WITH MULTINODULAR GOITER

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SUMMARY – The aim of the study was to compare the risk of thyroid malignancy in patients with a solitary thyroid nodule *vs.* patients with multinodular goiter. The prospective study included 406 patients who had one or more thyroid nodules and underwent ultrasound guided fine needle aspiration. There were 29 males and 377 females (male to female ratio 1:13). There were 117 (29%) patients (12 males and 105 females) with a solitary thyroid nodule, and 289 (71%) patients (17 males and 272 females) with multinodular goiter, age range 11-86 years, median 55 years. Upon cytologic examination definitive diagnosis of malignant tumor was made in six (5%) patients with a solitary thyroid nodule and in 15 (5%) patients with multinodular goiter. All patients with malignant tumors in both groups were females. It was concluded that there was no difference in the risk of thyroid malignancy between patients with a solitary thyroid nodule and patients with multinodular goiter.

Key words: *Thyroid neoplasms – pathology; Thyroid neoplasms – immunology; Carcinoma papillary; follicular – immunology; Goiter nodular – pathology; Biopsy needle - methods*

Introduction

Thyroid nodules are a common clinical problem but thyroid cancer is a relatively uncommon malignancy accounting for 1% of all new cancer cases[1]. More than 90% of thyroid carcinomas are well differentiated and have an overall favorable outcome, with only 9% of patients being terminal[2].

The key role of the physician evaluating thyroid nodularity is to determine which patients are at a risk of malignancy. Physical examination can only provide general clues: nodule that is fixed to the surrounding structures, hard nodule, paralysis of one of the vocal cords, or the presence of ipsilateral lymphadenopathy suggesting the presence of carcinoma. Nearly all patients with thyroid carcinoma have normal serum thyrotropin (TSH) concentrations, as do most patients with benign nodules. The thyroid radionuclide scan shows that most of thyroid carcinomas are hypofunctioning. Thyroid ultrasonography (USG) can be used to determine whether a nodule is solitary or is part of a multinodular goiter (MNG). Among patients with a solitary thyroid nodule (STN) on physical examination, about 50% have multiple nodules when evaluated by USG[3].

Traditionally, as well in some recent works, the main indication for fine needle aspiration (FNA) of the thyroid has been the presence of a solitary nodule[4,5]. Moreover, some authors who conducted research in rural Africa recommend routine excision of STNs due to the 16% malignancy rate found in this condition[6]. Although recent literature indicates that the prevalence rates of cancers in MNGs are lower than the rates in STNs, they are not sufficiently lower to allow for reliance only on these characteristics without FNA on deciding whether to recommend surgery[7-10].

The present study included patients who had one or more thyroid nodules on USG to compare the risk of thyroid malignancy between STN patients and MNG patients.

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Patients and Methods

This study included 406 consecutive patients who had one or more thyroid nodules on USG. All patients underwent ultrasound guided FNA. There were 29 males and 377 females (male to female (M:F) ratio 1:13), age range 11-86 years, median 55 years. Patients were divided into two groups according to their USG findings: STN group and MNG group. Patients with uncertain USG findings regarding nodularity and patients with previous thyroid operation were excluded from the study. Total number of nodules *per* patient was not recorded in patients with MNG. In patients with MNG, not all nodules (i.e. nodules less than 5 mm in greatest diameter and without USG suspect pattern) were cytologically evaluated. USG results concerning nodularity were compared with cytologic or histologic diagnosis.

Results

Ultrasonography

There were 117 (29%) patients with STN and 289 (71%) patients with MNG. In the STN group, nodule size was recorded in 97 (83%) patients and it was 2.2 ± 1.1 cm (median 1.9; range 0.5 to 8.3). In the MNG group, nodule size was recorded in 177 (61%) patients, 271 nodules were measured, with a mean nodule size of 1.9 ± 1.3 cm (median 1.5; range 0.5 to 10) (Table 1).

Age and sex

Age was similar in patients with STN (50 ± 15.7 years; median 50; range 11-81) and those with MNG (56 ± 12.5 years; median 56; range 13-86). According to sex distribution, there were 12 (11%) male and 105 (89%) female patients with STN (M:F ratio 1:9), and 17 (6%) male and 272 (94%) female patients with MNG (M:F ratio 1:16) (Table 2).

Cytologic/histologic diagnosis

In the STN group, there were six (5%) patients with definitive cytologic or histologic diagnosis of malignant tumor. Upon cytologic examination, definitive diagnosis of malignant tumor was made in five patients (all had cytologic diagnosis of papillary carcinoma; four were confirmed histologically, and one patient was without histologic finding). One patient with cytologically suspect follicular neoplasm had histologically verified papillary carcinoma.

In the MNG group, there were 16 (5%) patients with definitive cytologic or histologic diagnosis of malignant tumor. Upon cytologic examination, definitive diagnosis of malignant tumor was made in 15 patients (13 papillary carcinomas, one medullary carcinoma, and one poorly differentiated carcinoma). Of the 13 patients with cytologic diagnosis of papillary carcinoma, eight were histologically confirmed to have papillary carcinoma; one had mixed medullary and follicular carcinoma, and four were without histologic finding). The patient with cytologic diagnosis of poorly differentiated carcinoma had histologically verified anaplastic carcinoma, and the patient with cytologic diagnosis of medullary carcinoma was histologically confirmed to have medullary carcinoma. One patient with cytologically suspect papillary carcinoma had histologically verified papillary carcinoma.

All patients with malignant tumors in both groups were females.

Indeterminate cytologic findings were significantly more common in STN patients than in those with MNG (22/117 *vs.* 24/289; p=0.004) (Table 3).

In this study, the patient risk of thyroid malignancy was assessed against some other authors estimating the nodule chance to be malignant. To the best of our knowledge, this is the first study comparing the nodularity assessed

Table 1. Solitary thyroid nodule (STN) vs. multinodular goiter (MNG): distribution of patients and nodule size

	Patients	Nodule size		
		Mean	Median	Range
STN*	117 (29%)	2.2 ± 1.1	1.9	0.5 – 8.3
MNG**	289 (71%)	1.9 ± 1.3	1.5	0.5 – 10

*nodule size was recorded in 97 (83%) patients
**nodule size was recorded in 177 (61%) patients

Table 2. Solitary thyroid nodule (STN) vs. multinodular goiter (MNG): age and sex

	Age (yrs)			Sex		
	Mean	Median	Range	Male	Female	M : F
STN	50 ± 15.7	50	11 – 81	12 (11%)	105 (89%)	1 : 9
MNG	56 ±12.5	56	13 - 86	17 (6%)	272 (94%)	1 : 16

Table 3. Solitary thyroid nodule (STN) vs. multinodular goiter (MNG): cytologic/histologic diagnosis

	Cytologic/histologic diagnosis		
	Benign	Indeterminate*	Malignant
STN	89 (76%)	22 (19%)	6 (5%)
MNG	249 (87%)	24 (8%)	16 (5%)

*only for cytologic findings

exclusively by USG with cytologic or histologic diagnosis. The reason for using USG alone to assess thyroid nodularity was the fact that some 50% of patients with STN on physical examination have multiple nodules when evaluated by USG[3].

A comparable nodule size was observed in STN patients (median 1.9 cm) and MNG patients (median 1.5 cm). Patients with MNG were slightly older than those with STN (median 56 *vs.* 50 years), and showed a higher female predominance (M:F 1:16 *vs.* 1:9).

When the patient risk of thyroid malignancy was calculated, there was no difference between the two groups; it was 5% in both groups. Although Tollin *et al*. did not investigate these two groups of patients (i.e. patients with MNG and patients with STN), the malignancy rate in our MNG patients correlated with the malignancy rate they recorded in their MNG patients[9]. However, our findings were not in accordance with the rates reported by Franklyn *et al.*[8], who found a higher rate of malignancy in patients with STN (5.9% *vs.* 1.4%), and by Abu-Eshy *et al*.[11] (STN *vs*. MNG, 15% *vs*. 8%). These differences could be explained by different methods employed on assessing thyroid nodularity. Wagana *et al.* found 16% malignancy rate in STNs of patients undergoing thyroidectomy for STN[6]. Sachmechi *et al.*[12] investigated the risk of malignancy in STN *vs*. MNG only in nonfunctioning, cold nodules, and upon exclusion of patients with a history of neck irradiation, found an even higher rate of malignancy in MNG than in STN (9.8% *vs*.8%). In their study of nonpalpable thyroid nodules, Papini *et al.*[13] found a higher rate of malignancy in STN than in MNG (9.2% *vs*. 6.3%). These result variation between our and two papers mentioned above could be attributed to the different patient selection.

Interestingly, all patients with thyroid malignancies in our study were women. It could be attributed to the relatively small absolute number of male patients (n=29) in this study.

In conclusion, since we found the same risk of thyroid malignancy in patients with STN and those with MNG, the possibility of thyroid malignancy should be considered with the same caution in all patients with thyroid nodules irrespective of their number.

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Sažetak

RIZIK OD MALIGNITETA ŠTITNE ŽLIJEZDE U BOLESNIKA S POJEDINAČNIM ČVOROM ŠTITNE ŽLIJEZDE PREMA BOLESNICIMA S MULTINODULARNOM STRUMOM

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Cilj studije bio je usporediti rizik of maligniteta štitne žlijezde u bolesnika s pojedinačnim čvorom štitne žlijezde prema bolesnicima s multinodularnom strumom. U prospektivnu studiju bilo je uključeno 406 bolesnika koji su imali jedan ili više čvorova štitne žlijezde i podvrgnuti su ultrazvučno vođenoj tankoiglenoj biopsiji. Bilo je 29 muškaraca i 377 žena (omjer muških i ženskih bolesnika 1:13). Bilo je 117 (29%) bolesnika (12 muških i 105 ženskih) s pojedinačnim čvorom štitne žlijezde i 289 (71%) bolesnika (17 muških i 272 ženskih) s multinodularnom strumom, dobnoga raspona 11-86 godina, medijan 55 godina. Nakon citološke analize konačna dijagnoza zloćudnog tumora postavljena je u šestoro (5%) bolesnika s pojedinačnim čvorom štitne žlijezde i u 15 (5%) bolesnika s multinodularnom strumom. Sve osobe s malignim tumorom u objema skupinama bile su žene. Zaključeno je kako nema razlike u riziku od maligniteta štitne žlijezde među bolesnicima s pojedinačnim čvorom štitne žlijezde i onih s multinodularnom strumom.

Ključne riječi: *Neoplazme štitne žlijezde – patologija; Neoplazme štitne žlijezde – imunologija; Karcinom papilarni; folikularni – imunologija; Struma nodularna – patologija; Iglena biopsija – metode*