

RESEARCH ARTICLE

Editorial Process: Submission:26/01/2026 Acceptance:04/10/2026 Published:24/10/2026

Sonographic Features of Well-Differentiated Thyroid Cancer Recurrence in the Thyroid Bed After Thyroidectomy

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Abstract

Background: Thyroid cancer is the most common endocrine malignancy, with a steadily increasing incidence. Well-differentiated thyroid carcinoma, comprising papillary and follicular types, has an excellent prognosis but a relatively high recurrence rate, predominantly as local recurrence in the thyroid bed or cervical lymph nodes. Current surveillance relies on serum thyroglobulin measurement and ultrasound, both of which are accessible but prone to false-positive findings due to benign postoperative changes. This study aimed to identify ultrasound features of well-differentiated thyroid cancer recurrence in the thyroid bed after thyroidectomy and to compare the sensitivity of ultrasound with serum thyroglobulin for recurrence surveillance. **Methods:** In this retrospective study, we examined the sonographic features of thyroid bed lesions in two groups of patients (the recurrence group and the non-recurrence group) who had well-differentiated thyroid cancer from 2015 to 2023. The correlations between the sonographic features and recurrence were examined using the univariate and multivariate logistic regression analyses. **Results:** A total of 260 lesions were identified from 184 patients, with 32 in the recurrence group and 228 in the non-recurrence group. Certain sonographic features were significantly associated with recurrence, including microcalcification, hypoechogenicity, cystic components, lesion size ≥ 5 mm, internal vascularity, and taller-than-wide shape. Ultrasound examination (in lesions ≥ 5 mm) combined with thyroglobulin measurement had 100% sensitivity for identifying recurrence. **Conclusion:** Certain sonographic features, including microcalcification, hypoechogenicity, cystic components, lesion size ≥ 5 mm, internal vascularity, and a taller-than-wide shape, were associated with thyroid carcinoma recurrence after thyroidectomy. Therefore, ultrasound examination should be performed in combination with thyroglobulin assessment for the early detection and effective surveillance of local recurrence.

Keywords: Well-differentiated thyroid cancer, Thyroidectomy, Thyroid bed, Recurrence, Ultrasound

Asian Pac J Cancer Prev, 27 (10), 3731-3738

Introduction

Thyroid cancer is the most common type of endocrine cancer. Its incidence has increased in the last 30 years, with an annual increase of 3.8% [1]. Thyroid cancer can be classified into four main types: papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC), medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC) [2]. The most common form of thyroid cancer is well-differentiated thyroid carcinoma, which consists of PTC and FTC [3]. This group of thyroid cancers has a better prognosis than other thyroid cancers. It has been shown that PTC and FTC have 10-year survival rates of more than 95% and 85%, respectively [4, 5]. Because of these high survival rates, the local recurrence of this group of thyroid cancers is as high as 30%. Another study reported that the recurrence rate of

FTC is 43% [6, 7]. Well-differentiated thyroid cancer recurrence can present as both local or regional recurrence and distant metastasis, with around 76% of cases being local recurrence, including recurrence in the thyroid bed and cervical nodal chains [8].

Currently, there are two standard methods for the surveillance of thyroid cancer recurrence, including serum thyroglobulin (Tg) measurement and ultrasound (US) examination [9]. Both of these methods are easy, fast, and inexpensive, but they can produce false-positive results [10]. The sonographic features indicating local recurrence include hypoechogenicity, taller-than-wide shape, irregular margin, lesion cysts/microcalcification, and the presence of lesion blood flow [9, 11, 12]. Nonetheless, these sonographic features can also be identified in patients with non-recurrence, such as in patients with remnant thyroid tissue, suture granuloma, postoperative

fibrosis, and traumatic neuromas, amongst others [8, 13], frequently producing false-positive results. Hence, the local recurrence features of thyroid cancer are crucial for the examiner to reduce possible errors when interpreting the results.

The purpose of this study was to identify sonographic features associated with recurrence of well-differentiated thyroid carcinoma in the thyroid bed following thyroidectomy. In addition, we compared the sensitivity of ultrasound and serum Tg measurement in detecting recurrent disease. The findings aim to support more accurate ultrasound interpretation and optimize postoperative surveillance in patients with well-differentiated thyroid carcinoma.

Materials and Methods

Study Design and Patient Population

This retrospective observational cohort study was approved by the Chulabhorn Research Institute (EC079/2565) and was exempted from the requirement for individual informed consent. Patients who underwent thyroidectomy for well-differentiated thyroid carcinoma at Chulabhorn Hospital, Bangkok, Thailand, between January 2015 and December 2023 were eligible for inclusion.

During the study period, 224 patients underwent total or near-total thyroidectomy followed by postoperative radioactive iodine ablation. Forty patients without postoperative follow-up were excluded. The final study cohort consisted of 184 patients with 260 thyroid bed lesions. Among these, 32 lesions in 28 patients were confirmed as recurrent tumors, and 228 lesions in 156 patients were classified as nonrecurrent. This study focused specifically on lesions located within the thyroidectomy bed. Cervical lymph node lesions were not included as index lesions for sonographic feature analysis. When coexisting cervical nodal recurrence or distant metastasis was identified during postoperative surveillance, this information was recorded because disease outside the thyroid bed may influence serum Tg interpretation.

Recurrent lesions were confirmed by repeat surgery ($n = 2$) or ultrasound-guided fine-needle aspiration (FNA) with cytopathologic confirmation ($n = 30$). Nonrecurrent lesions were confirmed by benign cytology on FNA ($n = 16$) or stability on follow-up ultrasound for at least 2 years ($n = 212$). The interval between initial surgery and detection of recurrence, as well as follow-up duration, are summarized in Table 1.

Data Collection

Clinical data were retrospectively obtained from medical records, including patient sex, age at the time of ultrasound examination, histologic subtype of thyroid cancer, and history of radioactive iodine ablation. Pathologic results from FNA or surgery were recorded when available. Serum Tg levels measured within 6 months of the ultrasound examination were collected; values below the assay detection limit (<0.004 ng/mL) were recorded as zero. Information regarding distant

metastasis was also documented. Complete pretreatment staging information was not consistently available for all patients and was therefore not included in the comparative analysis.

For Tg-based diagnostic performance analysis, patients with disease outside the thyroid bed were excluded because serum Tg may be influenced by cervical nodal recurrence or distant metastasis. Therefore, 11 patients in the nonrecurrence group with distant metastasis and 5 patients in the recurrence group with coexisting thyroid bed recurrence, nodal recurrence, and distant metastasis were excluded from Tg and Tg+US analyses.

Ultrasound Imaging Variables

Sonographic characteristics of thyroid bed lesions were evaluated, including echogenicity relative to the surrounding strap muscles (hypoechoogenicity, isoechoogenicity, or hyperechoogenicity; Figures 1–3), maximum lesion diameter, shape (taller-than-wide or wider-than-tall; Figures 4–5), boundary, margin, cystic components, microcalcifications (Figure 6), and intralesional vascularity on Doppler imaging. Boundary referred to lesion demarcation from the surrounding thyroid bed tissue and was categorized as well-defined or ill-defined (Figures 7–8), whereas margin referred to the lesion contour and was categorized as regular or irregular (Figures 9–10). A taller-than-wide shape was defined as

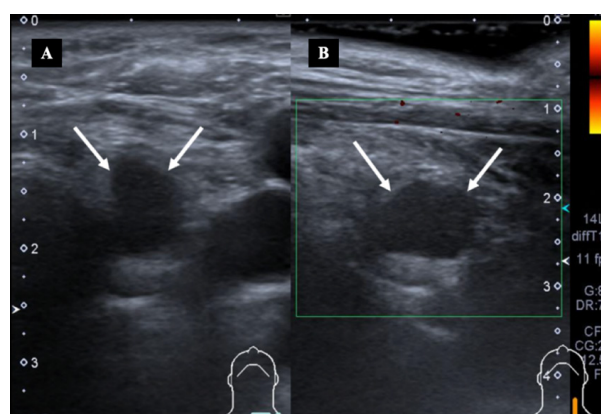


Figure 1. Transverse (A) and Sagittal (B) Sonograms Showing a Hypoechoogenicity Lesion (Arrows) Compared with the Strap Muscle on the Left Thyroid Bed.

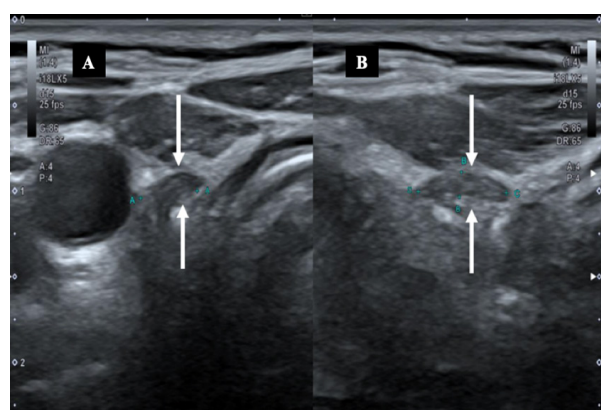


Figure 2. Transverse (A) and Sagittal (B) Sonograms Showing an Isoechoogenicity Lesion (Arrows) Compared with the Strap Muscle on the Right Thyroid Bed.

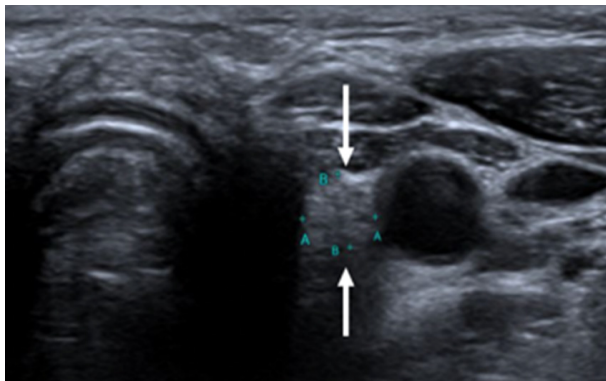


Figure 3. Transverse Sonograms Showing a Hyperechoic Lesion (Arrows) Compared with the Strap Muscle on the Left Thyroid Bed.

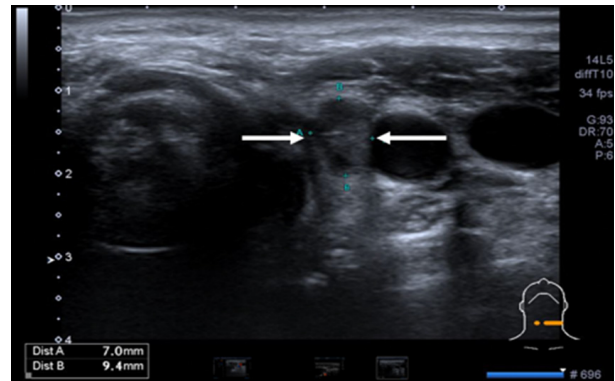


Figure 4. Transverse Sonogram Showing a 7.0 × 9.4 mm Taller-than-Wide Lesion (Arrows) on the Left Thyroid Bed.

an anteroposterior dimension equal to or greater than the transverse dimension on transverse images. Cystic components were defined as cystic areas measuring at least 2 mm. Microcalcifications were defined as punctate echogenic foci measuring ≤ 1 mm without posterior acoustic shadowing. Lesion growth was defined as an increase of ≥ 3 mm in the largest dimension compared with the initial examination, a threshold chosen to minimize measurement variability in high-resolution ultrasound.

All ultrasound images were retrospectively reviewed by a single radiologist with more than 15 years of experience in thyroid imaging, who was aware of the postoperative status but blinded to final recurrence outcomes at the time of image review.

Statistical Analysis

Statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, version 26.0; IBM Corp., Armonk, NY). Continuous variables are presented as mean $\pm$ standard deviation, and categorical variables as number and percentage. Comparisons between recurrent and nonrecurrent groups were performed using the independent t-test for continuous variables and the chi-square test for categorical variables.

Univariate and multivariate logistic regression analyses were conducted to evaluate associations between ultrasound features and thyroid cancer recurrence. The diagnostic performance of ultrasound and serum Tg measurement was assessed by calculating sensitivity, specificity, accuracy, positive predictive value, and negative predictive value. A p value < 0.05 was considered statistically significant.

Results

Sample Population

A total of 184 patients with well-differentiated thyroid carcinoma were included, comprising 260 thyroid bed lesions identified during postoperative surveillance. Local recurrence was confirmed in 28 patients (32 lesions), while 156 patients (228 lesions) had no evidence of recurrence. Recurrent lesions were confirmed by ultrasound-guided fine-needle aspiration or surgical pathology, whereas nonrecurrent lesions were confirmed by benign cytology

or stability on ultrasound follow-up for at least 2 years.

Patients in the recurrence group were significantly older than those in the non-recurrence group ($p = 0.010$). No significant differences were observed between groups with respect to sex or histologic subtype of thyroid cancer (Table 1). After exclusion of patients with disease outside the thyroid bed, Tg and Tg+US analyses were calculated from 168 patients, including 23 patients in the recurrence group and 145 patients in the nonrecurrence group. The reanalysis did not materially change the diagnostic performance results. Tg measurement alone remained less sensitive than ultrasound, whereas the combined use of Tg and ultrasound maintained 100% sensitivity for detecting local thyroid bed recurrence. Both baseline postoperative Tg levels and Tg levels at the time of lesion detection were significantly higher in the recurrence group than in the non-recurrence group ($p = 0.015$ and $p < 0.001$, respectively) (Table 1).

Sonographic Features of Thyroid Bed Lesions

Several ultrasound features differed significantly between recurrent and nonrecurrent lesions. Lesions in the recurrence group were more frequently ≥ 5 mm in size, hypoechogenicity, irregular margins, demonstrated cystic components or microcalcifications, and showed internal vascularity on Doppler imaging (all $p < 0.001$).

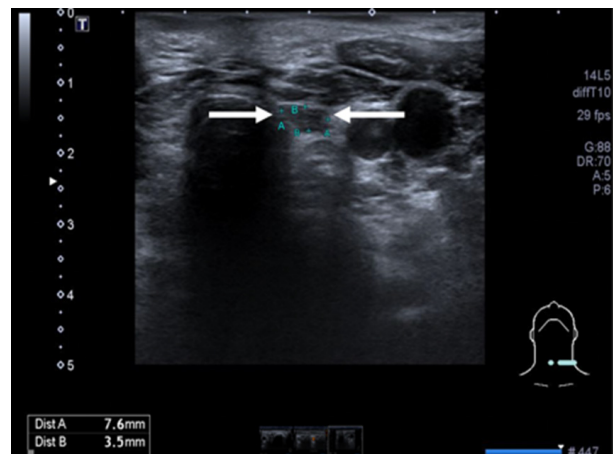


Figure 5. Transverse Sonogram Showing a 7.6 × 3.5 mm Wider-than-Tall Lesion (Arrows) on the Left Thyroid Bed.

Table 1. Demographic Data of the Study Population

	Recurrence (N = 28)	Non-recurrence (N = 156)	Total (N = 184)	p-value
Sex				
Female	21 (75.00)	129 (82.69)	150 (81.52)	0.071
Male	7 (25.00)	27 (17.31)	34 (18.48)	
Type of thyroid cancer				
PTC	24 (85.71)	137 (87.82)	161 (87.50)	0.119
FTC	2 (7.14)	16 (10.26)	18 (9.78)	
PTC + FTC	2 (7.14)	3 (1.92)	5 (2.72)	
Age	57.18 ± 16.09	49.35 ± 14.44	50.54 ± 14.92	0.010*
Postoperative Baseline Tg	1.82 ± 3.66	0.40 ± 2.59†	0.61 ± 2.81	0.015*
Tg during lesion detection	10.29 ± 20.03‡	1.52 ± 6.84†,‡	2.85 ± 10.43	<0.001*

PTC, papillary thyroid cancer; FTC, follicular thyroid cancer; Tg, thyroglobulin. The data are presented as the mean ± standard deviation or number (percentage). †Calculated from a total of 145 patients because 11 patients in the non-recurrence group had distant metastasis and were excluded. ‡Thyroglobulin while detecting the lesion (within 6 months after lesion detection) (14). *Indicates statistical significance ($p < 0.05$).

A taller-than-wide configuration was more frequently observed in recurrent lesions, although this difference did not reach statistical significance on univariate comparison (Supplementary Table 1).

Association Between Sonographic Features and Recurrence

On univariate logistic regression analysis, lesion size ≥ 5 mm, hypoechogenicity, cystic component, microcalcification, internal vascularity, irregular margin, and taller-than-wide shape were associated with recurrence

at a significance threshold of $p < 0.2$ (Table 2).

Multivariate logistic regression analysis identified six independent sonographic predictors of recurrence: microcalcification, hypoechogenicity, cystic component, lesion size ≥ 5 mm, internal vascularity, and taller-than-wide shape. Among these, microcalcification and hypoechogenicity demonstrated the strongest associations with recurrence (Table 2).

Diagnostic Performance of Ultrasound and Thyroglobulin

Ultrasound examination demonstrated higher

Table 2. Correlation of Sonographic Features with Recurrence

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Size	14.14	5.22–38.35	<0.001*	32.07	7.25–141.87	<0.001**
<5 mm						
≥ 5 mm						
Echogenicity	19.49	2.61–145.30	0.004*	163.62	5.34–5011.41	0.004**
Iso/hyperechogenicity						
Hypoechogenicity						
Aspect ratio	1.98	0.91–4.32	0.085*	4.59	1.17–18.10	0.029**
Wider than tall						
Taller than wide						
Margin	10.71	2.28–50.36	0.003*	8.98	0.50–160.63	0.136
Regular						
Irregular						
Cystic component	26.08	5.00–135.91	<0.001*	37.02	1.20–1142.84	0.039**
No						
Yes						
Microcalcification	32.43	3.50–300.44	0.002*	208.41	8.64–5028.83	0.001**
No						
Yes						
Blood flow	19.86	8.39–47.00	<0.001*	10.76	2.98–38.82	<0.001**
No						
Yes						

OR, odds ratio; CI, confidence interval. *Indicates statistical significance ($p < 0.2$). **Indicates statistical significance ($p < 0.05$). Note: Boundary was not included in the statistical analysis because all lesions in the recurrence group had clear boundaries (100%).

Table 3. Sensitivity, Specificity, Accuracy, PPV, and NPV of Thyroglobulin Measurement and Ultrasound Examination.

		Gold standard‡		Sensitivity	Specificity	Accuracy	PPV	NPV
		Positive	Negative					
Tg#	Positive	15	19	65.22	86.9	83.93	44.12	94.03
	Negative	8	126					
US##	Positive	24	22	85.71	84.83	84.97	52.17	96.85
	Negative	4	123					
Tg+US	Positive	23	39	100	73.1	76.79	37.1	100
	Negative	0	106					

Tg, thyroglobulin; US, ultrasound; PPV, positive predictive value; NPV, negative predictive value. ‡The gold standard for diagnosis is pathological outcomes obtained from needle aspiration/surgery. If the lesion has increased in size by <3 mm (15, 16) or there is no change in the sonographic appearance for at least 2 years at ultrasound follow-up (14, 17), the lesions are classified as non-recurrence lesions. #Recurrence was defined when thyroglobulin was >1 ng/mL (10, 11, 18). ##Recurrence was defined when the lesion on ultrasound had a size ≥ 5 mm with suspicious ultrasound features of lymph nodes were the following: hypoechogenicity, taller-than-wide shape, cystic component, microcalcification, or blood flow within the lesion (9, 12, 19, 20). Note: Diagnostic performance was calculated from 168 patients, including 23 patients in the recurrence group and 145 patients in the nonrecurrent group. In the nonrecurrent group, 11 patients and 5 patients were excluded from non-recurrence and recurrence group due to nodal or distant metastases.

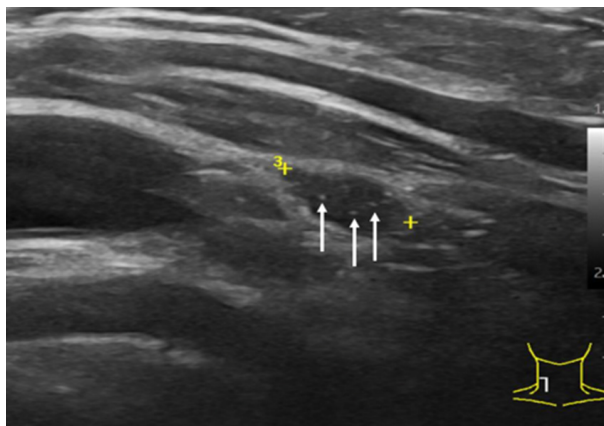


Figure 6. Sagittal Sonogram Showing a Hypoechogenicity Lesion (Calipers) with a Few Microcalcifications (Arrows) on the Right Thyroid Bed.

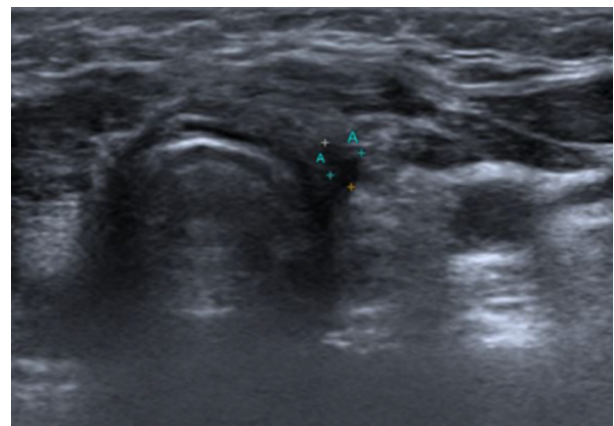


Figure 8. Transverse Sonogram Showing an Ill-Defined Hypoechogenicity Lesion (Calipers) on the Left Thyroid Bed.

sensitivity for detecting local recurrence than serum Tg measurement alone (85.7% vs. 65.2%). When ultrasound findings were combined with Tg measurement, sensitivity increased to 100% (Table 3).

Discussion

Current guidelines from the American Thyroid Association and the European Society for Medical Oncology recommend postoperative surveillance of

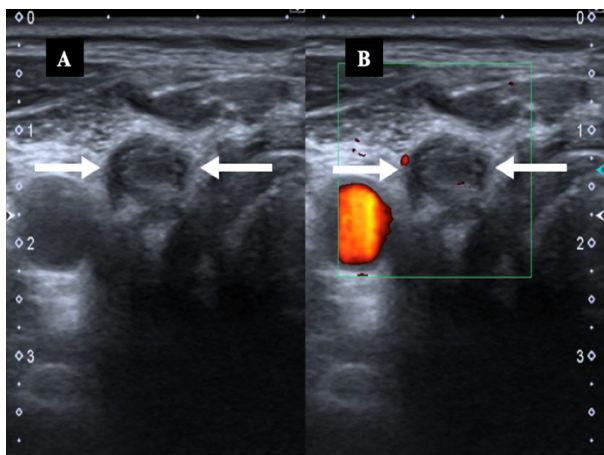


Figure 7. Grayscale (A) and Power Doppler (B) Transverse Sonogram Showing a Well-Defined Isoechoogenicity Lesion without Internal Vascularity (Arrows) on the Right Thyroid Bed.



Figure 9. Transverse Sonogram Showing a Regular Hypoechogenicity Lesion (Dotted Line) on the Right Thyroid Bed.

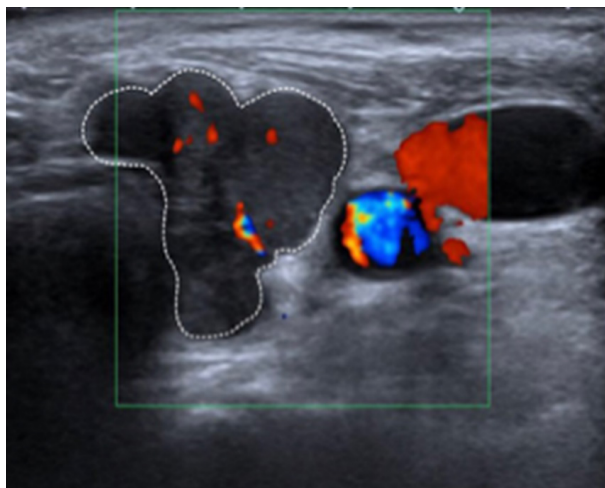


Figure 10. Transverse Sonogram Showing an Irregular Hypoechoogenicity Lesion (Dotted Line) on the Left Thyroid Bed. The results of fine-needle aspiration were positive for malignancy.

well-differentiated thyroid carcinoma using serum Tg measurement and periodic neck ultrasound, with attention to suspicious sonographic features such as hypoechoogenicity, taller-than-wide shape, irregular margins, cystic change or microcalcification, and intralesional vascularity. The findings of the present study are consistent with these recommendations and with prior reports [11, 12, 14, 15].

In this cohort, several ultrasound features were independently associated with local recurrence in the thyroid bed, including microcalcification, hypoechoogenicity, cystic components, lesion size ≥ 5 mm, internal vascularity, and a taller-than-wide configuration. Among these, microcalcification and hypoechoogenicity demonstrated the strongest associations with recurrence on multivariate analysis. Microcalcifications likely correspond to psammoma bodies, a characteristic histopathologic finding in papillary thyroid carcinoma [16, 17]. The high prevalence of hypoechoogenicity among recurrent lesions is also in agreement with previous studies and may reflect tumor hypercellularity and reduced acoustic interfaces compared with benign postoperative changes [14, 18, 19].

Cystic components were more frequently observed in recurrent lesions, which may be related to tumor necrosis or colloid accumulation following radioactive iodine therapy [20, 21]. Lesion size was another important discriminator; lesions measuring < 5 mm were rarely recurrent, consistent with prior studies demonstrating low malignant potential and limited clinical significance of very small thyroid bed nodules [22]. In addition, fine-needle aspiration of lesions < 5 mm is technically challenging and often yields nondiagnostic results, further supporting conservative management of these small lesions.

Internal vascularity was significantly associated with recurrence in the present study, although the observed frequency was higher than that reported in earlier literature [18]. This discrepancy may reflect improvements in Doppler sensitivity and microvascular imaging, as well as differences in imaging parameters and equipment. In

addition, it may be related to the fact that hypervascularity may exist in original thyroid tumors [23]. A taller-than-wide configuration was also independently associated with recurrence, consistent with the known growth pattern of malignant lesions across normal tissue planes [24], although this feature alone demonstrated limited discriminatory value on univariate analysis.

The multivariable analysis demonstrated that several sonographic features were independently associated with recurrence after adjustment for other imaging findings. Therefore, when multiple independent suspicious features coexist in the same thyroid bed lesion, the likelihood of recurrence should be considered higher in clinical practice. Although a formal scoring system based on the number of suspicious features was not performed, thyroid bed lesions measuring ≥ 5 mm with multiple suspicious features may warrant closer follow-up or tissue sampling, particularly when accompanied by elevated serum Tg.

In contrast, lesion boundaries were not useful for distinguishing recurrent from nonrecurrent lesions, as most lesions in both groups were well-defined. This finding is consistent with prior reports and likely reflects the well-differentiated nature of most recurrent tumors as well as the presence of benign, well-circumscribed postoperative structures in the thyroid bed.

From a diagnostic performance perspective, ultrasound demonstrated higher sensitivity than Tg measurement alone for detecting local recurrence. Importantly, the combined use of ultrasound and Tg measurement achieved 100% sensitivity, supporting their complementary roles in postoperative surveillance. However, ultrasound showed lower specificity, likely due to benign postoperative findings such as remnant thyroid tissue or suture granuloma, which are known sources of false-positive results [8, 18, 25].

This study has some limitations. First, complete pretreatment staging information was not consistently available for all patients, particularly because many patients were referred from other hospitals after initial surgery for postoperative radioactive iodine treatment. Therefore, baseline nodal status and distant metastasis could not be reliably compared between the recurrence and nonrecurrence groups, which may limit the interpretation of recurrence patterns in this retrospective cohort.

Another limitation is that nonrecurrent lesions were partly defined by stability on follow-up ultrasound for at least 2 years. Although this definition is consistent with prior thyroid bed imaging studies, well-differentiated thyroid carcinoma may recur or persist after a prolonged interval. Therefore, a 2-year follow-up period may not fully exclude very indolent residual disease or late recurrence. Longer-term follow-up studies are warranted.

In summary, this study reinforces the role of ultrasound as a primary modality for postoperative surveillance of thyroid bed recurrence following thyroidectomy. Recurrence is more likely in lesions measuring ≥ 5 mm and in those demonstrating suspicious sonographic features, including microcalcifications, hypoechoogenicity, cystic components, internal vascularity, and a taller-than-wide configuration. When used in conjunction with serum thyroglobulin measurement, ultrasound provides optimal

sensitivity for the detection of local recurrence and should be considered standard practice for effective postoperative surveillance of patients with well-differentiated thyroid carcinoma.

Author Contribution Statement

Nannapat Nuangchamnong^{1,2,3,4,5}, Nutsurang Promrach⁴, Pooriput Waongenngarm^{1,3}, Pantajaree Hiranrat³, Surachate Siripongsakun^{1,3,4,5}. Note: 1. Study concept and design 2. Acquisition of data 3. Analysis and interpretation of data 4. Drafting the manuscript 5. Critical revision of the manuscript

Acknowledgements

This study was supported by the Sonographer School, Faculty of Health Science Technology, Chulabhorn Royal Academy, and Chulabhorn Hospital, Thailand, for their facilitation and assistance in data collection, which contributed to the successful completion of this research.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author (SS). The data are not publicly available due to ethical restrictions.

Ethics approval statement

The study was approved by Human Research Ethics Committee of Chulabhorn Research Institute (EC079/2565) and the requirement for individual informed consent was waived due to the retrospective nature of the study.

Conflict of interest disclosure

The authors have no conflicts of interest corresponding to this article.

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