

## The Relationship between Calcification of Thyroid Nodules and Thyroid Malignancies in Patients Referred to Ayatollah Taleghani Hospital

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### ABSTRACT

**Aim:** Most thyroid nodules are benign and only 3% to 7% of these nodules show malignant behavior and therefore will be associated with adverse consequences in the short and long term. What is clinically important is to differentiate between benign and malignant nodules before the onset of tumor-related consequences and involvement of other tissues and organs. Recently, the presence of calcification and its pattern in nodules has been emphasized as an important parameter in differentiating benign from malignant nodules, and therefore the present study sought to investigate the role of nodular calcification in predicting thyroid cancer.

**Methods:** In this study, patients with thyroid disorders including thyroid nodules were studied and included in the study of thyroid nodules with thyroid nodules with calcification. In this evaluation, the type of nodule, the number of nodules, the presence of calcification in the nodules, the type of calcification as well as evidence of thyroid malignancy were examined. Relevant results were confirmed by pathology evaluation Fine Needle Aspiration sample (FNA). The ultimate goal was to evaluate the role of calcification in thyroid nodules with evidence of malignancy in the thyroid.

**Results:** Regarding the relationship between calcified nodules and thyroid malignancy, calcified nodules were confirmed in 51.1% of malignant lesions and in 25.0% of benign lesions, indicating a significant difference between the two groups ( $p$  value equal to 0.047). Accordingly, the probability of calcification of malignant nodules was 3.12 times that of benign nodules. Regarding the presence of calcified nodules with malignant type, the prevalence of calcified nodules in FTC is equal to 0.60%, in HTC equal to 66.7%, in ATC equal to 0.50%, in MTC equal to 33.3% and in PTC equal to 0.50% evaluated. The prevalence of microcalcification in anaplastic lesions was 0.0%, in FTC was 33.3%, in Hashimoto's thyroiditis was 0.60%, in HTC was 100%, in MTC was 100% and in PTC was 68.4%.

**Discussion:** The presence of calcification pattern, especially microcalcification, is significantly more common in malignant nodules than benign thyroid nodules. Thyroid is beneficial. Therefore, the presence of nodular calcification would be significantly associated with a higher risk of thyroid cancer.

**Keywords:** Thyroid; Calcified nodule; Microcalcification

### INTRODUCTION

The thyroid is made up of relatively spherical follicles lined by a cubic to short cylindrical epithelium filled with thyroglobulin-rich colloids, which in response to TSH convert thyroglobulin to thyroxine (T4) and lower amounts to triiodothyronine (T3).

They do. T4 and T3 hormones are released into the systemic circulation to be transported to peripheral tissues. The net effect of these processes is to increase basal metabolic the thyroid calcitonin. This hormone increases the absorption of calcium by the skeletal system and inhibits bone resorption by osteoclasts.

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Thyroid lesions are divided into two categories: neoplastic and non-neoplastic [1]. Non-neoplastic lesions include simple goiter, made up of relatively spherical follicles lined by a cubic to short cylindrical epithelium filled with thyroglobulin-rich colloids, which in response to TSH convert thyroglobulin to thyroxine (T4) and lower amounts to triiodothyronine (T3). They do. T4 and T3 hormones are released into the systemic circulation to be transported to peripheral tissues. The net effect of these processes is to increase basal metabolic rate [1]. The thyroid gland also contains a population of parafollicular cells, or C cells, that make and secrete the hormoneloid goiter, nodular goiter, cystic nodules, Graves' and thyroiditis. Neoplastic lesions into two benign categories and malignant are divided. Benign neoplasms such as follicular adenomas, follicular neoplasms, and Hertel cell adenomas. Malignant neoplasms include papillary carcinoma, follicular carcinoma, medullary carcinoma, and anaplastic carcinoma [2]. Thyroid carcinomas most often occur in adults, although some types of papillary carcinomas may be seen in childhood. The predominance of the female sex among patients with thyroid carcinoma has been observed in the early and mid-adult years, possibly due to the development of estrogen receptors on the neoplasm of the thyroid epithelium. In contrast, the prevalence in childhood and late adulthood between males and females and their relative prevalence are [3]:

1. Papillary carcinoma (85%-75% of cases)
2. Follicular carcinoma (10%-20% of cases)
3. Modular carcinoma (5% of cases)
4. Anaplastic carcinoma (less than 5% of cases)

Most thyroid carcinomas are derived from the follicular epithelium, with the exception of medullary carcinoma, which originates in Para follicular or C cells. In terms of pathogenicity, several genetic and environmental factors are involved in the pathogenicity of thyroid cancers. With the development of thyroid cancer in members of a family, the importance of genetic factors can be realized. Familial modular carcinomas of the thyroid are seen in multiple end carbon neoplasms of type 2 with RET mutations in the germ cell line [3-5].

Thyroid nodules are a separate lesion from normal thyroid tissue. Autopsy studies have reported the discovery of these nodules in more than 50% of thyroid assessments. The prevalence of malignancy is between 3% and 7%.

## MATERIALS AND METHODS

### Ultrasonography is an important diagnostic tool in the evaluation of thyroid nodules

However, biopsy and histological evaluation are essential to confirm or rule out malignancy in these nodules. Accordingly, some societies, such as the American Thyroid Association (ATA), have proposed a five-tier classification of thyroid nodules that describes the need for biopsy in addition to ultrasonography evaluation of these nodules [6,7]. A significant proportion of thyroid nodules is intangible and asymptomatic and has a prevalence of about 20% to 76% in the general population. These small thyroid nodules can be used as an

important diagnostic tool in the evaluation of thyroid nodules by gradually achieving ultrasonography.

However, biopsy and histological evaluation are essential to confirm or rule out malignancy in these nodules. Accordingly, some societies, such as the American Thyroid Association (ATA), have proposed a five-tier classification of thyroid nodules that describes the need for biopsy in addition to ultrasonography evaluation of these nodules. A significant proportion of thyroid nodules is intangible and asymptomatic and has a prevalence of about 20% to 76% in the general population. More tracking and detection in 2015, the American Thyroid Association published its updated guidelines for assessing and treating thyroid nodules and assessing the risk of these nodules becoming cancerous [8,9].

This guideline describes the combined use of ultrasonography presentation of thyroid nodules along with their size to determine whether a biopsy will be necessary in addition to ultrasound for diagnosis. Based on the ultrasonography evidence of nodules on ultrasound, there are five levels of risk for malignant thyroid nodules in the form of high risk (70% to 90%), moderate risk (10% to 20%), low risk (5% to 10%), and very low risk (below 3%) and defined quite benign (below 1%).

**High suspicion nodules:** In terms of ultrasonography presentation, these nodules are large and hypotactic with one or more cases of the following features: irregular margin (infiltrative-micro bubble), microcalcification, more than wide in shape, rim calcification with little distribution of soft tissue and evidence of Extra-Thyroid Proliferation or ETE. In this classification, the risk of malignancy will be between 70% and 90% and the cut-off point for FNA will be the same size or more than 1 cm.

**Nodules with suspected moderate malignancy (intermediate):** In terms of ultrasonography manifestations, these nodules are hypotactic solid nodules with a smooth margin without microcalcification, extend beyond the thyroid, or are longer than wide. The risk of malignancy of this type of nodule is estimated between 10% and 20% and the cutting point for Fine Needle Aspiration (FNA) will be the same size or more than 1 cm.

**Nodules with suspected low malignancy (low):** These nodules are solid isoequic or hypovacuic nodules or cystic in nature with solid eccentric surfaces without microcalcification, with an irregular margin or extending beyond the thyroid gland, or longer than wide. The risk of malignancy of this type of nodules is estimated between 5% and 10% and the cutting point for FNA size will be equal to or more than 1.5 cm nodules with very little suspected malignancy.

These nodules will be completely spongy or almost cystic nodules without any of the ultrasonographic evidence described in the above classifications. In these cases, the risk of malignancy of this type of nodule is estimated to be less than 3% and the cut-off point for FNA size will be equal to or more than 2 cm. However, failure to perform FNA has also been declared acceptable [10,11].

**Benign nodules (benign:** These nodules will be completely cystic nodules without any evidence or solid components. The risk of malignancy of these nodules is estimated to be less than 1% and no biopsy is required for diagnosis. In general, calcification is seen in approximately 19.8% to 32.1% of thyroid nodules and is seen in both benign and malignant nodules.

Some patterns can be seen in the calcification of these nodules, such as the pattern of ovoid or marginal peripheral skin, dense intracranial calcifications, calcified spots, and microcalcification. Based on this point, microcalcification is strongly associated with papillary thyroid carcinoma and its histological type can be easily detected and examined by FNA with ultrasound guide. However, for other patterns of calcification, it is difficult to assess the features of the nodule based on ultrasound, and second, which pattern is more associated with the risk of malignancy. Methods: in this study, patients with thyroid disorders, including thyroid nodules, were examined and peripheral skin, dense intracranial calcifications, calcified spots, and microcalcification. Based on this point, micro calcification is strongly associated with papillary thyroid carcinoma and its histological type can be easily detected and examined by FNA with ultrasound guide. However, for other patterns of calcification, it is difficult to assess the features of the nodule based on ultrasound, and second, which pattern is more associated with the risk of malignancy. Methods: in this study, patients with included in the study of thyroid nodule peripheral skin, dense intracranial calcifications, calcified spots, and microcalcification. Based on this point, micro calcification is strongly associated with papillary thyroid carcinoma and its histological type can be easily detected and examined by FNA with ultrasound guide. However, for other patterns of calcification, it is difficult to assess the features of the nodule based on ultrasound, and second, which pattern is more associated with the risk of malignancy. Methods: in this study, patients with thyroid disorders, includes with thyroid nodules with calcification. In this evaluation, the type of nodule, the number of nodules, the presence of calcification in the nodules, the type of calcification as well as evidence of thyroid malignancy were examined. Relevant results were confirmed by pathology evaluation (FNA sample). The ultimate goal was to evaluate the role of calcification in thyroid nodules with evidence of malignancy in the thyroid. 3-5-data analysis method: the results were expressed as mean and standard deviation (mean  $\pm$  SD) for quantitative variables and as a percentage for stratified qualitative variables.

The t test was used to compare quantitative variables and the chi-square test was used to compare qualitative variables. Significance level was considered less than 0.05. For statistical analysis of data, SPSS software version 23 was used. Ethical considerations: At the 3-5-data analysis method: the results were expressed as mean and standard deviation (mean  $\pm$  SD) for quantitative variables and as a percentage for stratified qualitative variables.

The t test was used to compare quantitative variables and the chi-square test was used to compare qualitative variables. Significance level was considered less than 0.05. For statistical analysis of data, SPSS software version 23 was used. Time of the

study, patients were used t-test to compare quantitative variables and chi-square test to compare qualitative variables.

Data from the software their parents were explained about the goals and how to carry out the project, and it was ensured that information about them would only be provided to the project manager. Also, no cost was imposed on them in this study.

## RESULTS AND DISCUSSION

### Data from the project findings software

In this study, a total of 71 patients were included in the study. The mean age of patients was 43.15, 15, 15.39 years in the range of 20 years to 82 years. In terms of sex distribution, 15 cases (21.1%) were male and 56 cases (78.9%) were female. In terms of the total number of thyroid lymph nodes, 27 cases (38.0%) had one lymph node, 18 cases (25.4%) had two lymph nodes and 26 cases (36.6%) had more than two lymph node cases. In terms of lymph node type, in CT scan view, 43 cases (60.6%) were hippocampal, 5 cases (0.7%) were iso/hippocampus and 23 cases (32.4%). In total, calcified lymph nodes were reported in 31 cases (43.7%) (Table 1). Regarding the form of calcification, in 31 cases observed calcification, in 20 cases (64.5%) in the form of microcalcification, in 4 cases (12.9%) in the form of RIM, in 2 cases (6.5%) in the form of course, In 1 case (3.2%) in the form Internal, in 1 case (3.2%) in the form of macrocalcification, in 1 Regarding the form of calcification, in 31 cases observed calcification, in 20 cases (64.5%) in the form of microcalcification, in 4 cases (12.9%) in the form of RIM, in 2 cases (6.5%) in the form of coarse In 1 case (3.2%) in cc form (3.2%) in punctuate form, in 1 case (3.2%) in RIM mix and microcalcification and in 1 case (3.2%) the shape was round.

Regarding the observed malignancies, the highest frequency of malignancies was related to PTC in 38 cases (53.5%) and other malignancies were: FTC in 5 cases (0.7%), HTC in 3 cases (2/2). 4%), MTC was reported in 3 cases (4.2%) and anaplastic or ATC in 2 cases (2.8%). Other pathological lesions were benign and were: Hashimoto's thyroiditis in 13 cases (18.3%), follicular adenoma in 4 cases (5.6%), benign cysts in 1 case (1.4%), Colloid goiter in 1 case (1.4%) and colloid nodules in 1 case (1.4%). Regarding the margin of lesions, 46 cases (64.8%) had irregular margins and 25 cases (35.2%) had regular margins (Table 2). In terms of the relationship between calcified nodules and thyroid malignancy, calcified nodules were confirmed in 51.1% of malignant lesions and in 25.0% of benign lesions, indicating a significant difference between the two groups (p-value equal to 0.047). Accordingly, the probability of calcification of malignant nodules was 3.12 times that of benign nodules (Table 3). In terms of the presence of calcified nodules with malignancy, the prevalence of calcified nodules in FTC (Familial Tumoral Calcinosis) is equal to 0.60%, in HTC (Hyperphosphatemic Tumoral Calcinosis) equal to 66.7%, in ATC (Anaplastic Thyroid Cancer) equal to 0.50%, in MTC (Metastatic Tumoral Calcinosis) equal to 33.3% and in Pseudo Tumoral Calcinosis (PTC) equal to 0.50% evaluated

In contrast, the prevalence of calcified nodules in benign lesions was 38.5% in Hashimoto's thyroiditis, while nodules in other

lesions including follicular adenoma, colloid goiter, and colloidal nodules were completely non-calcified. In terms of calcification form and benign and malignant lesions, first of 20 microcalcified nodules, 19 (61.3%) related to PTC, 3.2% related to MTC, 6.5% related to HTC, 3.2% were related to ATC, 15% were related to Hashimoto's thyroiditis and 5% were related to FTC, and therefore 83.9% of microcalcifications were observed in malignant lesions.

In this regard, the prevalence of microcalcification in anaplastic lesions is 0.0%, in FTC is 33.3%, in Hashimoto's thyroiditis is 0.60%, in HTC is 100%, in MTC is 100% and in PTC is 68.4% evaluated. In our evaluation, the frequency of irregular margins in benign and malignant masses was 0.0% and 84.6%, respectively, which showed a significant difference (p-value less than 0.001). Also, in malignant and benign lesions, the frequency of hypovaco form is 84.6% and 0.40%, respectively, the frequency of hypo/iso form is 3.8% and 0.0% and the frequency of iso echo form is equal to 0.5 (Table 4). It was 11% and 60%, respectively, which indicated a significant difference between the two groups (p value was 0.042) According to the data presented in Table 4, what differentiated malignant and benign lesions from each other included nodule calcification (51.1% and 0.25%, Pvalue of 0.047, respectively), irregular margin (88.2% and 0.5%, respectively, p-value less than 0.001) and leukocytic echogenicity of the lesion in the form of lesion (78.4% and 0.15%, respectively, p-value less than 0.001) has been denoted.

Column 1	Column 2
Myangin Sun	39/15 ± Study 15/43
<b>Sexual distribution</b>	
Male	15 cases (1/21%)
female	Female 56 cases (78.9%)
<b>Number of lymph nodes</b>	
Two	18 items (4/25%)
More than two	26 cases (36.6%)
<b>Lymph node echogenicity</b>	
Hippo	43 cases (60.6%)
ISO/Hippo	5 items (0.7%)
Izwako	23 items (32.4%)
<b>Calcification</b>	
Calcified nodules	31 items (43.7%)
Non-calcified nodules	40 cases (56.3%)
<b>Pattern of calcification</b>	
Microcalcification	20 items (64.5%)

RIM	4 items (12.9%)
Coarse	2 items (6.5%)
Internal	1 item (2/3%)
Macrocalcification	1 item (2/3%)
Punctuate	1 item (2/3%)
RIM and microcalcification	1 item (2/3%)
Round	1 item (2/3%)

**Table 1:** Background characteristics of the studied patients.

Column 1	Column 2	Column 3
Benign lesion	Malignant lesion	Form of calcification
0/5%	0/2%	coarse
0/0%	0/2%	internal
0/0%	0/2%	macro-calcification
0/15%	3/33%	micro-calcification
0/0%	0/2%	punctuate
0/5%	9/5%	RIM
0/0%	0/2%	RIM/ microcalcification
0/0%	0/2%	Round

**Table 2:** Characteristics of the calcification form in benign and malignant lesions.

Non-calcified nodules	Calcified nodules	Type of lesion
5/47%	3/61%	PTC
0/5%	2/3%	MTC
5/2%	5/6%	HTC
0/5%	7/9%	FTC
0/20%	1/16%	Hashimoto's thyroiditis
5/2%	2/3%	Anaplastic lesions
5/2%	0/0%	Who is benign
5/2%	0/0%	Colloid goiter
5/2%	0/0%	Colloid nodules

0/10%	0/0%	Follicular adenoma
Total		
0/60%	6/80%	Malignant lesions
0/40%	4/19%	Benign lesions

**Table 3:** Relationship between calcification and type of benign lesions malignant and malignant.

Column 1	Column 2	Column 3	Column 4
Value P	Property	Malignant lesion	Benign lesion
204/0	2 items (0/10%)	13 items (25/25%)	Abundance of males
			Average age, years
272/0			Number of nodules involved
	7 items (0/35%)	20 items (39.2%)	One
	3 items (0/15%)	15 cases (29.4%)	Two
	10 items (0/50%)	16 cases (31.4%)	More
047/0	5 items (0/25%)	26 items (0.51%)	Nodule calcification
001/0>			Echogenicity of nodules
	3 items (0/15%)	40 cases (78.4%)	Hippo Echo
	0 items (0/0%)	5 items (9/8%)	Hypo/ISO Echo
	17 items (0.85%)	6 items (11.8%)	Hippo
001/0>			Lesion margin form
	1 item (0.5%)	45 items (88.2%)	Irregular

19 items (0/95%)	6 items (11.8%)	Regular
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**Table 4:** Comparison of benign and malignant lesion characteristics.

### CONCLUSION

As a final conclusion, the presence of calcification pattern, especially microcalcification, is significantly more common in malignant nodules than benign thyroid nodules. Malignant thyroid malignancy is beneficial. Therefore, the presence of nodular calcification with a high risk of thyroid cancer would be significant.

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