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Original Article

Associations of demographic, anthropometric, and laboratory factors with Korean Thyroid Imaging Reporting and Data System (K-TIRADS) ultrasonographic risk stratification in patients with thyroid nodules

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Abstract

Thyroid nodules are commonly detected by ultrasonography and require standardized imaging-based risk stratification. The Korean Thyroid Imaging Reporting and Data System (K-TIRADS) classifies thyroid nodules according to ultrasonographic features associated with suspected malignancy; however, factors associated with higher K-TIRADS classification remain incompletely understood. The aim of this study was to evaluate the associations of demographic, anthropometric, and laboratory factors with K-TIRADS ultrasonographic risk stratification in patients with thyroid nodules. A cross-sectional study was conducted at Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia. Adult patients with clinically suspected thyroid nodules were included using total sampling. Thyroid ultrasonography was performed using a standardized protocol, and nodules were classified according to the 2021 K-TIRADS. Demographic, anthropometric, and laboratory factors included age, sex, body mass index (BMI), and serum thyroid-stimulating hormone (TSH) level. Generalized estimating equations (GEE) were used to assess associations while accounting for clustering of multiple nodules within the same patient. A total of 109 patients with 171 thyroid nodules were included. Most patients were female (81.7%), with a median age of 46 years (IQR 34–59). Most nodules were classified as K-TIRADS 3 (48.0%) or K-TIRADS 4 (35.7%). Univariate analyses suggested that age was significantly associated with higher K-TIRADS classification (β=0.010; 95%CI: 0.003–0.018; p=0.008), whereas sex, BMI, and serum TSH level were not significant. In multivariable analysis, increasing age (β=0.010; 95%CI: 0.002–0.018; p=0.012) and higher serum TSH level (β=0.007; 95%CI: 0.002–0.011; p=0.002) were independently associated with higher K-TIRADS classification. No significant associations were observed for sex or BMI. The findings highlight that increasing age and higher serum TSH level were independently associated with higher K-TIRADS ultrasonographic risk stratification in patients with thyroid nodules. Selected demographic and laboratory factors may complement the ultrasonography-based classification system.

Keywords: K-TIRADS, age, sex, body mass index, TSH

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Introduction

Increasing detection of thyroid nodules represents a growing clinical and public health concern [1]. While palpation identifies nodules in only 4%–7% of the population, high-resolution ultrasonography (USG) detects up to 68%, indicating that many thyroid nodules are clinically undetected [2]. Although most thyroid nodules are benign, thyroid malignancy is identified in approximately 5–15% of cases, necessitating accurate risk stratification to avoid both underdiagnosis of cancer and overuse of invasive procedures [1,3]. The widespread use of USG has led to a marked rise in thyroid nodule detection globally, including in Indonesia, where the disease burden remains significant, with an estimated prevalence affecting millions of individuals, accompanied by notable mortality from thyroid cancer [3]. This epidemiological shift has created an urgent need for reliable, accessible, and context-specific diagnostic frameworks to guide clinical decision-making. Korean Thyroid Imaging Reporting and Data System (K-TIRADS) classification offers a standardized ultrasonographic approach; however, its applicability across different populations remains uncertain [4-9].

Beyond imaging, demographic, anthropometric, and laboratory factors such as body mass index (BMI), age, sex, and serum thyroid-stimulating hormone (TSH) may influence malignancy risk. Serum TSH, as a thyroid growth regulator, has been implicated in tumorigenesis, yet existing evidence remains inconsistent [10-14]. TSH functions as a growth factor for thyroid follicular cells, and elevated TSH levels are hypothesized to promote abnormal cellular proliferation [11,13]. Some studies suggest that higher TSH levels are associated with increased malignancy risk [10,11,13], whereas lower levels are more commonly associated with benign nodules [12,14]. Similarly, BMI-related metabolic and inflammatory pathways may contribute to thyroid pathology through mechanisms involving endocrine dysregulation, insulin resistance, and chronic inflammation [15,16]. Nevertheless, the association between BMI and K-TIRADS classification remains controversial, with heterogeneous findings across different populations [15-19].

Age and sex further complicate risk stratification, with differing patterns in nodule prevalence and malignancy risk [20-22]. Increasing age has been associated with a higher risk of malignancy, although its correlation with TIRADS classification remains inconclusive [20-24]. Furthermore, thyroid nodules are more prevalent in females, yet some studies report a higher likelihood of malignancy in males [20-23]. In Indonesia, evidence regarding the validity of K-TIRADS and association of demographic, anthropometric, and laboratory factors—including serum TSH levels, age, sex, and BMI—remains limited. Local data are needed to assess the applicability of K-TIRADS in the Indonesian population, considering for epidemiological and clinical differences, and to improve diagnostic accuracy and patient management. Therefore, the aim of this study was to evaluate the association between demographic, anthropometric, and laboratory factors with ultrasonographic features of thyroid nodules based on the K-TIRADS classification.

Methods

Study design and setting

A cross-sectional study was conducted at Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, from October to December 2025. Eligible participants were adult patients with clinically suspected thyroid nodules referred from outpatient clinics or inpatient wards to the hospital's Radiology Department after eligibility screening and written informed consent. Participants were enrolled after eligibility screening and written informed consent. Thyroid ultrasonography was performed using a standardized protocol, and nodules were classified according to the 2021 Korean Thyroid Imaging Reporting and Data System (K-TIRADS). In patients with multiple nodules, the most suspicious nodule in each thyroid lobe was selected as the unit of analysis.

Sampling method and patients' criteria

A total sampling approach was employed, including all patients presenting with suspected thyroid nodules who underwent thyroid USG at the Radiology Department during the study period. The

inclusion criteria were: adult patients aged ≥18 years with clinically suspected thyroid nodules; patients who underwent standardized thyroid ultrasonography with clearly visualized nodules; availability of serum thyroid-stimulating hormone (TSH) results obtained within ±2 weeks of ultrasonographic examination; and provision of written informed consent. Patients were excluded if they had ectopic thyroid lesions, purely cystic nodules on ultrasonography, incomplete clinical, imaging, or laboratory data, a history of thyroid surgery or thyroid malignancy, current or recent use of medications known to affect thyroid function within the previous three months, or severe systemic illness or other conditions that could interfere with accurate clinical or laboratory assessment such as had or having any type of other cancers.

Data collection

Baseline demographic and clinical characteristics were systematically recorded using a standardized data collection form, including age, sex, BMI, and relevant clinical history such as prior thyroid disease, medication use, smoking status, menopausal status, and family history of thyroid malignancy. Anthropometric measurements, including body weight and height, were obtained using a calibrated digital weighing scale and a wall-mounted stadiometer, with patients measured in light clothing and without footwear. BMI was subsequently calculated as weight (kg) divided by height squared (m^2) and categorized according to the Asian-specific criteria recommended by the World Health Organization [25].

Thyroid ultrasonography examination

Thyroid ultrasonography was performed using a high-resolution ultrasound system (GE Voluson S8; GE HealthCare, Chicago, IL, USA) with a 7.5–12 MHz linear transducer. Patients were examined in the supine position with slight neck extension. Both thyroid lobes and the isthmus were evaluated in longitudinal and transverse planes using a standardized protocol. Each nodule was assessed for composition (solid, cystic, or mixed), echogenicity (hypoechoic, isoechoic, or hyperechoic relative to surrounding thyroid parenchyma), orientation (parallel or non-parallel/taller-than-wide), margin characteristics (smooth, ill-defined, lobulated, or irregular), presence of echogenic foci (including microcalcifications, macrocalcifications, or comet-tail artifacts), internal vascularity and size in three dimensions. Representative images were stored for documentation and quality verification. All examinations and interpretations were performed in real time by a radiology resident under the supervision of a board-certified radiologist experienced in thyroid imaging.

Korean Thyroid Imaging Reporting and Data System (K-TIRADS)

Thyroid nodules were subsequently classified according to the 2021 K-TIRADS, a structured risk stratification system that integrates key ultrasonographic features to estimate the probability of malignancy and guide clinical management [26]. Classification was based on a combination of nodule composition (solid, predominantly solid, partially cystic, or cystic), echogenicity relative to the surrounding thyroid parenchyma, and the presence of suspicious sonographic features, including non-parallel orientation (taller-than-wide shape), irregular or spiculated margins, and punctate echogenic foci suggestive of microcalcifications. Based on these characteristics, nodules were categorized into four principal risk groups: K-TIRADS 2 (benign), typically including purely cystic or spongiform nodules with negligible malignancy risk; K-TIRADS 3 (low suspicion), generally comprising partially cystic or isoechoic/hyperechoic nodules without suspicious features; K-TIRADS 4 (intermediate suspicion), including hypoechoic nodules without overtly suspicious features or partially cystic/isoechoic nodules with suspicious features; and K-TIRADS 5 (high suspicion), defined by solid hypoechoic nodules with one or more suspicious features, indicating a high likelihood of malignancy. In patients with multiple nodules, a lesion-based analytical approach was applied. Each thyroid lobe was assessed independently, and the nodule demonstrating the highest-risk sonographic profile—based on the presence and combination of suspicious features—was designated as the index nodule for that lobe.

Serum thyroid-stimulating hormone (TSH) measurement

Peripheral venous blood samples were obtained under standardized pre-analytical conditions, typically between 07:00 and 09:00 after an overnight fast. Approximately 3–5 mL of blood was

collected from the antecubital vein into serum separator tubes (SST), allowed to clot for 20–30 minutes at room temperature, and centrifuged at 3000 rpm for 10 minutes within 1 hour of collection. The separated serum was immediately analyzed or stored at 2–8°C if analysis was performed within 24 hours. Serum TSH levels were measured using a chemiluminescent microparticle immunoassay (CMIA) on an automated analyzer (ARCHITECT i2000SR, Abbott Laboratories, Abbott Park, IL, USA). All assays were conducted in accordance with manufacturer specifications, and results were reported in μIU/mL.

Study variable

The independent variables included age, sex, BMI, and serum TSH levels. Age was categorized into three groups: young adults (18–44 years), middle-aged adults (45–59 years), and older adults (≥60 years). Sex was recorded as a biological variable based on medical records and classified as male or female. BMI was categorized according to Asian-specific cut-off values [25]: underweight (<18.5 kg/m²), normal (18.5–22.9 kg/m²), overweight (23.0–24.9 kg/m²), obesity class I (25.0–29.9 kg/m²), and obesity class II (≥30.0 kg/m²). Serum TSH levels were measured in μIU/mL and categorized into quartiles based on the distribution within the study population: Q1 (<0.92 μIU/mL), Q2 (0.92–1.07 μIU/mL), Q3 (1.07–3.10 μIU/mL), and Q4 (>3.10 μIU/mL).

The primary dependent variable in this study was the ultrasonographic classification of thyroid nodules based on the 2021 K-TIRADS. Each nodule was evaluated using standardized sonographic criteria and assigned to one of four ordinal categories reflecting increasing risk of malignancy: K-TIRADS 2 (benign), K-TIRADS 3 (low suspicion), K-TIRADS 4 (intermediate suspicion), and K-TIRADS 5 (high suspicion). The unit of analysis was the thyroid nodule, allowing for multiple nodules to be included per patient.

Potential confounding variables included history of thyroid medication use (yes/no, defined as use within the previous three months), menopausal status (yes/no, defined as absence of menstruation for ≥12 consecutive months in women aged >40 years), smoking history (yes/no, defined as regular smoking within the previous six months), family history of thyroid cancer (yes/no, defined as presence in first-degree relatives), and comorbid conditions (yes/no, including chronic diseases such as diabetes mellitus, dyslipidemia, or metabolic syndrome).

Statistical analysis

Given that the unit of analysis was the thyroid nodule and multiple nodules could originate from a single patient, association within clusters was addressed using generalized estimating equations (GEE). Univariate analyses were performed to examine the association between age, sex, BMI, and serum TSH levels with K-TIRADS classification. An appropriate link function and working correlation structure were specified, with patient-level clustering applied to account for intra-individual correlation. Effect estimates were reported as regression coefficients (β) with corresponding 95% confidence intervals (95%CI) and *p*-values. Multivariable analysis was subsequently conducted using GEE to adjust for potential confounding and to evaluate the independent association between variables and K-TIRADS classification. Variables included in the multivariable model were selected based on clinical relevance and the distribution of the data, with consideration given to the event-to-variable ratio to reduce the risk of model overfitting. Potential confounding variables, including history of thyroid medication use, menopausal status, smoking history, family history of thyroid cancer, and comorbid conditions, were primarily analyzed descriptively due to sample size limitations and variability in distribution. These variables were not fully incorporated into the multivariable model to preserve model stability. All statistical tests were two-sided, and a *p*-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA).

Results

Characteristics of the included patients

A total of 109 patients were included, contributing 171 thyroid nodules for analysis (**Table 1**). As multiple nodules were present in several patients (62/109), the unit of analysis was defined at the nodule level. Among 109 patients, predominantly female (81.7%), with a median age of 46 years

(IQR 34–59) (**Table 1**). The largest age group was 18–44 years (45.0%), followed by 45–59 years (36.7%) and ≥60 years (18.3%). The mean BMI was 25.7±3.9 kg/m², with obesity class I and normal BMI each representing 31.2% of the cohort, while obesity class II accounted for 12.8%. Median serum TSH level was 1.41 µIU/mL (IQR 0.67–2.75), with the majority of values within the third quartile (45.0%). Based on 2021 K-TIRADS classification of 171 nodules, most lesions were categorized as K-TIRADS 3 (48.0%) and 4 (35.7%), whereas high-suspicion nodules (K-TIRADS 5) comprised 12.3%. Thyroid medication use was uncommon (5.5%). A history of smoking was present in 12.8%, and a family history of thyroid cancer in 7.3%. Comorbid conditions were reported in 39.4% of patients. Among female patients (n=89), the majority were premenopausal (79.8%), with 20.2% classified as postmenopausal (**Table 1**).

Table 1. Characteristics of patients with thyroid nodules included in the study (n=109)

Variable	Frequency (%)
Sex	
Male	20 (18.3)
Female	89 (81.7)
Age (years), median (interquartile range, IQR)	46 (34–59.0)
18–44 years	49 (45.0)
45–59 years	40 (36.7)
≥60 years	20 (18.3)
Body mass index (kg/m²), mean±SD [a]	25.7 ± 3.9
Underweight (<18.5)	6 (5.5)
Normal (18.5–22.9)	34 (31.2)
Overweight (23.0–24.9)	21 (19.3)
Obesity class I (25.0–29.9)	34 (31.2)
Obesity class II (≥30.0)	14 (12.8)
Serum thyroid-stimulating hormone level (µIU/mL), median (IQR)	1.41 (0.67–2.75)
Q1 (<0.92)	34 (31.2)
Q2 (0.92–1.07)	6 (5.5)
Q3 (1.07–3.10)	49 (45.0)
Q4 (>3.10)	20 (18.3)
K-TIRADS, median (IQR)[#]	3 (3-4)
K-TIRADS 1	0 (0)
K-TIRADS 2	7 (4.1)
K-TIRADS 3	82 (48.0)
K-TIRADS 4	61 (35.7)
K-TIRADS 5	21 (12.3)
Thyroid medication use	
Yes	6 (5.5)
No	103 (94.5)
Smoking history	
Yes	14 (12.8)
No	95 (87.2)
Family history of thyroid cancer	
Yes	8 (7.3)
No	101 (92.7)
Comorbidities	
Yes	43 (39.4)
No	66 (60.6)
Menopausal status*	
Postmenopausal	18 (20.2)
Premenopausal	71 (79.8)

K-TIRADS: Korean Thyroid Imaging Reporting and Data System
[a] BMI categorized using Asian-specific cut-offs
* Menopausal status calculated among female patients only (n=89)
[#] Calculated for all included thyroid nodules (n=171)

Associations of demographic, anthropometric, and laboratory factors with K-TIRADS risk stratification

GEE demonstrated that age was significantly associated with K-TIRADS classification (β: 0.010; 95%CI: 0.003–0.018; p=0.008) (**Table 2**). Each one-year increase in age was associated with a 0.010-point increase in mean K-TIRADS score. No significant associations were observed for sex (β: −0.104; 95%CI: −0.389 to 0.181; p=0.473), BMI (β: 0.025; 95%CI: −0.011 to 0.062; p=0.170), or serum TSH levels (β: 0.006; 95%CI: −0.001 to 0.012; p=0.084).

Table 2. Factors associated with 2021 Korean Thyroid Imaging Reporting and Data System (K-TIRADS) classification using generalized estimating equations (GEE)

Variable	Regression coefficient (β)	Standard error (SE)	95% confidence interval (95%CI)	*p*-value [a]
Age (years)	0.010	0.0038	0.003 to 0.018	0.008*
Sex (male vs female)	−0.104	0.1455	−0.389 to 0.181	0.473
Body mass index (kg/m²)	0.025	0.0185	−0.011 to 0.062	0.170
Serum TSH level (µIU/mL)	0.006	0.0034	−0.001 to 0.012	0.084

TSH: Thyroid-Stimulating Hormone; K-TIRADS: Korean Thyroid Imaging Reporting and Data System.
[a] Generalized estimating equations (GEE) with exchangeable correlation structure were used to account for clustering of nodules within patients
* Statistically significant at $p<0.05$

Multivariable analysis factors associated with K-TIRADS risk stratification

Multicollinearity assessment was performed prior to multivariable modeling to ensure the independence of predictor variables and the stability of regression estimates. Screening using a linear regression model demonstrated that all predictors—sex, age, BMI, and serum TSH levels—had tolerance values >0.10 and variance inflation factor (VIF) values close to 1.0 (range: 1.006–1.045).

After adjustment for potential confounders, including smoking history, menopausal status, thyroid medication use, family history of thyroid cancer, and comorbid conditions, age remained significantly associated with K-TIRADS classification (β: 0.010; 95%CI: 0.002–0.018; $p=0.012$) (**Table 3**). Each one-year increase in age was associated with a 0.010-point increase in K-TIRADS score. Serum TSH levels also showed a significant independent association after adjustment (β: 0.007; 95%CI: 0.002–0.011; $p=0.002$), indicating that each 1 µIU/L increase in serum TSH level corresponded to a 0.007-point increase in K-TIRADS score. In contrast, sex was not significantly associated with K-TIRADS after adjustment (β: −0.118; 95%CI: −0.415 to 0.179; $p=0.435$), although the direction suggested slightly lower scores in males. BMI also did not demonstrate a significant association (β: 0.017; 95%CI: −0.019 to 0.053; $p=0.364$).

Table 3. Multivariable generalized estimating equations (GEE) analysis of factors associated with 2021 Korean Thyroid Imaging Reporting and Data System (K-TIRADS) classification after adjustment for confounders

Variable	Regression coefficient (β)	Standard error (SE)	95% confidence interval (95%CI)	*p*-value [a]
Age (years)	0.010	0.0040	0.002 to 0.018	0.012*
Sex (male vs female)	−0.118	0.1515	−0.415 to 0.179	0.435
Body mass index (kg/m²)	0.017	0.0184	−0.019 to 0.053	0.364
Serum TSH level (µIU/mL)	0.007	0.0021	0.002 to 0.011	0.002*

TSH: thyroid-stimulating hormone.
[a] Analyzed using multivariable generalized estimating equations (GEE) with robust standard errors to account for within-patient association; models were adjusted for smoking history, menopausal status, thyroid medication use, family history of thyroid cancer, and comorbidities.
*Statistically significant at $p<0.05$

Discussion

This study evaluated the association between age, sex, BMI, and serum TSH levels with ultrasonographic risk stratification of thyroid nodules based on the 2021 K-TIRADS. The findings demonstrate that age and serum TSH level are independently associated with higher K-TIRADS classification after adjustment for confounding variables, whereas sex and BMI are not significantly associated.

Age demonstrated a consistent and independent association with K-TIRADS classification, with increasing age associated with higher ultrasonographic risk. This finding is biologically plausible, as advancing age is associated with cumulative cellular and molecular alterations, including genetic mutations and changes in the tissue microenvironment. These processes may manifest as high-risk ultrasonographic features—such as marked hypoechogenicity, irregular margins, and microcalcifications—which are key components of the K-TIRADS system [26]. Further support is provided by previous studies, which reported that thyroid nodules in older

populations are more frequently classified into higher K-TIRADS categories and are associated with a greater proportion of malignancy compared to younger groups [26,30]. In addition to increased prevalence, age is also associated with changes in the biological behavior and morphology of thyroid nodules. A study noted that while certain malignancy risks may occur in younger patients, nodules in older individuals more often exhibit aggressive morphological features [29]. The persistence of this association after adjustment indicates that age exerts an independent effect on nodule morphology, rather than acting solely as a proxy for other clinical variables. Although K-TIRADS is a morphology-based system, these findings suggest that age-related biological processes contribute to structural changes in thyroid nodules that are captured by ultrasonographic risk stratification.

The absence of a significant association between K-TIRADS classification and sex is consistent with the underlying principle of TIRADS-based systems, which rely on morphological features rather than demographic characteristics [26]. Although thyroid nodules were more prevalent in females, the proportion of higher-risk nodules (K-TIRADS 4–5) was comparable between sexes in the present study. Previous studies have similarly reported higher nodule prevalence in females but a relatively higher malignancy risk per nodule in males, likely related to hormonal and reproductive factors [27,28]. Estrogen has been shown to regulate the metastatic phenotype of thyroid cancer cells, and expression of estrogen receptor α and β has been identified in human thyroid cancer tissues [28]. In contrast, solitary nodules in males may carry a higher risk of malignancy [29]. However, K-TIRADS does not incorporate hormonal or molecular factors, as it is based solely on ultrasonographic imaging features [7,26]. In the present study, adjustment for menopausal status and other confounders, including age, serum TSH level, BMI, smoking history, thyroid medication use, family history of thyroid cancer, and comorbidities, did not alter the non-significant association between sex and K-TIRADS. These findings support the role of K-TIRADS as an objective, morphology-based risk stratification system that is largely independent of demographic and hormonal factors, reflecting imaging-based malignancy risk rather than underlying biological variation.

The present study also found that BMI was not significantly associated with K-TIRADS classification, despite a higher absolute number of nodules observed in overweight and obese individuals. Although several studies have reported an association between obesity and thyroid cancer risk, this relationship is not consistently reflected in TIRADS-based scoring systems [15-19]. BMI may influence systemic inflammatory and hormonal status; however, evidence suggests that the thyroid tumor microenvironment is more strongly driven by local immune–inflammatory interactions than by anthropometric factors alone [30]. This may explain the absence of a significant association between BMI and K-TIRADS classification, indicating that BMI is not an independent determinant of suspicious ultrasonographic morphology. Higher BMI has been associated with increased thyroid nodule prevalence and larger thyroid volume [16-19]. Previous studies have shown that individuals with higher BMI tend to have a greater number of thyroid nodules [16-19]. Another study also reported increased thyroid volume and nodularity in patients with obesity, potentially mediated by elevated leptin levels [31]. However, increased nodule prevalence does not necessarily correspond to higher malignancy risk or more suspicious ultrasonographic features, as reflected in K-TIRADS scores. Obesity is associated with systemic metabolic and inflammatory alterations, including insulin resistance, hyperinsulinemia, and increased adipokine activity [19,30]. These factors may promote thyroid growth and nodular formation; however, not necessarily drive the morphological changes associated with malignancy. The lack of association in the present study reinforces the concept that K-TIRADS classification is largely independent of anthropometric factors and instead reflects intrinsic structural characteristics of the nodule.

Serum TSH levels demonstrated a significant independent association with K-TIRADS classification after multivariable adjustment, although this association was not apparent in unadjusted analysis. This pattern suggests the presence of confounding variables that may obscure the true association between serum TSH level and ultrasonographic risk when not controlled. After adjustment, higher serum TSH levels were associated with increased K-TIRADS scores, indicating a greater likelihood of suspicious sonographic features. This finding is consistent with the established role of TSH as a trophic hormone that stimulates thyroid follicular

cell proliferation through activation of intracellular signaling pathways, including cyclic AMP and protein kinase A [32]. Chronic or elevated TSH stimulation may promote cellular proliferation, angiogenesis, and architectural remodeling, which could manifest as high-risk ultrasonographic features [32,33]. The discrepancy between unadjusted and adjusted findings highlights the importance of comprehensive statistical modeling in studies of thyroid nodules. Serum TSH levels are influenced by multiple factors, including age, sex, metabolic status, and underlying thyroid function, which may confound crude associations [10-14]. The emergence of a significant association after adjustment suggests that TSH exerts an independent effect on nodule characteristics when these factors are accounted for. From a clinical perspective, this supports the integration of serum TSH level assessment into the overall evaluation of thyroid nodules, alongside imaging-based risk stratification.

Several limitations should be considered. The cross-sectional design precludes causal inference and limits evaluation of temporal relationships between clinical variables and evolution of ultrasonographic features, such that the roles of age and TSH in driving, rather than accompanying, suspicious morphology cannot be determined. The absence of systematic histopathological confirmation is a key limitation, as K-TIRADS served as a surrogate for malignancy risk without validation against fine-needle aspiration biopsy or surgical pathology outcomes. Serum TSH level was assessed at a single time point, which may not reflect dynamic thyroid function influenced by circadian variation, subclinical dysfunction, or systemic conditions. Longitudinal measurements could provide more precise characterization of this relationship. In addition, although several confounders were included, other relevant factors—such as iodine status, thyroid autoantibodies, prior radiation exposure, and molecular alterations (e.g., BRAF or RAS mutations)—were not evaluated, leaving the possibility of residual confounding.

Future research should adopt prospective longitudinal cohort designs to evaluate changes in K-TIRADS classification over time and to determine whether age- and TSH-related effects predict progression to malignancy. Integration of histopathological outcomes is essential to validate the predictive performance of combined clinical and ultrasonographic parameters. Studies incorporating serial thyroid function testing, including TSH, free T4, free T3, and autoantibody profiles, may better characterize the hormonal milieu associated with nodule evolution. In addition, multimodal approaches combining conventional ultrasonography with advanced imaging techniques, such as elastography or contrast-enhanced ultrasound, should be explored to improve diagnostic accuracy. The inclusion of molecular and genetic profiling may further refine risk stratification by linking biological pathways with imaging phenotypes. Finally, large-scale, multicenter studies across diverse populations are needed to enhance external validity and to evaluate potential geographic or ethnic variability in the relationship between clinical parameters and K-TIRADS classification.

Conclusion

Increasing age and higher serum TSH levels were independently associated with higher K-TIRADS classification, whereas no independent associations were observed for sex or BMI. Although K-TIRADS provides a reliable morphology-based framework for risk stratification, the addition of selected clinical parameters may further improve risk assessment. Integrating ultrasonographic findings with age and serum TSH may enhance the accuracy of malignancy prediction and facilitate more tailored management strategies for patients with thyroid nodules.

Ethics approval

Protocol of the present study was reviewed and approved by Ethical Committee of Health Research, Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia (Approval number: 317/ETIK-RSUDZA/2025).

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

Artificial intelligence (AI) tool, ChatGPT, was employed in the language refinement (improving grammar, sentence structure, and readability of the manuscript). Authors confirmed that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

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