Original Article

The impact of nodule size on malignancy risk in indeterminate thyroid nodules

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Background: The association between malignancy risk and nodule size in indeterminate thyroid nodules (ITNs) remains controversial. Thus, we aimed to explore the impact of nodule size as a predictor of cancer in patients with ITNs.

Methods: This cross-sectional study assessed 113 patients who underwent surgical intervention for ITNs, comparing two groups based on nodule size (≥4 or <4 cm). The correlation between nodule size and malignancy risk was examined. Other variables of interest included demographics, thyroid-stimulating hormone (TSH) levels, type of surgery, and ultrasound features.

Results: Of the 113 patients, 88.5% were aged <55 years, 76.1% were women, and 65.5% had nodules <4 cm. Mean nodule size was 3.4±2.3 cm. There was no significant correlation between malignancy risk and nodule size (P=0.55). An association was observed between <4 cm nodules and elevated TSH levels (P=0.03) and between ≥4 cm nodules and the presence of hypervascularity (P=0.04). Nodules <4 cm were more likely to have extrathyroidal extension, lymphovascular invasion, and positive margins than those ≥4 cm; however, this was not significant.

Conclusions: Our findings showed no association between nodule size and malignancy risk, suggesting that size alone is not a predictor of cancer development. Further prospective studies are required to confirm these results.

Keywords: Fine needle aspiration (FNA); malignancy risk; thyroid nodule (TN); thyroid nodule size

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Introduction

Background

Thyroid nodules (TNs) are a common phenomenon observed in daily practice, with the vast majority discovered by radiological studies, particularly ultrasonography (US). The first step in the evaluation of TNs includes physical examination and the collection of the patient's history. This is followed by neck US with or without fine needle aspiration (FNA) (1).

Both US and FNA are diagnostic techniques commonly used for the clinical assessment of TNs (2). US characterizes

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the nodules in terms of size, echogenicity, echotexture, composition, margins, calcification, shape, and lymph node status. Furthermore, it aids in risk stratification of TNs and, as a result, determines the necessity for FNA (1). The sensitivity of FNA has been reported to vary between 80% and 94%, whereas false negative rates range from 1.9% to 12.7% across different institutions. These variations can be attributed to the procedural methods used, namely US-guided or palpation-based biopsies (2). However, approximately 25% of all FNAs have uncertain cytology, and these are referred to as indeterminate TNs (ITNs). Surprisingly, these tend to be clinically challenging (1). Repeat FNA, molecular testing, or diagnostic thyroid lobectomy (TL) are recommended to exclude malignancy in ITNs (3). Of note, 70–80% of ITNs exhibit benign histology after thyroidectomy, suggesting unnecessary diagnostic procedures (1,4).

Whether larger TNs increase the risk of malignancy (ROM) remains controversial. Traditionally, a nodule ≥3 cm is considered to be a risk factor for malignancy. In 1995, Meko and Norton assessed the cytology results of 52 nodules that were ≥3 cm and found that the ROM was 21% and the rate of false negatives was 30% in benign FNAs (5). Most recent reports have confirmed that for large nodules (≥4 cm), there is a high ROM (6-8) as well as a high rate of false negatives in benign FNAs (8,9). McCoy *et al.* conducted a study including a cohort of 223 patients who presented with ≥4 cm nodules. These patients were prospectively managed and had histological diagnoses with a ROM of 19%. Notably, the ROM was 13% in ≥4 cm nodules with benign cytology, implying a high false negative rate (10).

Notably, Wharry *et al.* found that when FNA yielded a diagnosis of indeterminate cytology, there was a 29.6% likelihood of clinically relevant malignancy. In addition, the ROM associated with nodule size was higher in oncocytic neoplasms (11). In a study conducted by Banks *et al.* including 639 patients with suspicious or indeterminate cytological and histological results, the multivariable analysis showed that nodule size, patient age, and "suspicious for malignancy" cytology were significant indicators of thyroid cancer (TC) (12). Additionally, for each 1 cm increase in nodule size, nodules >2.5 cm had a 39% higher likelihood of being malignant. Nevertheless, when conducting predictive modeling, focusing solely on the size of a nodule was found to be insufficient to classify it as a high-risk indicator of malignancy (12).

Rationale and knowledge gap

Currently, no established criteria can effectively differentiate between malignant and benign lesions in the context of ITNs (1). Over the last decade, numerous diagnostic tools, including clinical, radiological, biochemical, and cytological features, have been investigated as predictors of malignancy in ITNs. However, it is unclear whether these tools are sufficiently reliable for guiding the management of patients with ITNs. In addition, there is an ongoing debate regarding the extent to which the nodule size can be used as the only criterion for determining the need for thyroidectomy (11). Considering the high rate of benign histology in ITNs after thyroidectomy, confirming risk factors that can predict the presence of malignancy in these nodules is imperative (1).

Objective

The objective of this study was to investigate the influence of nodule size as a predictive determinant for cancer in ITNs and to compare the aggressiveness features of malignant nodules <4 and ≥4 cm. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-12/rc).

Methods

The current investigation was a cross-sectional study conducted at King Faisal Specialist Hospital & Research

Highlight box

Key findings
- Nodule size was not associated with the risk of malignancy (ROM) in indeterminate thyroid nodules (ITNs).

What is known and what is new?
- Reports regarding the association between nodule size and malignancy are conflicting, although nodules ≥4 cm are generally considered to be a risk factor for cancer.
- There is a high rate of benign histology in indeterminate nodules after thyroidectomy.
- This study sought to confirm the impact of nodule size on the ROM in ITNs.

What is the implication, and what should change now?
- Our findings suggest that size alone should not be used as a predictor of malignancy in ITNs.

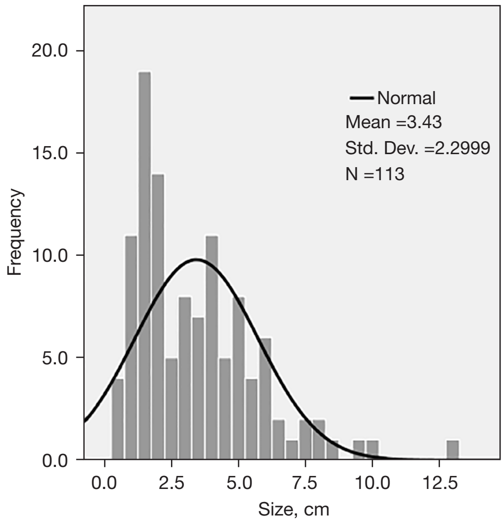

Figure 1 Histogram of nodule size in cm.

Centre, Riyadh, Saudi Arabia, which is known for its extensive expertise in TC surgery. Following the acquisition of ethics approval from the Regional Research and Ethics Committee of King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia (protocol code: 2235446; date of approval: November 6, 2023), an analysis was conducted on 113 patients who underwent thyroidectomies for Bethesda III TNs [scored according to The Bethesda System for Reporting Thyroid Cytopathology (13)] between January 2011 and December 2014. We used a dataset gathered from our previously published study (14), although two of the reported cases were excluded from the present study due to the unavailability of nodule size. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). As this was a retrospective analysis, informed consent was not required.

A data collection sheet was used to systematically capture and arrange the acquired data. The data encompassed several parameters, including patient demographics, US-based assessment of nodules, thyroid-stimulating hormone (TSH) levels, type of surgical procedure, and final histopathological diagnosis (benign *vs.* malignant).

The primary objective was to explore the correlation between the size of nodules and the histopathological outcomes following surgery. Additionally, we analyzed the influence of patient demographics, US-based assessment of nodules, TSH levels, and the type of surgical procedure [TL *vs.* total thyroidectomy (TT)]. The analysis also incorporated aggressive tumor characteristics, such as extrathyroidal extension, lymphovascular invasion, lymph node metastasis, and positive margins, whenever available. The analysis was conducted on the entire dataset, after which the patients were stratified into two groups based on the preoperative size of the index tumor (≥4 *vs.* <4 cm). In addition, we divided the participants based on their age at diagnosis (<55 or ≥55 years), according to the eighth edition of the American Joint Committee on Cancer/tumor-node-metastasis (TNM) cancer staging system (15).

Statistical analysis

Descriptive data are presented as counts and percentages for nominal variables and as mean ± standard deviation (SD) for numerical variables. Two comparisons were performed in this study. The first comparison involved binary data, specifically the differentiation between nodules measuring <4 cm and those measuring ≥4 cm on preoperative US imaging. The second comparison used continuous data, specifically the actual size of the nodules measured in cm. Associations were assessed using χ^2 and Fisher exact tests for categorical data and independent *t*-tests or Mann-Whitney *U* tests for continuous variables. Effect sizes are expressed as odds ratios (ORs) or as mean differences with 95% confidence intervals (CIs). Statistical analyses were performed using R (version 3.4.3; developed by the R Foundation for Statistical Computing, Vienna, Austria) and SPSS (version 23; IBM, Armonk, NY, USA). A threshold of P<0.05 was set for statistical significance.

Results

This study included a total of 113 participants with the majority <55 years (n=100, 88.5%) and the remaining ≥55 years (n=13, 11.5%). Of the total, 76.1% (n=86) were female. The distribution of nodules by laterality was as follows: 54.0% (n=61) were located in the right lobe, 42.5% (n=48) in the left lobe, and 3.5% (n=4) in the isthmus.

In terms of TSH levels, most of the patients (n=90, 82.6%) fell within the normal range (0.27–4.2 mIU/L), whereas 11.0% (n=12) had high levels (>4.2 mIU/L) and 6.4% (n=7) had low levels (<0.27 mIU/L). When considering the type of surgical intervention, 28.3% (n=32) of the participants underwent TT, whereas 71.7% (n=81) underwent TL.

The results of the pathological examination showed that 52.2% (n=59) of the nodules were benign and 47.8% (n=54) were malignant. In terms of nodule size, the mean was 3.4±2.3 cm, as shown in *Figure 1*; 65.5% (n=74) of the

Table 1 The pathological types and subtypes of malignant nodules (n=54)

Features	N (%)	<4 cm (n=37), n/N (%)	≥4 cm (n=17), n/N (%)	P value
Papillary thyroid carcinoma	49 (90.7)	35/37 (94.6)	14/17 (82.4)	0.10[†]
Classic	9	7/9 (77.8)	2/9 (22.2)	
Follicular variant	29	21/29 (72.4)	8/29 (27.6)	
Columnar cell	1	0	1/1 (100.0)	
Tall cell	3	3/3 (100.0)	0	
Oncocytic	4	2/4 (50.0)	2/4 (50.0)	
Not reported	3	2/3 (66.7)	1/3 (33.3)	
Follicular thyroid carcinoma	3 (5.6)	2/37 (5.4)	1/17 (5.9)	
Oncocytic	2	2/2 (100.0)	0	
Not reported	1	0	1/1 (100.0)	
Lymphoma (mucosa-associated lymphoid tissue)	2 (3.7)	0	2/17 (11.8)	

[†], the P value was estimated using the Chi-square test and assessed the correlation between pathological types (3×2 contingency table) and nodule size.

Table 2 Comparison of aggressiveness features between malignant nodules <4 and ≥4 cm (n=54)

Aggressiveness features	All malignant cases (n=54), n (%)	<4 cm (n=37), n (%)	≥4 cm (n=17), n (%)	Effect size (95% CI)	P value
Extrathyroidal extension				0.67 (0.55–0.81)	0.99
Yes	2 (3.7)	2 (5.4)	0		
No	52 (96.3)	35 (94.3)	17 (100.0)		
Lymphovascular invasion				0.77 (0.17–3.39)	0.99
Yes	11 (20.4)	8 (21.6)	3 (17.6)		
No	43 (79.6)	29 (78.4)	14 (82.4)		
LN metastasis				1.51 (0.22–9.9)	0.64
Yes	5 (9.3)	3 (8.1)	2 (11.8)		
No	49 (90.7)	34 (91.9)	15 (88.2)		
Positive margins				0.51 (0.05–4.9)	0.99
Yes	5 (9.3)	4 (10.8)	1 (5.9)		
No	49 (90.7)	33 (89.2)	16 (94.1)		

CI, confidence interval; LN, lymph node.

nodules were <4 cm, and 34.5% (n=39) were ≥4 cm.

In malignant cases (n=54), the pathological types and subtypes were compared according to the size of the nodules, as shown in *Table 1*. There was no statistically significant difference between the types of pathology and nodule size (P=0.10). Papillary TC (PTC) was the predominant type of TC.

Table 2 shows the comparison between malignant nodules <4 and ≥4 cm in terms of aggressiveness features. Nodules <4 cm were more likely to have extrathyroidal extension, lymphovascular invasion, and positive margins than those ≥4 cm. However, no statistically significant differences were observed.

The tabulated data comparing several variables with the size of the nodules, as both a continuous and binary variable, is shown in *Table 3*. In the group of patients aged

Table 3 Comparison between nodules (n=113) stratified by size (<4 *vs.* ≥4 cm)

Variables	Size (cm)†	<4 cm (n=74)‡	≥4 cm (n=39)‡	Effect size (95% CI)	P value
Age (years)				1.74 (0.54–5.6)	0.36
<55	3.4±2.3	67 (90.5)	33 (84.6)		
≥55	3.7±2.4	7 (9.5)	6 (15.4)		
Gender				0.86 (0.35–2.21)	0.81
Male	3.2±1.9	17 (23.0)	10 (25.6)		
Female	3.4±2.4	57 (77.0)	29 (74.4)		
Pathology				0.77 (0.35–1.68)	0.55
Benign	3.5±2.1	37 (50.0)	22 (56.4)		
Malignant	3.4±2.5	37 (50.0)	17 (43.6)		
TSH (mIU/L)^				0.36§ (0.15–0.88)	0.03
<1	4.5±2.5§	13 (18.6)	15 (38.5)		
≥1	3.2±2.1	57 (81.4)	24 (61.5)		
Presence of thyroiditis				–	0.54
Yes	1.7±0.07	2 (2.7)	0		
No	3.5±2.3	72 (97.3)	39 (100.0)		
Type of surgery				0.99 (0.41–2.34)	>0.99
Total thyroidectomy	3.6±2.8	21 (28.4)	11 (28.2)		
Thyroid lobectomy	3.4±2.0	53 (71.6)	28 (71.8)		
US features^					
Echogenicity				0.196	–
Hypoechoic	3.5±2.3	39 (54.2)	19 (52.8)		
Isoechoic	3.8±2.3	9 (12.5)	9 (25.0)		
Hyperechoic	2.9±2.2	24 (33.3)	8 (22.2)		
Content				0.39	–
Solid	2.6±2.3	44 (61.1)	25 (69.4)		
Predominantly solid	3.3±2.3	21 (29.2)	10 (27.8)		
Predominantly cyst-like	2.2±1.4	7 (9.7)	1 (2.8)		
Shape				1.5 (0.69–3.5)	0.40
Ovoid	3.6±2.5	43 (59.7)	25 (69.4)		
Irregular	3.1±1.7	29 (40.3)	11 (30.6)		
Echotexture				0.50 (0.22–1.14)	0.10
Homogenous	3.7±2.5	26 (36.1)	19 (52.8)		
Heterogenous	3.2±2.1	46 (63.9)	17 (47.2)		
Margins				0.53 (0.31–1.16)	–
Smooth	3.7±2.5	40 (55.6)	23 (63.9)		
Ill-defined	3.01±1.8	32 (44.4)	13 (36.1)		

Table 3 (*continued*)

Table 3 (*continued*)

Variables	Size (cm)†	<4 cm (n=74)‡	≥4 cm (n=39)‡	Effect size (95% CI)	P value
Calcification				0.64 (0.23–1.81)	0.46
Yes	2.7±2.0	17 (23.6)	6 (16.7)		
No	3.6±2.3	55 (76.4)	30 (83.3)		
Vascularity				0.41 (0.17–0.97)	0.04
Hypervascular	3.8±2.7§	35 (48.6)	25 (69.4)		
Hypovascular	2.9±1.5	37 (51.4)	11 (30.6)		
Lymphadenopathy				2.12 (0.49–9.04)	0.43
Yes	4.4±2.4	4 (5.6)	4 (11.4)		
No	3.3±2.3	68 (94.4)	32 (88.9)		
Peripheral halo				1.5 (0.69–3.54)	0.31
Yes	3.6±2.3	36 (50.0)	22 (61.1)		
No	3.2±2.3	36 (50.0)	14 (38.9)		

†, nodule size as a continuous variable, was presented as mean ± standard deviation; ‡, nodule size as a binary variable, was presented as n (%); ^, of 113 patients, only 109 had available TSH levels and only 108 had available US results; §, these P values are estimated by independent *t*-test, and the mean difference with 95% CI is reported. CI, confidence interval; TSH, thyroid-stimulating hormone; US, ultrasonography.

<55 years, a total of 33 patients (33.0%) presented with nodules measuring ≥4 cm, whereas 67 (67.0%) had nodules <4 cm in size. Within the group with nodules measuring ≥4 cm, there were 10 (25.6%) male patients and 29 (74.4%) female patients. With respect to the pathological diagnosis of nodules ≥4 cm, 22 cases (56.4%) were classified as benign and 17 cases (43.6%) as malignant. Conversely, for the subset of nodules measuring <4 cm, 37 cases (50.0%) were benign, whereas the remaining 37 cases (50.0%) were malignant. No correlation was observed between malignancy and nodule size.

An association was observed between a smaller nodule size and higher mean TSH levels. Nodules <4 cm had TSH levels ≥1 mIU/L in 81.4% of cases, whereas ≥4 cm nodules had TSH levels ≥1 mIU/L in only 61.5% of cases. A notable difference was observed when the size was examined as a continuous variable. Specifically, nodules with TSH levels ≥1 mIU/L exhibited a smaller average size (mean, 3.2 cm) than nodules with TSH levels <1 mIU/L (mean, 4.5 cm), and this difference was statistically significant (P=0.03).

Interestingly, two nodules, accounting for 2.7% of the sample, exhibited thyroiditis and measured <4 cm. In addition, within the group of patients who received TT, 11 cases (28.2%) had nodules ≥4 cm, whereas 21 cases (28.4%) presented with nodules <4 cm. However, these correlations were not statistically significant.

Table 3 also presents data pertaining to the US characteristics of the nodules, specifically echogenicity, content, shape, echotexture, margins, calcification, lymphadenopathy, and peripheral halos. The presence of vascularity was associated with nodule size, indicating that larger nodules (mean, 3.8 cm) had hypervascularity, whereas smaller nodules (mean, 2.9 cm) had hypovascularity, with a statistically significant P value of 0.04. The distribution of these traits was presented in distinct categories for nodules measuring <4 and ≥4 cm in size.

Discussion

Key findings

The correlation between nodule size and ROM in ITNs remains a topic of debate, with discordant results and conflicting conclusions. Therefore, this study aimed to investigate the influence of nodule size as a predictive determinant of TC. Our findings indicated that nodule size was not associated with the ROM in ITNs. However, smaller TNs were associated with elevated TSH levels and larger TNs with the presence of hypervascularity. Moreover, although not statistically significant, nodules

<4 cm were more likely to have extrathyroidal extension, lymphovascular invasion, and positive margins than those ≥4 cm.

Strengths and limitations

Our study is among a limited number of studies that specifically investigated the impact of nodule size on the ROM in ITNs. However, there were some limitations to our study. The inclusion criteria were limited to surgically removed nodules, resulting in a selection bias. Additionally, the occurrence of type II statistical errors was unavoidable because of the limited sample size.

Comparison with similar researches

FNA is a useful method to assess TNs. It demonstrates high accuracy rates in detecting most benign and malignant nodules, especially when used in conjunction with US, leading to decreased sampling errors in large nodules (1,2). Notably, core-needle biopsy is an alternative method that is currently under extensive debate. Nevertheless, the optimal management strategy for nodules that are ≥4 cm remains unclear (2). Some authors recommend (2) diagnostic lobectomies for TNs that are ≥4 cm because of the higher likelihood of false-negative FNA results. They also contend that the size of a nodule is an independent determinant for TC and that a nodule measuring ≥4 cm carries a greater risk of being malignant. In contrast, other investigators advocate the use of US-guided FNA for any nodules that are ≥1 cm as they share similar characteristics and should be examined using the same approach (2). Previous studies have reported comparable sensitivities and predictive values of FNA for nodules measuring <4 cm and those measuring ≥4 cm. Furthermore, the results of US-guided FNA can potentially alter the course of treatment by providing evidence to support the decision between surgical intervention or surveillance (2).

A study including 382 TNs ≥4 cm found that the clinically relevant ROM was 22%, and this nodule size was considered to be an independent indication for thyroidectomy. In the same study, histologically identified malignancy was discovered in 20% of nodules with no worrisome US features and in 10.4% of nodules with benign cytology on FNA, resulting in the recommendation for diagnostic thyroidectomy (LT or TT) in all ≥4 cm TNs (11). Moreover, a meta-analysis of 19 studies found that male sex and nodule size >4 cm were risk factors for malignancy in ITNs. Conversely, nodules with a diameter <4 cm were correlated with a benign outcome (16). According to Mehta *et al.*, nodule size is an independent risk factor for malignancy in mutation-negative atypia of undetermined significance/follicular lesions of undetermined significance (AUS/FLUS) TNs. Furthermore, the probability of malignancy was observed to rise by 4.3% for each additional mm increase in nodule size. Thus, in certain cases, individuals who have small TNs with no detectable mutations and fall under the AUS/FLUS category may be effectively treated with US surveillance instead of thyroidectomy (17).

Similar to our results, some investigators have found that the ROM in TNs exhibits an inverse relationship with nodule size, whereby larger nodules tend to have lower rates of cancer (18). Furthermore, a study of 1,023 patients revealed no significant correlation between nodule size and ROM. This finding suggests that relying solely on nodule size rather than FNA as a basis for treatment decision-making is inadvisable (19). Additionally, Cozzani *et al.* demonstrated no correlation between size of ITNs and ROM, features of tumor aggressiveness, and oncological outcomes in the setting of differentiated TC (DTC) (20). Similarly, Valderrabano *et al.* established that the size of an ITN measuring ≥4 cm did not exhibit any significant association with an elevated ROM, increased tumor aggressiveness, or worse clinical outcomes; these conclusions were accompanied by an expression of confidence in the representativeness of their research and an assertion that the findings possessed broad applicability despite the inherent limitations of their study methodology. Indeed, most ITNs, irrespective of their size, were found to be benign or low-risk malignant tumors, indicating that TL could serve as an adequate initial therapeutic option (4).

Explanations of findings

This phenomenon can be attributed to several factors. First, in contrast to other cytological categories (suspicious for malignancy or malignancy) that typically correlate with a poorer thyroid differentiation score and PTC, most malignant ITNs are characterized as low-risk malignant lesions. Second, the reclassification of noninvasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTP) affected the rates of cancer within institutional settings. Hence, NIFTPs are no longer classified as malignant, which should result in a notable reduction in inter-institutional variability in the incidence rates of uncertain cytological categories of malignancy. Lastly, TT is no longer recommended for all DTCs >1 cm. TL may be sufficient as an appropriate therapy for NIFTP of any size, intrathyroidal DTCs <4 cm, minimally invasive follicular TCs, and intrathyroidal encapsulated follicular variants of PTCs (21). This therapeutic de-escalation strategy for low-risk malignant lesions is supported by the evidence that the extent of surgery does not appear to alter recurrence or survival rates and that TLs have a lower rate of complications than TTs (11% *vs.* 20%, respectively) (4). Additionally, a more conservative surgical approach allows for the preservation of thyroid function in approximately 80% of cases, and the results and possible complication rate of a two-step thyroidectomy are comparable to those of TT (4). A retrospective study of 652 ITNs (106 nodules >4 cm and 546 nodules <4 cm) found that malignant ITN lesions of any size were frequently well-differentiated, with low-risk follicular patterns and favorable prognoses. Therefore, in the absence of other indications for TT, TL was suggested to be an acceptable procedure for >90% of solitary ITN, regardless of lesion size (4).

Furthermore, performing TT for ITNs based on lesion size alone leads to overtreatment, increasing the likelihood of postoperative complications and necessitating lifetime thyroid hormone replacement therapy (4). A recent meta-analysis of seven studies involving 10,817 lesions found that TNs measuring 3–5.9 cm had a 26% greater ROM than nodules measuring <3 cm. In contrast, the ROM decreased by 16% when the size of the nodule was ≥6 cm (22). Our findings showed that the ROM in <4 cm nodules was higher than those ≥4 cm, which is in accordance with the results of Varshney *et al.* (2). In addition, the aggressiveness features (except lymph node metastasis) were more likely to be found in nodules <4 cm than in those ≥4 cm; although not statistically significant, these differences are in line with a previously published study (4). Furthermore, the presence of thyroiditis was associated with nodules <4 cm, which is in accordance with the study by Osborne *et al.* (23).

Currently, therapeutic approaches have expanded beyond surgery and surveillance. Radiofrequency ablation, a newly proposed minimally invasive technique, is currently a subject of ongoing international debate. It is performed under US guidance and considered a viable option for individuals with benign or low-risk TNs. Moreover, the technique is believed to decrease the nodule volume from 60% to 100% (24). Nonetheless, further research is required to elucidate the risks and advantages of this procedure compared with more conventional surgeries.

Implications and actions needed

Overall, TL is the most appropriate surgical approach for ITNs (3). Although some authors suggest that TT should be indicated in ITNs with nodule sizes >4 cm because of the increased ROM (21), this procedure is associated with postoperative complications such as hypothyroidism, hypoparathyroidism, and recurrent laryngeal nerve injury (1) and should be avoided if possible. Furthermore, as the majority of ITNs (70–80%) have benign final histopathology, those patients who received TT and had benign pathology were overtreated. Other factors that influence surgical decision-making for ITNs (TL *vs.* TT) include the presurgical likelihood of malignancy based on clinical risk factors (family history and/or history of radiation), sonographic features, cytological diagnosis, molecular testing status, patient preference, comorbidities, and the presence of hyperthyroidism and contralateral nodules (21). This demonstrates the ongoing challenges in the setting of ITNs, and further research is required to clarify the optimal treatment strategies.

Conclusions

The results of our study indicate that there is no correlation between nodule size and ROM, suggesting that nodule size alone is not a determining factor for TC. However, extensive and thorough prospective studies are required to validate these findings.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-12/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-12/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.

com/article/view/10.21037/gs-24-12/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Regional Research and Ethics Committee of King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia (protocol code: 2235446; date of approval: November 6, 2023). Patient consent was waived due to the retrospective nature of the study.

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