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ORIGINAL RESEARCH ARTICLE

High rates of aggressive features in young Vietnamese females with papillary thyroid carcinoma: Associations with preoperative risk factors

Nguyen Van De*, Dao Thi Huyen, Dinh Huu Tam

Department of Pathology, 108 Military Central Hospital, Hanoi 11650, Viet Nam

*** Corresponding author:** Nguyen Van De, Doctorde108@gmail.com

ABSTRACT

Background: Thyroid carcinoma represents a significant global health burden, rising worldwide incidence. Papillary thyroid carcinoma (PTC) accounts for most cases, but aggressive variants with capsular invasion and nodal metastases require more intensive treatment. Reported rates of these capsular invasion and cervical lymph node metastasis vary widely. This study aimed to elucidate associations between clinical/tumor characteristics, capsular invasion, and nodal metastasis in Vietnamese PTC patients. **Methods:** This retrospective cohort study examined 1626 patients with cytologically/histologically confirmed thyroid carcinoma at a referral center in Vietnam during 2018–2020. Data collected included demographics, imaging, cytology, tumor features, capsular invasion, and nodal metastasis. Associations were analyzed using chi-squared tests and binary logistic regression. **Results:** Most patients were young (≤ 45) females with small papillary carcinomas. High rates of capsular invasion (58.7%) and nodal metastasis (28.5%) were observed. Capsular invasion was associated with higher TIRADS categories, Bethesda cytological categories, larger tumors, and papillary histology. Nodal metastasis was linked to younger age, male sex, higher TIRADS categories, larger tumors, papillary histology, and capsular invasion. Binary logistic regression identified TIRADS categories, Bethesda cytological categories, larger tumor size, younger age, male sex, and capsular invasion as independent predictors. **Conclusion:** Unexpectedly high rates of capsular invasion and cervical lymph node metastasis were found. TIRADS, Bethesda system, tumor size, age, sex, and capsular invasion were significant preoperative risk factors for aggressive PTC behaviors.

Keywords: papillary thyroid carcinoma; capsular invasion; cervical lymph node metastasis; TIRADS; Bethesda; tumor size; age; sex

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1. Introduction

Thyroid carcinoma represents a significant global public health burden, with rising incidence rates worldwide in recent years[1,2]. Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, representing approximately 80%–90% of all primary thyroid neoplasms[3]. While most PTCs follow an indolent clinical course with excellent prognosis, more aggressive variants exhibit capsular invasion, extrathyroidal extension, and cervical lymph node metastases, necessitating more intensive treatment approaches[4].

Despite considerable research, gaps in knowledge remain regarding the prevalence and predictors of aggressive disease characteristics. Reported rates of capsular invasion in PTC vary widely in the literature, ranging from 10%–40% across studies[5,6]. Similarly, reported cervical lymph node metastasis rates range from 15%–90%, reflecting differences in study populations, disease staging, and

diagnostic criteria[7–9]. The factors driving this heterogeneity, particularly the independent contributions of variables like age, sex, and cytologic findings, remain poorly characterized[10,11]. Importantly, clinical management differs considerably between regions. Asian countries like Japan have seen increasing popularity of active surveillance for small papillary microcarcinomas[12]. However, surgical resection remains the predominant approach in Vietnam, with active surveillance rarely utilized for papillary microcarcinomas under 10 mm based on local registry data. Few studies have evaluated these associations in Vietnamese patients, who may differ from Western populations[13].

Accordingly, the present study sought to delineate the clinicopathological profile of thyroid carcinoma and elucidate associations between clinical and tumor characteristics and capsular invasion and cervical lymph node metastasis, specifically among Vietnamese patients diagnosed at a major referral center. We hypothesized that sonographic features concerning for malignancy, large tumor size, and high-grade cytology would independently predict capsular and lymphovascular invasion. By clarifying these relationships in a unique patient population, the results of this study aim to provide novel insights into aggressive disease patterns in Vietnamese patients with PTC. Findings may enable more accurate preoperative risk stratification and optimize individualized management decisions.

2. Materials and methods

2.1. Study population and design

This retrospective, single-center cohort study examined the association between clinicopathologic factors and capsular invasion and cervical lymph node metastasis in 1626 patients diagnosed with thyroid carcinoma at the Department of Pathology, 108 Military Central Hospital, Hanoi, Vietnam, between 1 December 2018, and 31 December 2020. Eligible participants were patients with cytologically or histologically confirmed thyroid carcinoma. Patients were excluded if they had incomplete medical records. The study protocol was approved by the Institutional Review Board at 108 Military Central Hospital (reference number 3228/QĐ-BV) and adhered to the ethical standards outlined in the 1964 Declaration of Helsinki. As this was a retrospective study, the requirement for informed consent was waived.

2.2. Variables

Data collected included patient demographics, preoperative thyroid imaging results, fine needle aspiration cytology, tumor size, location, and histologic type. Preoperative thyroid imaging results were categorized based on the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS)[14]. Fine needle aspiration cytology was classified using the Bethesda System for Reporting Thyroid Cytopathology[15]. Tumor size was measured by millimeters using a calibrated ruler on gross pathological examination. Tumor location and histologic type were determined by examination of hematoxylin and eosin (H&E) stained sections of formalin-fixed paraffin-embedded tissue using light microscopy and categorized as papillary, follicular, or medullary carcinoma[16]. Capsular invasion was defined as tumor extension beyond the thyroid capsule into the surrounding extrathyroidal soft tissues[6]. Capsular invasion and cervical lymph node metastasis were evaluated through histopathological examination of the surgical specimens.

2.3. Statistical analysis

Categorical variables were expressed as numbers (percentages). Associations were analyzed using Pearson's chi-squared test. Binary logistic regression models identified predictors of outcomes. Variables with $p < 0.05$ on univariate analysis were entered into multivariate models. Odds ratios and 95% confidence intervals were calculated. Analyses were performed using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). A two-tailed $p < 0.05$ was considered statistically significant.

3. Results

3.1. Clinicopathologic features of thyroid carcinoma

In the present study, we examined the clinicopathologic features of 1626 patients diagnosed with thyroid carcinoma at our institution (**Table 1**). The majority were female (82.3%) and aged 45 years or younger (52.6%). Based on preoperative thyroid imaging, most nodules were moderately suspicious (79.0%) for malignancy. Cytology showed over half (51.6%) were suspicious and 29.9% were malignant. Tumors were equally distributed between the thyroid lobes (left 45.5%, right 49.8%), with few in the isthmus (4.7%). Just over half (53.9%) were ≤8 mm. Histopathology revealed papillary carcinoma dominated (98.8%), with uncommon follicular (1.0%) and rare medullary (0.2%) carcinomas. Capsular invasion was present in 58.7% (**Figure 1**). Cervical lymph node metastases were seen in 28.5% (**Figure 2**).

Table 1. Clinicopathologic characteristics of patients with thyroid carcinoma.

Characteristics		**n (%)**
Age		
	≤ 45	856 (52.6)
	> 45	770 (47.4)
Sex		
	Male	287 (17.7)
	Female	1339 (82.3)
ACR TIRADS		
	TR3	166 (10.2)
	TR4	1284 (79.0)
	TR5	176 (10.8)
Bethesda category		
	I	50 (3.1)
	II	80 (4.9)
	III	141 (8.7)
	IV	30 (1.8)
	V	839 (51.6)
	VI	486 (29.9)
Tumor location		
	Left lobe	740 (45.5)
	Right lobe	810 (49.8)
	Isthmus	76 (4.7)
Tumor size		
	≤ 8 mm	877 (53.9)
	> 8 mm	749 (46.1)
Histology thyroid carcinoma types		
	Papillary carcinoma	1606 (98.8)
	Follicular carcinoma	17 (1.0)
	Medullary carcinoma	3 (0.2)
Capsular invasion		
	Absent	672 (41.3)
	Present	954 (58.7)
Cervical lymph node metastasis		
	Absent	1163 (71.5)
	Present	463 (28.5)

ACR TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System; TR3: Mildly suspicious; TR4: Moderately suspicious; TR5: Highly suspicious; Bethesda category: The Bethesda System for Reporting Thyroid Cytopathology; I: Nondiagnostic; II: Benign; III: Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS); IV: Follicular neoplasm (FN)/Suspicious for follicular neoplasm (SFN); V: Suspicious for malignancy (SM); VI: Malignant.

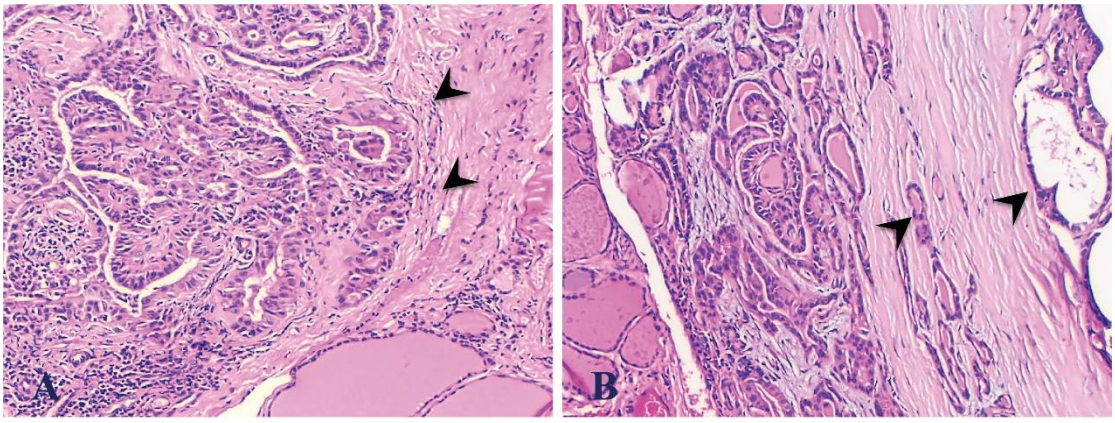

Figure 1. Histopathological examination of capsular invasion in papillary thyroid carcinoma. Representative hematoxylin and eosin (H&E) stained sections of papillary thyroid carcinoma at 200× magnification. **(A)** Tumor without evidence of capsular invasion. The tumor is confined within an intact capsule (black arrows); **(B)** Tumor exhibiting capsular invasion. The tumor cells breach the capsule and extend into the pericapsular (black arrows).

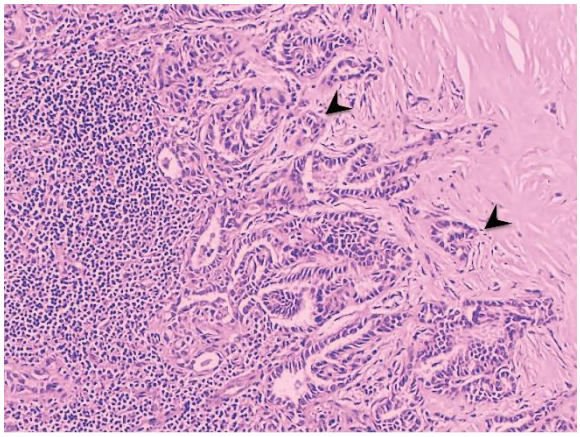

Figure 2. Histopathological identification of cervical lymph node metastasis in papillary thyroid carcinoma. Representative H&E stained section of a cervical lymph node with metastatic papillary thyroid carcinoma at 100× magnification. The lymph node shows effacement of the normal architecture by metastatic papillary thyroid carcinoma cells (black arrows).

In summary, we observed a high prevalence of small papillary carcinomas in young female patients, with over half demonstrating capsular invasion and just under one-third having cervical lymph node metastases.

3.2. Associations of clinicopathologic features with capsular invasion and cervical lymph node metastasis in thyroid carcinoma

Our examination of the associations between clinicopathologic features and capsular invasion in thyroid carcinoma revealed several significant findings (**Table 2**). We did not find significant differences in capsular invasion rates based on patient age or sex. However, capsular invasion rates did vary significantly according to ACR TIRADS categories ($p < 0.001$). The rates were 4.7% for TR3 nodules, 46.3% for TR4 nodules, and 7.7% for TR5 nodules. Bethesda cytology categories also showed significant associations with capsular invasion ($p = 0.003$), with rates of 1.4% for Bethesda I, 2.6% for Bethesda II, 4.6% for Bethesda III, 0.9% for Bethesda IV, 29.9% for Bethesda V, and 19.4% for Bethesda VI. Tumor location was not significantly linked to capsular invasion. However, tumor size did have a significant association ($p < 0.001$), with capsular invasion rates of 25.3% for tumors ≤8 mm and 33.4% for tumors >8 mm. Furthermore, histology showed a significant relationship ($p = 0.001$), with capsular invasion present in 57.5% of papillary carcinomas, 1.0% of follicular carcinomas, and 0.2% of medullary carcinomas.

Table 2. Associations between clinicopathologic features and capsular invasion in thyroid carcinoma.

Characteristics		Capsular invasion, n (%)		*p*
		Absent	Present	
Age				
	≤ 45	351 (21.6)	505 (31.1)	0.780
	> 45	321 (19.7)	449 (27.6)	
Sex				
	Male	122 (7.5)	165 (10.2)	0.655
	Female	550 (33.8)	789 (48.5)	
ACR TIRADS				
	TR3	90 (5.5)	76 (4.7)	< 0.001
	TR4	531 (32.7)	753 (46.3)	
	TR5	51 (3.1)	125 (7.7)	
Bethesda category				
	I	28 (1.7)	22 (1.4)	0.003
	II	38 (2.3)	42 (2.6)	
	III	67 (4.1)	74 (4.6)	
	IV	16 (1.0)	14 (0.9)	
	V	353 (21.7)	486 (29.9)	
	VI	170 (10.5)	316 (19.4)	
Tumor location				
	Left lobe	315 (19.4)	425 (26.1)	0.643
	Right lobe	327 (20.1)	483 (29.7)	
	Isthmus	30 (1.8)	46 (2.8)	
Tumor size				
	≤ 8 mm	466 (28.7)	411 (25.3)	< 0.001
	> 8 mm	206 (12.6)	543 (33.4)	
Histology thyroid carcinoma types				
	Papillary carcinoma	672 (41.3)	934 (57.5)	0.001
	Follicular carcinoma	0 (0)	17 (1.0)	
	Medullary carcinoma	0 (0)	3 (0.2)	

ACR TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System; TR3: Mildly suspicious; TR4: Moderately suspicious; TR5: Highly suspicious; Bethesda category: The Bethesda System for Reporting Thyroid Cytopathology; I: Nondiagnostic; II: Benign; III: Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS); IV: Follicular neoplasm (FN)/Suspicious for follicular neoplasm (SFN); V: Suspicious for malignancy (SM); VI: Malignant; *p* values were determined using the Pearson Chi-square test.

Shifting focus to cervical lymph node metastasis, our analysis found several clinicopathologic features to be significantly associated (**Table 3**). Patient age and sex were correlated with cervical lymph node metastasis ($p < 0.001$ and $p = 0.003$, respectively). ACR TIRADS categories also showed significant relationships ($p < 0.001$), with metastasis rates of 1.7% for TR3, 22.9% for TR4, and 3.9% for TR5. Similar associations emerged for Bethesda cytology categories ($p < 0.001$). The metastasis rate was 0.8% for Bethesda I, 0.7% for Bethesda II, 1.8% for Bethesda III, 0.4% for Bethesda IV, 13.7% for Bethesda V, and 11.1% for Bethesda VI. Additionally, tumor size had a significant association ($p < 0.001$), with metastasis rates of 17.4% for tumors >8 mm and 11.1% for tumors ≤8 mm. Histology also showed a significant relationship ($p = 0.032$), with metastasis present in 28.4% of papillary carcinomas and 0.1% of medullary carcinomas. Lastly, capsular invasion was significantly linked to cervical lymph node metastasis ($p < 0.001$), occurring in 20.8% of cases with metastasis versus 7.7% without metastasis. The only clinicopathologic feature not significantly associated with cervical lymph node metastasis was tumor location.

Table 3. Associations between clinicopathologic features and cervical lymph node metastasis in thyroid carcinoma.

Characteristics		Cervical lymph node metastasis, n (%)		*p*
		Absent	Present	
Age				
	≤ 45	559 (34.4)	297 (18.3)	< 0.001
	> 45	604 (37.1)	166 (10.2)	
Sex				
	Male	185 (11.4)	102 (6.3)	0.003
	Female	978 (60.1)	361 (22.2)	
ACR TIRADS				
	TR3	139 (8.5)	27 (1.7)	< 0.001
	TR4	912 (56.1)	372 (22.9)	
	TR5	112 (6.9)	64 (3.9)	
Bethesda category				
	I	37 (2.3)	13 (0.8)	< 0.001
	II	69 (4.2)	11 (0.7)	
	III	112 (6.9)	29 (1.8)	
	IV	24 (1.5)	6 (0.4)	
	V	616 (37.9)	223 (13.7)	
	VI	305 (18.8)	181 (11.1)	
Tumor location				
	Left lobe	521 (32.0)	219 (13.5)	0.632
	Right lobe	588 (36.2)	222 (13.6)	
	Isthmus	54 (3.3)	22 (1.4)	
Tumor size				
	≤ 8 mm	697 (42.9)	180 (11.1)	< 0.001
	> 8 mm	466 (28.7)	283 (17.4)	
Histology thyroid carcinoma types				
	Papillary carcinoma	1144 (70.4)	462 (28.4)	0.032
	Follicular carcinoma	17 (1.0)	0 (0)	
	Medullary carcinoma	2 (0.1)	1 (0.1)	
Capsular invasion				
	Absent	546 (33.6)	126 (7.7)	< 0.001
	Present	617 (37.9)	337 (20.8)	

ACR TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System; TR3: Mildly suspicious; TR4: Moderately suspicious; TR5: Highly suspicious; Bethesda category: The Bethesda System for Reporting Thyroid Cytopathology; I: Nondiagnostic; II: Benign; III: Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS); IV: Follicular neoplasm (FN)/Suspicious for follicular neoplasm (SFN); V: Suspicious for malignancy (SM); VI: Malignant; *p* values were determined using the Pearson Chi-square test.

In summary, we identified several clinicopathologic characteristics associated with capsular invasion and cervical lymph node metastasis that may help guide prognosis and treatment decisions in thyroid cancer patients.

3.3. Identification of risk factors for capsular invasion and cervical lymph node metastasis in thyroid cancer using binary logistic regression

We performed binary logistic regression analyses to identify risk factors for capsular. Our analyses identified several significant risk factors for capsular invasion and cervical lymph node metastasis in thyroid cancer patients. Regarding capsular invasion, our binary logistic regression analysis revealed that higher ACR TIRADS categories, higher Bethesda cytopathology categories, and larger tumor sizes were associated with increased odds. Specifically, compared to TR3 nodules, TR4 and TR5 nodules had 1.679 and 2.902 times higher odds of capsular invasion, respectively ($p = 0.002$ and $p < 0.001$). Patients with Bethesda category VI

nodules had 2.366 times higher odds of capsular invasion relative to category I ($p = 0.004$). Tumors larger than 8 mm had 2.989 times higher odds of capsular invasion compared to smaller tumors ($p < 0.001$), as shown in **Table 4**.

Table 4. Binary logistic regression analysis of risk factors for capsular invasion in thyroid carcinoma.

Variables		Odds ratio	95% Confidence interval	*p*
ACR TIRADS				
	TR3	1	-	-
	TR4	1.679	1.213–2.324	0.002
	TR5	2.902	1.857–4.536	< 0.001
Bethesda category				
	I	1	-	-
	II	1.407	0.691–2.862	0.346
	III	1.406	0.735–2.690	0.304
	IV	1.114	0.449–2.764	0.816
	V	1.752	0.986–3.114	0.056
	VI	2.366	1.313–4.262	0.004
Tumor size				
	≤ 8 mm	1	-	-
	> 8 mm	2.989	2.427–3.680	< 0.001
Histology thyroid carcinoma types				
	Papillary carcinoma	1	-	-
	Follicular carcinoma	1	-	-
	Medullary carcinoma	1	-	-

ACR TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System; TR3: Mildly suspicious; TR4: Moderately suspicious; TR5: Highly suspicious; Bethesda category: The Bethesda System for Reporting Thyroid Cytopathology; I: Nondiagnostic; II: Benign; III: Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS); IV: Follicular neoplasm (FN)/Suspicious for follicular neoplasm (SFN); V: Suspicious for malignancy (SM); VI: Malignant; *p* values were determined using the Binary Logistic Regression analyses. (-): omitted.

For cervical lymph node metastasis, our analysis found that younger age, male sex, higher TIRADS categories, larger tumor sizes, and presence of capsular invasion were predictive of increased odds, as summarized in **Table 5**. Patients above 45 years had 0.517 times lower odds of metastasis than younger patients ($p < 0.001$). Females had 0.669 times lower odds than males ($p = 0.004$). TR4 and TR5 nodules had 2.100 and 2.942 times higher odds of metastasis than TR3 nodules ($p = 0.001$ and $p < 0.001$). Tumors over 8 mm had 2.352 times higher odds than smaller tumors ($p < 0.001$). Presence of capsular invasion was associated with 2.367 times higher odds of metastasis ($p < 0.001$).

Table 5. Binary logistic regression analysis of risk factors for cervical lymph node metastasis in thyroid carcinoma.

Variables		Odds ratio	95% Confidence interval	*p*
Age				
	≤ 45	1	-	-
	> 45	0.517	0.414–0.646	< 0.001
Sex				
	Male	1	-	-
	Female	0.669	0.511–0.877	0.004
ACR TIRADS				
	TR3	1	-	-
	TR4	2.100	1.367–3.226	0.001
	TR5	2.942	1.759–4.919	< 0.001

Table 5. (*Continued*).

Variables		Odds ratio	95% Confidence interval	*p*
Bethesda category				
	I	1	-	-
	II	0.454	0.185–1.112	0.084
	III	0.737	0.347–1.564	0.427
	IV	0.712	0.238–2.128	0.543
	V	1.030	0.538–1.974	0.928
	VI	1.689	0.875–3.262	0.119
Tumor size				
	≤ 8 mm	1	-	-
	> 8 mm	2.352	1.886–2.932	< 0.001
Histology thyroid carcinoma types				
	Papillary carcinoma	1	-	-
	Follicular carcinoma	1	-	-
	Medullary carcinoma	1.238	0.112–13.687	0.862
Capsular invasion				
	Absent	11	-	-
	Present	2.367	1.871–2.993	< 0.001

ACR TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System; TR3: Mildly suspicious; TR4: Moderately suspicious; TR5: Highly suspicious; Bethesda category: The Bethesda System for Reporting Thyroid Cytopathology; I: Nondiagnostic; II: Benign; III: Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS); IV: Follicular neoplasm (FN)/Suspicious for follicular neoplasm (SFN); V: Suspicious for malignancy (SM); VI: Malignant; *p* values were determined using the Binary Logistic Regression analyses. (-): omitted.

In summary, our binary logistic regression analyses identified several patient and tumor characteristics as significant predictors of capsular invasion and cervical lymph node metastasis in thyroid cancer patients. Key factors included age, sex, ACR TIRADS categories, Bethesda cytopathology grading, tumor size, and capsular invasion. Our findings offer valuable insights into the risk factors for aggressive disease in thyroid carcinoma.

4. Discussion

4.1. Key findings and implications from a study of thyroid carcinoma clinicopathological feature

Consistent with previous literature, our cohort showed a predominance of younger women[2,17] and papillary histology[4,18]. The TIRADS malignancy risk stratification also aligned with prior studies, with most cancers arising from moderately suspicious nodules[19,20]. However, our study found a high prevalence of capsular invasion (58.7%) and cervical lymph node metastasis (28.5%) among patients with thyroid carcinoma. These findings diverge from some recent literature reporting lower rates of capsular invasion (around 30%)[6,21] and nodal metastases (15%–50%) in similar cohorts[22–24]. The elevated incidence of capsular breach indicates more aggressive tumor behavior, with implications for increased extrathyroidal extension and lymphatic spread[25,26].

Plausible factors contributing to the discrepancy include advanced disease at presentation, variances in diagnostic criteria, and unique characteristics of our patient population. Regardless of the underlying reasons, the high rate of capsular invasion signifies a need to tailor diagnostic and therapeutic approaches to this group. Our results advocate continued adoption of ACR TIRADS for malignancy risk stratification. The system performed well in our cohort, with most cancers arising from moderately suspicious nodules.

Overall, this study largely confirms established knowledge but reveals a concerning pattern of capsular invasion warranting further research. The findings provide valuable insights into the clinicopathological profile of thyroid malignancy in our patients. Key areas for additional investigation include elucidating the factors

influencing capsular invasion patterns and examining long-term prognostic implications.

4.2. Associations between clinicopathologic features and aggressive disease in thyroid carcinoma

Our findings confirm and extend previous research showing associations between tumor characteristics and aggressive features like capsular invasion and cervical lymph node metastasis in thyroid carcinoma. We found capsular invasion rates were significantly linked to ACR TIRADS categories, Bethesda cytology, tumor size, and histology. These results support prior studies showing higher invasion rates in nodules with more suspicious imaging and cytology[6,27,28]. The increased frequency of invasion in larger tumors also aligns with earlier reports[29]. While some studies associate invasion more with follicular carcinoma[30], others report significant capsular invasion in aggressive papillary thyroid carcinoma subtypes[29,31]. Our analysis of cervical lymph node metastasis revealed significant associations with patient age, sex, ACR TIRADS categories, Bethesda cytology, tumor size, histology, and capsular invasion presence. These findings parallel patterns reported in the literature. Specifically, the higher nodal metastasis rates in men, younger patients[32,33], and tumors with suspicious ultrasound patterns, cytology, and larger size[34–37], match previous research.

Taken together, our results suggest thyroid nodules with more suspicious ultrasound patterns, cytology, larger size, and papillary histology are more likely to exhibit aggressive features like capsular invasion and cervical lymph node metastasis. While papillary carcinoma often has an excellent prognosis[38,39], our study confirms it may demonstrate concerning characteristics more frequently than other histologic subtypes[40–42]. These findings could help clinicians identify higher risk thyroid cancers that are not suitable for non-surgical follow-up. Our study also highlights the potential value of TIRADS and Bethesda systems for preoperative risk assessment. Further research is needed to clarify discrepancies between studies and better understand the complex interplay between tumor features and aggressive disease progression.

4.3. Preoperative risk factors for capsular invasion and nodal metastases in thyroid cancer

Our study identified several key risk factors for capsular invasion and cervical lymph node metastasis in patients with thyroid cancer. The binary logistic regression analyses revealed that higher ACR TIRADS categories, Bethesda cytopathology categories, and larger tumor sizes were significant predictors of increased odds of capsular invasion. Additionally, younger age, male sex, higher TIRADS categories, larger tumor sizes, and presence of capsular invasion were associated with greater odds of cervical lymph node metastasis.

These findings align with and expand upon previous research identifying associations between higher TIRADS categories, increased tumor size, extrathyroidal extension, and lymph node metastases[27,43]. Our study confirms these relationships and further identifies young age and male sex as independent risk factors for nodal spread[44,45]. The positive association between Bethesda cytological categories and capsular invasion has also been suggested previously[28,46]. Taken together, our results emphasize the prognostic value of certain clinical and tumor characteristics in predicting aggressive disease behaviors in thyroid carcinoma patients.

Our findings differ somewhat from a few studies that did not identify male sex as an independent risk factor[47,48]. And our findings diverge from some publications that found no independent association between ACR TIRADS and capsular invasion after adjusting for nodule size[49,50]. These discrepancies may relate to differences in methods or sample characteristics between studies. Additional large, multicenter studies are needed to clarify these relationships.

In summary, our analyses have defined several readily available preoperative factors that may allow more accurate risk assessment and tailored management approaches in thyroid cancer. The results largely confirm previous observations while also suggesting expanded roles for Bethesda cytological categories, age, and sex in risk stratification. Further investigation into the mechanisms underlying these associations is warranted.

4.4. Study limitations

While this study provides valuable insights, some limitations should be acknowledged. The single-center retrospective design and modest sample size preclude broad generalizability. The lack of long-term follow-up data also constrains assessment of definitive patient outcomes. Additional large, multicenter studies with diverse populations and long-term follow-up are warranted to clarify discrepancies between existing studies and better elucidate prognostic implications.

5. Conclusions and future research

In summary, our findings largely confirm established knowledge but reveal an unexpectedly high incidence of aggressive features like capsular invasion in thyroid carcinoma at our institution. We identified suspicious ultrasound patterns, large tumor size, and high-grade cytology as significant preoperative risk factors for capsular breach and cervical metastasis. These results align with and expand upon previous observations in the literature.

However, discrepancies between our data and some prior studies regarding invasion rates and independent risk factors merit further clarification through large multicenter cohorts with long-term follow-up. Additional research should explore mutational and molecular profiles associated with aggressive disease. Elucidating prognostic biomarkers could facilitate more personalized risk stratification and management. Exploring relationships with environmental exposures and genetics may shed light on etiological mechanisms.

Our data emphasize tailoring of diagnostic, therapeutic, and surveillance strategies based on preoperative risk factors. However, ongoing work is needed given study limitations. We recommend continued validation of TIRADS and Bethesda systems for preoperative characterization. Future investigations should focus on replicating our findings, clarifying discrepancies in the literature, and delineating prognosis based on tumor behaviors. Ultimately, a better understanding of clinicopathological associations and molecular drivers may enable more precise individualized care in thyroid carcinoma.

Author contributions

Conceptualization, NVD and DTH; methodology, NVD and DHT; software, DHT; validation, NVD and DTH; formal analysis, NVD and DHT; investigation, NVD; Resources, NVD and DTH; data curation, NVD; writing—original draft preparation, NVD and DHT; writing—review and editing, NVD; visualization, DTH; supervision, NVD; project administration, NVD; funding acquisition, DHT. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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