



## Research Article

# Retrospective Study Evaluating Histopathological Thyroid Findings in an Iodine-Sufficient Area: Correlation with Anthropometric Characteristics and Thyroid Gland Morphological Parameters

Ioannis Legakis<sup>1\*</sup>, Theodoros Bourchas<sup>2</sup>, Stylianos Archontakis<sup>2</sup>, Vasilis Psaltakos<sup>2</sup> and GP Chrousos<sup>3</sup>

<sup>1</sup>Endocrinology Department, Henry Dunant Hospital, Greece

<sup>2</sup>Head & Neck Clinic, Henry Dunant Hospital, Greece

<sup>3</sup>Professor Emeritus of Pediatrics and Endocrinology, National and Kapodistrian University of Athens School of Medicine, Athens, Greece

Submitted : 02 March, 2026

Accepted : 10 March, 2026

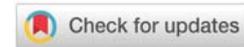
Published : 11 March, 2026

\*Corresponding author: Ioannis Legakis, Endocrinology Department, Henry Dunant Hospital, Greece, E-mail: ilegak@med.uoa.gr

**Keywords:** Nodular goiter; Thyroid; Follicular adenoma; Papillary carcinoma

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## Abstract

**Objectives:** To examine the association between thyroid nodular formation and histopathological outcomes in an iodine-sufficient region, we retrospectively reviewed histopathological findings from surgically excised thyroid specimens collected over three years (2021–2023) at Henry Dunant Hospital in the metropolitan area of Athens. Histological diagnoses, along with patient anthropometric characteristics and thyroid morphological parameters, were analysed to evaluate malignancy risk and enhance prognostic assessment.

**Methods:** Histopathological reports from 192 patients (138 men and 54 women) were retrospectively reviewed. Patients were categorised into three age groups: Group A (<40 years: 42 men, 14 women), Group B (40–69 years: 87 men, 35 women), and Group C (≥69 years: 9 men, 5 women). Correlations were performed between anthropometric characteristics and thyroid morphological parameters, including gland weight, gland dimensions, and the number of nodules per lobe.

**Results:** An age-related increase in thyroid gland weight was observed, which was more pronounced in the female population ( $p < 0.027$ ). Multinodular goitre was present in more than 80% of patients across all age groups. In women aged 40–49 years, a significantly larger nodule diameter was observed in the right thyroid lobe. In contrast, an increase in the number of nodules was noted exclusively in the left lobe of men aged ≥69 years.

The prevalence of a solitary thyroid nodule was similar in men aged <40 and 40–69 years (23.8% and 24.1%, respectively), while women showed a higher prevalence in the <40-year age group (42.9%).

No statistically significant sex-related differences were observed in the incidence of papillary or follicular thyroid carcinoma. However, papillary carcinoma predominated over follicular carcinoma in both sexes within the <40 and 40–69 age groups. Metastatic disease was more frequently observed in men aged 40–69 years. Medullary carcinoma was identified exclusively in men, with a prevalence of 2.3% in the 40–69-year age group. Follicular adenoma was the most common histopathological diagnosis across all age groups.

**Conclusions:** Consistent with previous reports, follicular adenoma was the most frequent histopathological finding in patients with multinodular goitre, while papillary carcinoma represented the predominant thyroid cancer subtype. Thyroid gland weight increased with age, particularly among women, but this increase was not associated with a higher risk of malignancy. Further studies are required to confirm these findings and better define their implications for long-term clinical outcomes.



## Introduction

Epidemiological and clinical evidence indicate that the prevalence of thyroid nodules varies with anthropometric factors, including sex, body mass index, and age, as well as with the method of detection (self-detection, palpation, ultrasonography, or autopsy) and geographic region. In recent years, incidence rates have increased, particularly among asymptomatic individuals undergoing routine screening, contributing to overdiagnosis and, in many cases, subsequent medical overuse [1].

The clinical evaluation of thyroid nodules relies on established diagnostic tools and management algorithms supported by cost-effectiveness analyses. Despite advances in ultrasound-based risk stratification systems—including improvements in ultrasonographic technology, shear-wave elastography, three-dimensional (3D) ultrasound imaging, and modern surgical techniques—considerable variability persists in the diagnosis and management of thyroid nodules [2,3].

To assess the malignant potential of thyroid nodules in an iodine-sufficient population, a retrospective study was conducted involving patients who underwent thyroidectomy at Henry Dunant Hospital over 3 years. Postoperative histopathological findings were correlated with patients' anthropometric characteristics and thyroid morphological parameters.

## Materials and methods

Histopathological reports from 192 patients (138 men and 54 women) were retrospectively reviewed. Patients were categorised into three age groups: Group A (<40 years: 42 men, 14 women), Group B (40–69 years: 87 men, 35 women), and Group C (≥69 years: 9 men, 5 women).

The anthropometric characteristics evaluated in this study included age and sex. Age was categorised into three groups (<40 years, 40–69 years, and ≥69 years), and sex was recorded as male or female. These variables were incorporated into the statistical analysis as grouping factors to examine their associations with thyroid morphological parameters, including gland weight, lobe volumes, and the number and diameter of nodules. Correlations were performed between anthropometric characteristics and thyroid morphological parameters, including gland weight, gland dimensions, and the number of nodules per lobe.

## Statistical analysis

Quantitative variables are presented using measures of central tendency and dispersion (mean, median, standard deviation, minimum, and maximum), whereas categorical variables are summarised using absolute frequencies and percentages. The Mann–Whitney U test was used to compare continuous variables between groups, and the Kruskal–Wallis test was used to compare continuous variables across more than two groups when appropriate.

Associations between categorical variables were evaluated using the Pearson chi-square test. When contingency tables contained small expected cell counts, particularly in analyses involving the ≥69-year age group, chi-square tests with Monte Carlo simulation were applied to obtain reliable *p*-values.

All statistical tests were two-sided, and a *p*-value <0.05 was considered statistically significant. In addition to *p*-values, effect size measures (risk differences, odds ratios or Cohen's *d*, where appropriate) were examined to facilitate clinical interpretation of observed group differences. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA).

## Results

Thyroid gland weight demonstrated a significant age-related increase, with a more pronounced effect observed in women (*p* < 0.027) (Table 1). Multinodular goitre was highly prevalent, occurring in more than 80% of cases across all age groups.

Among women aged 40–49 years, nodule diameter was significantly greater in the right thyroid lobe (*p* < 0.038) (Tables 2a,b), and corresponded to a small-to-moderate effect size (Cohen's *d* = 0.32). In contrast, in men, a significant increase in the number of nodules was observed exclusively in the left lobe in individuals older than 69 years (*p* < 0.022) (Table 1).

The prevalence of solitary thyroid nodules in men was comparable between the <40 and 40–69 age groups (23.8% and 24.1%, respectively). In women, solitary nodules were most frequently observed in the <40 age group (42.9%) (Table 3). Hence, the absolute risk difference between genders for the solitary nodules in the <40-year age group was 19.1%.

**Table 1:** Quantitative variables by age group and gender.

Variable	Gender	<i>p</i> -value (overall)	<i>p</i> -value (groups 1-2)	<i>p</i> -value (groups 1-3)	<i>p</i> -value (groups 2-3)
Right lobe volume (RLV)	Female	0.530			
	Male	0.399			
Left lobe volume (LLV)	Female	0.259			
	Male	0.188			
Thyroid gland weight (gr)	Female	0.049	0.198	0.027	0.051
	Male	0.160			
Right lobe nodules (RLN) (cm)	Female	0.149			
	Male	0.078			
RLN diameter (cm)	Female	0.311			
	Male	0.647			
Left lobe nodules (LLN)(cm)	Female	0.922			
	Male	0.033	0.109	0.022	0.059
LLN diameter (cm)	Female	0.519			
	Male	0.373			
Isthmus	Female	0.197			
	Male	0.791			
Isthmus nodules diameter(IND) (cm)	Female	0.516			
	Male	0.791			

- *p*-value (overall) compares if there is a difference between the 3 groups (Kruskal-Wallis' test). Pairwise comparisons were performed with Mann-Whitney test.
- Group 1: age<40years old
- Group 2: 40≤age<69
- Group 3: age≥69



**Table 2a:** Quantitative variables by gender and age group.

Variable	Age groups	Gender	N	Mean	Median	SD	Min	Max	p-value
Right lobe volume	Age<40	Male	42	36.85	18.00	41.97	0.00	216.00	0.150
		Female	14	53.96	40.35	52.12	8.75	200.00	
		Total	56	41.12	23.20	44.85	0.00	216.00	
	40≤Age<69	Male	87	42.94	22.50	53.95	0.00	356.25	0.775
		Female	35	57.80	30.00	139.03	0.00	840.00	
		Total	122	47.20	23.44	86.86	0.00	840.00	
	Age≥69	Male	9	81.26	70.00	91.77	0.00	250.00	1.000
		Female	5	52.20	66.00	28.83	15.00	80.00	
		Total	14	70.88	68.00	75.15	0.00	250.00	
	Total	Male	138	43.58	21.63	54.35	0.00	356.25	0.206
		Female	54	56.29	31.19	114.60	0.00	840.00	
		Total	192	47.16	24.60	76.13	0.00	840.00	
Left lobe volume	Age<40	Male	42	37.23	19.00	50.24	0.00	270.00	0.374
		Female	14	27.81	13.56	37.92	0.00	133.00	
		Total	56	34.88	17.25	47.31	0.00	270.00	
	40≤Age<69	Male	87	35.06	24.00	36.72	0.00	200.00	0.318
		Female	35	50.34	16.20	126.78	0.00	756.00	
		Total	122	39.44	23.50	74.31	0.00	756.00	
	Age≥69	Male	9	57.51	42.00	57.38	4.60	189.00	0.898
		Female	5	73.52	48.00	86.96	12.35	225.00	
		Total	14	63.23	45.00	66.46	4.60	225.00	
	Total	Male	138	37.19	24.00	42.71	0.00	270.00	0.309
		Female	54	46.64	16.10	106.79	0.00	756.00	
		Total	192	39.85	22.50	67.02	0.00	756.00	
Thyroid gland weight (gr)	Age<40	Male	42	28.54	19.25	28.40	0.50	174.00	0.188
		Female	14	37.47	24.50	31.02	10.70	108.00	
		Total	56	30.77	20.00	29.05	0.50	174.00	
	40≤Age<69	Male	87	34.70	23.00	34.64	7.00	200.00	0.755
		Female	35	31.23	26.00	20.61	8.00	100.00	
		Total	122	33.70	24.00	31.22	7.00	200.00	
	Age≥69	Male	9	68.69	49.00	56.07	8.20	160.00	1.000
		Female	5	56.54	52.00	35.12	20.70	113.00	
		Total	14	64.35	50.50	48.48	8.20	160.00	
	Total	Male	138	35.04	23.00	35.58	0.50	200.00	0.274
		Female	54	35.19	27.00	25.62	8.00	113.00	
		Total	192	35.08	24.00	33.02	0.50	200.00	
Right lobe nodules (RLN)(cm)	Age<40	Male	42	1.62	1.00	1.25	0.00	5.00	0.456
		Female	14	1.36	1.00	1.22	0.00	4.00	
		Total	56	1.55	1.00	1.23	0.00	5.00	
	40≤Age<69	Male	87	1.44	1.00	1.06	0.00	4.00	0.022
		Female	35	1.91	2.00	1.12	0.00	4.00	
		Total	122	1.57	1.00	1.10	0.00	4.00	
	Age≥69	Male	9	2.11	2.00	0.93	1.00	3.00	0.438
		Female	5	2.60	3.00	1.14	1.00	4.00	
		Total	14	2.29	2.50	0.99	1.00	4.00	
	Total	Male	138	1.54	1.00	1.12	0.00	5.00	0.097
		Female	54	1.83	2.00	1.18	0.00	4.00	
		Total	192	1.62	1.00	1.14	0.00	5.00	
RLN diameter (cm)	Age<40	Male	42	1.25	1.00	1.13	0.00	5.50	0.231
		Female	14	1.59	1.50	1.24	0.00	4.00	
		Total	56	1.33	1.00	1.16	0.00	5.50	
	40≤Age<69	Male	87	1.44	1.40	1.14	0.00	4.60	0.065
		Female	35	1.87	1.70	1.18	0.00	4.30	
		Total	122	1.56	1.50	1.16	0.00	4.60	
	Age≥69	Male	9	1.66	1.50	0.94	0.50	3.00	0.699
		Female	5	1.44	0.80	0.92	0.80	2.80	
		Total	14	1.58	1.30	0.90	0.50	3.00	
	Total	Male	138	1.40	1.25	1.12	0.00	5.50	0.038
		Female	54	1.76	1.50	1.17	0.00	4.30	
		Total	192	1.50	1.40	1.14	0.00	5.50	



Left lobe nodules (LLN) (cm)	Age<40	Male	42	1.67	1.00	1.41	0.00	4.00	0.190	
		Female	14	1.14	1.00	1.35	0.00	4.00		
		Total	56	1.54	1.00	1.40	0.00	4.00		
	40≤Age<69	Male	87	1.62	1.00	1.40	0.00	5.00	0.438	
		Female	35	1.80	2.00	1.35	0.00	5.00		
		Total	122	1.67	1.00	1.38	0.00	5.00		
	Age≥69	Male	9	1.78	2.00	1.39	0.00	4.00	0.147	
		Female	5	3.00	3.00	1.22	1.00	4.00		
		Total	14	2.21	2.50	1.42	0.00	4.00		
	Total	Male	138	1.64	1.00	1.39	0.00	5.00	0.674	
		Female	54	1.74	1.50	1.40	0.00	5.00		
		Total	192	1.67	1.00	1.39	0.00	5.00		
LLN diameter (cm)	Age<40	Male	42	0.98	0.70	1.05	0.00	3.60	0.515	
		Female	14	0.87	0.40	1.20	0.00	4.30		
		Total	56	0.95	0.65	1.08	0.00	4.30		
	40≤Age<69	Male	87	1.19	1.00	1.24	0.00	7.00	0.745	
		Female	35	1.28	0.90	1.27	0.00	5.00		
		Total	122	1.22	1.00	1.24	0.00	7.00		
	Age≥69	Male	9	1.37	1.20	1.32	0.00	3.60	0.797	
		Female	5	1.66	0.50	2.34	0.40	5.80		
		Total	14	1.47	0.90	1.67	0.00	5.80		
	Total	Male	138	1.14	0.80	1.19	0.00	7.00	0.981	
		Female	54	1.21	0.80	1.36	0.00	5.80		
		Total	192	1.16	0.80	1.24	0.00	7.00		
	Isthmus	Age<40	Male	41	0.20	0.00	0.60	0.00	3.00	0.580
			Female	14	0.07	0.00	0.27	0.00	1.00	
			Total	55	0.16	0.00	0.54	0.00	3.00	
40≤Age<69		Male	87	0.13	0.00	0.37	0.00	2.00	0.664	
		Female	35	0.11	0.00	0.40	0.00	2.00		
		Total	122	0.12	0.00	0.38	0.00	2.00		
Age≥69		Male	9	0.367	0.000	0.6964	0.0	2.0	0.364	
		Female	5	0.000	0.000	0.0000	0.0	0.0		
		Total	14	0.236	0.000	0.5759	0.0	2.0		
Total		Male	137	0.163	0.000	0.4733	0.0	3.0	0.270	
		Female	54	0.093	0.000	0.3512	0.0	2.0		
		Total	191	0.143	0.000	0.4424	0.0	3.0		
Isthmus nodules diameter (IND) (cm)		Age<40	Male	42	0.12	0.00	0.36	0.00	1.80	0.561
			Female	14	0.03	0.00	0.11	0.00	0.40	
			Total	56	0.09	0.00	0.31	0.00	1.80	
	40≤Age<69	Male	87	0.09	0.00	0.29	0.00	1.50	0.563	
		Female	35	0.12	0.00	0.48	0.00	2.50		
		Total	122	0.10	0.00	0.35	0.00	2.50		
	Age≥69	Male	8	0.26	0.00	0.49	0.00	1.10	0.524	
		Female	5	0.00	0.00	0.00	0.00	0.00		
		Total	13	0.16	0.00	0.39	0.00	1.10		
	Total	Male	137	0.11	0.00	0.32	0.00	1.80	0.267	
		Female	54	0.09	0.00	0.39	0.00	2.50		
		Total	191	0.10	0.00	0.34	0.00	2.50		

- Mann-Whitney test was implemented

**Table 2b:** Quantitative variables by gender.

Variable	Gender	N	Mean	Median	SD	Min	Max	p-value
Right lobe volume	Male	138	43.58	21.63	54.35	0.00	356.25	0.206
	Female	54	56.29	31.19	114.60	0.00	840.00	
	Total	192	47.16	24.60	76.13	0.00	840.00	
Left lobe volume	Male	138	37.19	24.00	42.71	0.00	270.00	0.309
	Female	54	46.64	16.10	106.79	0.00	756.00	
	Total	192	39.85	22.50	67.02	0.00	756.00	
Thyroid gland weight (gr)	Male	138	35.04	23.00	35.58	0.50	200.00	0.274
	Female	54	35.19	27.00	25.62	8.00	113.00	
	Total	192	35.08	24.00	33.02	0.50	200.00	
Right lobe nodules (RLN) (cm)	Male	138	1.54	1.00	1.12	0.00	5.00	0.097
	Female	54	1.83	2.00	1.18	0.00	4.00	
	Total	192	1.62	1.00	1.14	0.00	5.00	



RLN diameter (cm)	Male	138	1.40	<b>1.25</b>	1.12	0.00	5.50	<b>0.038</b>
	Female	54	1.76	<b>1.50</b>	1.17	0.00	4.30	
	Total	192	1.50	1.40	1.14	0.00	5.50	
Left lobe nodules (LLN) (cm)	Male	138	1.64	1.00	1.39	0.00	5.00	0.674
	Female	54	1.74	1.50	1.40	0.00	5.00	
	Total	192	1.67	1.00	1.39	0.00	5.00	
LLN diameter (cm)	Male	138	1.14	0.80	1.19	0.00	7.00	0.981
	Female	54	1.21	0.80	1.36	0.00	5.80	
	Total	192	1.16	0.80	1.24	0.00	7.00	
Isthmus	Male	137	0.16	0.00	0.47	0.00	3.00	0.270
	Female	54	0.09	0.00	0.35	0.00	2.00	
	Total	191	0.14	0.00	0.44	0.00	3.00	
Isthmus nodules diameter (IND)(cm)	Male	137	0.11	0.00	0.32	0.00	1.80	0.267
	Female	54	0.09	0.00	0.39	0.00	2.50	
	Total	191	0.10	0.00	0.34	0.00	2.50	

- Mann-Whitney test was implemented

**Table 3:** Qualitative variables by gender and age group.

Variable		N	%	N	%	% difference	p-value
<b>Age group: Age &lt; 40</b>							
<b>Gender</b>		<b>Males</b>		<b>Females</b>			
		42	100.0	14	100.0		
Subtotal thyroidectomy left lobe	No	40	97.6	14	100.0	-2.4	0.555
	Yes	1	2.4	0	0.0	2.4	
Subtotal thyroidectomy right lobe	No	40	97.6	14	100.0	-2.4	0.555
	Yes	1	2.4	0	0.0	2.4	
Total Thyroidectomy	No	3	7.1	0	0.0	7.1	0.304
	Yes	39	92.9	14	100.0	-7.1	
Multi-nodular Goitre (MNG)	No	8	19.0	4	28.6	-9.5	0.452
	Yes	34	81.0	10	71.4	9.5	
Single nodule	No	32	76.2	8	57.1	19.0	0.172
	Yes	10	23.8	6	42.9	-19.0	
In situ_ca	No	33	78.6	14	100.0	-21.4	0.059
	Yes	9	21.4	0	0.0	21.4	
Papillary_ca	No	29	69.0	11	78.6	-9.5	0.495
	Yes	13	31.0	3	21.4	9.5	
Follicular ca	No	36	85.7	12	85.7	0.0	1.000
	Yes	6	14.3	2	14.3	0.0	
Mixed_ca	No	36	85.7	12	85.7	0.0	1.000
	Yes	6	14.3	2	14.3	0.0	
Follicular adenoma	No	20	47.6	6	42.9	4.8	0.757
	Yes	22	52.4	8	57.1	-4.8	
Metastases lymph	No	40	95.2	14	100.0	-4.8	0.406
	Yes	2	4.8	0	0.0	4.8	
Hyperplastic_MNG	No	11	26.2	5	35.7	-9.5	0.495
	Yes	31	73.8	9	64.3	9.5	
Hurth cell adenoma	No						
	Yes						

Acidophilic adenoma	No	41	97.6	12	85.7	11.9	0.087
	Yes	1	2.4	2	14.3	-11.9	
Medullary_ca	No	40	95.2	12	85.7	9.5	0.231
	Yes	2	4.8	2	14.3	-9.5	
Pyramoid lobe	No	42	100.0	13	92.9	7.1	0.081
	Yes	0	0.0	1	7.1	-7.1	
	No	41	97.6	13	92.9	4.8	0.406
	Yes	1	2.4	1	7.1	-4.8	
<b>Age group: 40 ≤ Age &lt; 69</b>							
<b>Gender</b>		<b>Males</b>		<b>Females</b>			
		87	100.0	35	100.0		
Subtotal thyroidectomy left lobe	No	84	96.6	35	100.0	-3.4	0.266
	Yes	3	3.4	0	0.0	3.4	
Subtotal thyroidectomy right lobe	No	86	98.9	33	94.3	4.6	0.141
	Yes	1	1.1	2	5.7	-4.6	
Total Thyroidectomy	No	4	4.6	2	5.7	-1.1	0.796
	Yes	83	95.4	33	94.3	1.1	
Multi-nodular Goitre (MNG)	No	16	18.4	3	8.6	9.8	0.176
	Yes	71	81.6	32	91.4	-9.8	
Single nodule	No	65	74.7	29	82.9	-8.1	0.557
	Yes	21	24.1	6	17.1	7.0	
In situ_ca	No	77	88.5	30	85.7	2.8	0.671
	Yes	10	11.5	5	14.3	-2.8	
Papillary_ca	No	63	72.4	25	71.4	1.0	0.913
	Yes	24	27.6	10	28.6	-1.0	
Follicular_ca	No	71	81.6	28	80.0	1.6	0.837
	Yes	16	18.4	7	20.0	-1.6	
Mixed_ca	No	73	83.9	29	82.9	1.1	0.785
	Yes	14	16.1	6	17.1	-1.1	



Follicular adenoma							
	No	46	52.9	14	40.0	12.9	0.198
	Yes	41	47.1	21	60.0	-12.9	
Metastases lymph							
	No	81	93.1	31	88.6	4.5	0.145
	Yes	5	5.7	0	0.0	5.7	
Hyperplastic_MNG							
	No	22	25.3	4	11.4	13.9	0.091
	Yes	65	74.7	31	88.6	-13.9	
Hurth cell adenoma							
	No	80	92.0	31	88.6	3.4	0.555
	Yes	7	8.0	4	11.4	-3.4	
Acidophilic adenoma							
	No	84	96.6	31	88.6	8.0	0.086
	Yes	3	3.4	4	11.4	-8.0	
Medullary_ca							
	No	85	97.7	35	100.0	-2.3	0.366
	Yes	2	2.3	0	0.0	2.3	
Pyramid lobe							
	No	83	95.4	33	94.3	1.1	0.796
	Yes	4	4.6	2	5.7	-1.1	
<b>Age group: Age≥69</b>							
<b>Gender</b>		<b>Males</b>		<b>Females</b>			
		9	100.0	5	100.0		
Subtotal thyroidectomy left lobe							
	No	9	100.0	5	100.0	0.0	1.000
	Yes	0	0.0	0	0.0	0.0	
Subtotal thyroidectomy right lobe							
	No	9	100.0	5	100.0	0.0	1.000
	Yes	0	0.0	0	0.0	0.0	
Total Thyroidectomy							
	No	0	0.0	0	0.0	0.0	1.000
	Yes	9	100.0	5	100.0	0.0	
Multi-nodular Goitre							
	No	0	0.0	0	0.0	0.0	1.000
	Yes	9	100.0	5	100.0	0.0	
Single nodule							
	No	8	88.9	5	100.0	-11.1	0.439
	Yes	1	11.1	0	0.0	11.1	
In situ_ca							
	No	9	100.0	3	60.0	40.0	0.040
	Yes	0	0.0	2	40.0	-40.0	
Papillary_ca							
	No	8	88.9	3	60.0	28.9	0.052
	Yes	0	0.0	2	40.0	-40.0	
Follicular_ca							
	No	9	100.0	3	60.0	40.0	0.040
	Yes	0	0.0	2	40.0	-40.0	
Mixed_ca							
	No	9	100.0	3	60.0	40.0	0.040
	Yes	0	0.0	2	40.0	-40.0	
Follicular adenoma							
	No	3	33.3	1	20.0	13.3	0.597
	Yes	6	66.7	4	80.0	-13.3	
Metastases lymph							
	No	9	100.0	5	100.0	0.0	1.000
	Yes	0	0.0	0	0.0	0.0	
Hyperplastic_MNG							

	No	1	11.1	1	20.0	-8.9	0.649
	Yes	8	88.9	4	80.0	8.9	
Hurth cell adenoma							
	No	7	77.8	4	80.0	-2.2	0.923
	Yes	2	22.2	1	20.0	2.2	
Acidophilic adenoma							
	No	7	77.8	4	80.0	-2.2	0.923
	Yes	2	22.2	1	20.0	2.2	
Medullary_ca							
	No	9	100.0	5	100.0	0.0	1.000
	Yes	0	0.0	0	0.0	0.0	
Pyramid lobe							
	No	9	100.0	5	100.0	0.0	1.000
	Yes	0	0.0	0	0.0	0.0	

The chi-square test was implemented; when expected cell counts were small, Monte Carlo-simulated *p*-values were used.

No statistically significant sex-based differences were identified in the incidence of papillary or follicular thyroid carcinoma (Table 4). Papillary carcinoma appeared more frequent than follicular carcinoma in both sexes within the <40 and 40–69 age groups (Table 3); however, these observations should be interpreted descriptively unless supported by statistically significant differences. Metastatic disease was more frequently observed in men aged 40–69 years, although this difference did not reach statistical significance.

Medullary thyroid carcinoma was identified exclusively in men, with a prevalence of 2.3% in the 40–69 age group (Table 3). However, the number of cases was small, and no statistical inference can be drawn for the general population. Metastatic lymph node involvement was observed only among men in the 40–69-year age group (5.7%), corresponding to an absolute risk difference of 5.7% (OR ≈ 4.5); however, the small number of cases limits definitive inference.

Across all age groups, follicular adenoma was the most common histopathological diagnosis among resected thyroid specimens (Table 4).

## Discussion

Recent progress in the diagnosis and treatment of thyroid cancer has substantially transformed current management paradigms. Ultrasound-based risk stratification systems for thyroid nodules, together with minimally invasive therapeutic approaches for low-risk thyroid malignancies, have become integral components of routine clinical practice. Consequently, there is an increasing demand for well-designed randomised controlled trials and large-scale population-based observational studies to strengthen evidence-based decision-making and inform the development of clinical management guidelines for thyroid cancer [4–6].

Thyroid nodules are a common finding in the general population and are most frequently assessed using ultrasonography (US). Previous studies comparing solitary thyroid nodules (STNs) and multinodular goitre (MNG) have yielded heterogeneous results, particularly regarding patient age and sex [7].

**Table 4:** Quantitative variables by age group and gender.

Variable	Gender	p-value (overall)
Subtotal thyroidectomy left lobe	Female	0.823
	Male	-
Subtotal thyroidectomy right lobe	Female	0.793
	Male	0.569
Total thyroidectomy	Female	0.639
	Male	0.569
Multi-nodular Goitre	Female	0.361
	Male	0.113
Single nodule	Female	0.843
	Male	0.067
In situ_ca	Female	0.143
	Male	0.068
Papillary_ca	Female	0.191
	Male	0.717
Follicular_ca	Female	0.336
	Male	0.470
Mixed_ca	Female	0.705
	Male	0.419
Follicular adenoma	Female	0.501
	Male	0.650
Metastases lymph	Female	0.747
	Male	-
Hyperplastic_MNG	Female	0.618
	Male	0.141
Hurth cell adenoma	Female	0.102
	Male	0.855
Acidophilic adenoma	Female	0.050
	Male	0.855
Medullary_ca	Female	0.552
	Male	0.233
Pyramid lobe	Female	0.684
	Male	0.834

- p-value (overall) tests for a difference among the 3 groups (Chi-square test was implemented; when expected cell counts were small, Monte Carlo-simulated p-values were used). Pairwise comparisons were also performed using the Chi-square test.

- Group 1: age < 40 years old

- Group 2: 40 ≤ age < 69

- Group 3: age ≥ 69

Epidemiological evidence suggests that the prevalence of thyroid nodules may exceed 67%, depending on the diagnostic approach used (palpation, ultrasonography, or autopsy), with marked variation across geographic regions [8,9]. Estimates based on ultrasound screening and autopsy studies report prevalence rates ranging from 34% to 66% [10]. Several determinants, including female sex, higher body mass index (BMI), and increasing age, have consistently been associated with a greater likelihood of thyroid nodule development [11]. Moreover, women tend to develop thyroid nodules at an earlier age than men, while multinodular goitre has been more frequently linked to multicentric malignancy, particularly in papillary thyroid carcinoma [12].

Marked geographic differences have been reported, with Denmark and South Africa documenting nodular presentation rates of 54% and 79%, respectively, whereas substantially lower rates of approximately 30% have been observed in Canada and the United States [13].

Despite the high prevalence of thyroid nodules, the majority

are benign or lack ultrasonographic features indicative of malignancy and therefore have limited clinical relevance [14].

In agreement with previously published data, our findings showed that multinodular goitre was present in more than 80% of patients, irrespective of sex or age group. Thyroid gland weight increased progressively with age (with mean values rising from 30.8 g in individuals younger than 40 years to 64.4 g in those aged ≥69 years, representing a moderate-to-large standardised difference (Cohen's  $d \approx 0.8$ )), a trend that was more pronounced among female patients.

Sex-related differences in nodule characteristics were also identified. Women aged 40–49 years exhibited a significant increase in nodule diameter in the right thyroid lobe ( $p < 0.038$ ). In contrast, men showed an age-related increase in the number of nodules confined to the left thyroid lobe after age 69 years.

Age-dependent variation was also evident in the prevalence of solitary thyroid nodules. Among women, the highest frequency was observed in those younger than 40 years (42.9%), whereas men showed comparable prevalence rates in the <40-year (23.8%) and 40–69-year (24.1%) age categories. Some of our findings, though, are derived from small age strata, particularly the ≥69-year group, and should be interpreted cautiously and viewed as exploratory observations that require confirmation in larger cohorts.

The incidence of malignancy among thyroid nodules reported in the literature has risen substantially following the widespread implementation of thyroid ultrasonography. Reported malignancy rates range from 4% to 42%. They are influenced by regional cancer prevalence, incidental detection, environmental and endemic factors, inequalities in healthcare access, radiation exposure, and iodine deficiency, particularly in low- and middle-income countries [16,17]. Despite these regional disparities, the female-to-male ratio of thyroid cancer remains relatively stable worldwide at approximately 3:1 [18].

A retrospective analysis conducted at the Ankara Oncology Training and Research Hospital assessed thyroid nodularity and malignancy in a high-risk population. Clinically significant nodules were detected in 6.4% of female and 1.5% of male patients, while malignant lesions accounted for approximately 4% – 6% of all thyroid nodules [19].

Global incidence data from the *Cancer Incidence in Five Continents* database, spanning 1973 to 2007 and including 24 populations from the Americas, Asia, Europe, Africa, and Oceania, revealed a worldwide increase in thyroid cancer incidence. The highest rates were observed among women, particularly in Israel and within the United States Surveillance, Epidemiology, and End Results (SEER) registry [20].

A prospective cohort study conducted at the Brigham & Women's Hospital Thyroid Nodule Clinic between 1995 and 2011 further examined the relationship between age, thyroid nodularity, and cancer risk. The investigators reported that while the prevalence of thyroid nodules increased with age,

well-differentiated thyroid cancers were more likely to develop earlier in life. Conversely, older individuals more frequently presented with aggressive histological subtypes, including variants of papillary thyroid carcinoma, poorly differentiated carcinoma, and anaplastic carcinoma [21].

In China, thyroid cancer has become the fastest-growing malignancy, with an estimated annual increase in incidence of approximately 20% between 2003 and 2011 [22]. Subsequent analyses of temporal trends from 1990 to 2021 demonstrated a pronounced rise in incidence accompanied by a plateau in mortality reduction. This divergence from global trends is thought to reflect intensified diagnostic activity aimed at expanding screening coverage, as well as persistent concerns related to overdiagnosis [23]. Observational cross-sectional analyses based on Global Burden of Disease data further indicate that the overall burden of thyroid cancer across EU15+ countries is declining [24,25]. In contrast, the United States and Australia have shown increasing trends in age-standardised mortality rates (ASMR) and disability-adjusted life years (DALYs) over 30 years [26].

In line with the existing literature, our study demonstrated a modest female predominance, with women accounting for 79.7% of overall thyroid cancer cases compared with 70.3% in men. Nevertheless, no statistically significant sex-based differences were observed in the distribution of cancer subtypes. Specifically, ocular cancer accounted for 13.8% of cases in men and 13.0% in women; papillary carcinoma for 26.8% in men versus 27.8% in women; follicular carcinoma for 15.9% in men versus 20.4% in women; and mixed carcinoma for 13.8% in men versus 18.5% in women. Papillary carcinoma predominated over follicular carcinoma in both sexes within the <40 and 40–69-year age groups. An increased frequency of metastatic disease was observed exclusively among men aged 40–69 years.

Recent developments in molecular diagnostics have markedly improved both preoperative and postoperative accuracy in thyroid tumour characterisation and risk stratification, enabling more personalised clinical management [27,28]. However, conventional morphological assessment continues to face limitations related to reproducibility and quantitative evaluation in routine practice. With ongoing advances in artificial intelligence, the integration of morphological, clinical, molecular, and epigenetic data at the individual patient level may further enhance prognostic precision and optimise therapeutic decision-making [29].

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