THE JOURNAL OF SURGICAL RADIOLOGY

Journal of Surgical Radiology

Site: https://journalsurgrad.com/

ISSN Print 2156-213X| ISSN Online: 2156-4566 Volume: 05Issue: 04 Open Access

Research Article

Role of Ultrasound and Doppler Parameters in Differentiating Benign and Malignant Thyroid Nodules: A Cross-Sectional Study

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Article History

Received: 15.01.2026
Revised: 22.02.2026
Accepted: 18.03.2026
Published: 11.04.2026

Citations:
Sune, S., Pawar, A., & Narote, V. (n.d.). Role of ultrasound and Doppler parameters in differentiating benign and malignant thyroid nodules: A cross-sectional study.J Surg Radiol, V5(4) 35-41

Abstract: ***Introduction:*** Thyroid nodules are common clinical findings, with a small but significant proportion harboring malignancy. Accurate, non-invasive differentiation between benign and malignant nodules is essential to guide further management and avoid unnecessary invasive procedures. **Aim:** To evaluate the role of ultrasound and Doppler parameters in differentiating benign and malignant thyroid nodules. **Materials and Methods:** This hospital-based cross-sectional study included 120 patients with thyroid nodules evaluated using high-resolution gray-scale ultrasound and Doppler imaging. Ultrasound features such as composition, echogenicity, margins, calcifications, shape, halo, and extrathyroidal extension were assessed. Doppler evaluation included vascular patterns and spectral indices such as resistive index, pulsatility index, and peak systolic velocity. Findings were correlated with fine-needle aspiration cytology and/or histopathology. Statistical analysis included comparison of variables, calculation of effect sizes, and assessment of diagnostic accuracy. **Results:** Malignant nodules were associated with older age, larger size, suspicious cervical lymphadenopathy, higher TIRADS categories, and high-risk Doppler patterns. Gray-scale ultrasound features including solid composition, hypoechogenicity, irregular margins, microcalcifications, taller-than-wide shape, absent halo, and extrathyroidal extension showed significant associations with malignancy ($p < 0.05$). Doppler indices were significantly higher in malignant nodules, and chaotic intranodular flow was strongly predictive of malignancy. Combined ultrasound and Doppler assessment demonstrated the highest diagnostic accuracy (85.8%), outperforming either modality alone. **Conclusion:** A combined gray-scale ultrasound and Doppler approach provides superior diagnostic accuracy in differentiating benign and malignant thyroid nodules. This multiparametric evaluation can enhance risk stratification and guide appropriate clinical decision-making.

Keywords: Thyroid nodules. Doppler ultrasound. Thyroid malignancy.

INTRODUCTION

Thyroid nodules are a common clinical finding, with a reported prevalence ranging from 19-68% in the general population when detected by high-resolution ultrasonography. Although the majority of thyroid nodules are benign, approximately 5-15% harbor malignancy, making accurate risk stratification essential to guide further diagnostic and therapeutic decisions. The increasing use of imaging modalities has led to a rising detection rate of incidental thyroid nodules, posing challenges in differentiating benign from malignant lesions while avoiding unnecessary invasive procedures.[1]

Ultrasonography (USG) is the first-line imaging modality for the evaluation of thyroid nodules due to its non-invasiveness, wide availability, cost-effectiveness, and excellent spatial resolution. Gray-scale ultrasound provides valuable information regarding nodule size, echogenicity, margins, shape, calcifications, and internal composition. Certain sonographic features such as hypoechogenicity, irregular margins, microcalcifications, taller-than-wide shape, and absence of a peripheral halo have been consistently associated with an increased risk of malignancy. However, no single ultrasound feature alone is sufficiently sensitive or specific, necessitating a combination of parameters for improved diagnostic accuracy.[2]

Color Doppler and spectral Doppler ultrasound add a functional dimension to morphological assessment by evaluating vascular patterns within and around thyroid nodules. Malignant nodules often demonstrate increased internal vascularity, chaotic flow patterns, and elevated resistive and pulsatility indices due to tumor-induced neoangiogenesis. In contrast, benign nodules typically show peripheral or absent vascularity with relatively lower Doppler indices. The integration of Doppler parameters with gray-scale ultrasound findings has been shown to enhance diagnostic confidence and reduce false-negative rates.[3]

Fine-needle aspiration cytology (FNAC) remains the gold standard for diagnosing thyroid malignancy; however, it is invasive, operator-dependent, and may yield indeterminate or non-diagnostic results in a significant proportion of cases. Hence, there is growing emphasis on optimizing non-invasive imaging criteria to triage nodules requiring FNAC and surgical intervention. Risk stratification systems such as TIRADS have further emphasized the role of ultrasound-based assessment, though variability in interpretation and overlap of features between benign and malignant nodules persist.[4]

Aim
To evaluate the role of ultrasound and Doppler parameters in differentiating benign and malignant thyroid nodules.

Objectives
1. To assess gray-scale ultrasound features of thyroid nodules and their association with benign and malignant pathology.
2. To evaluate Doppler vascular patterns and indices in thyroid nodules and correlate them with cytological or histopathological diagnosis.
3. To determine the diagnostic accuracy of combined ultrasound and Doppler parameters in differentiating benign from malignant thyroid nodules.

MATERIALS AND METHODS

Source of Data
The study data were obtained from patients presenting with clinically or incidentally detected thyroid nodules who were referred to the Department of Radiodiagnosis for ultrasound evaluation.

Study Design
This was a hospital-based cross-sectional observational study.

Study Location
The study was conducted in the Department of Radiodiagnosis in collaboration with the Departments of ENT, Surgery, and Pathology at a tertiary care teaching hospital.

Study Duration
The study was carried out over a period of 18 months.

Sample Size
A total of 120 patients with thyroid nodules were included in the study.

Inclusion Criteria
- Patients aged 18 years and above
- Patients with one or more thyroid nodules detected clinically or incidentally
- Patients who consented to undergo ultrasound, Doppler evaluation, and FNAC or surgery

Exclusion Criteria
- Patients with diffuse thyroid disease without discrete nodules
- Previously diagnosed or treated cases of thyroid malignancy
- Patients who had undergone prior thyroid surgery or radioiodine therapy
- Patients unwilling to provide informed consent

Procedure and Methodology
All patients underwent detailed clinical evaluation followed by high-resolution gray-scale ultrasound of the thyroid gland using a high-frequency linear transducer. Nodules were evaluated for size, number, composition, echogenicity, margins, shape, presence of calcifications, and halo sign. Color Doppler imaging was performed to assess vascularity patterns (peripheral, central, mixed, or absent). Spectral Doppler analysis was used to measure resistive index (RI) and pulsatility index (PI) of intranodular vessels.

Sample Processing
Ultrasound-guided FNAC was performed for all nodules using standard aseptic techniques. Cytological smears were prepared, stained, and reported according to the Bethesda System. Histopathological examination was considered when surgical specimens were available.

Data Collection
All clinical, ultrasound, Doppler, and cytological or histopathological findings were systematically recorded in a pre-designed proforma.

Statistical Methods
Data were entered into Microsoft Excel and analyzed using statistical software. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. The Chi-square test and independent t-test were used to assess associations. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Clinicodemographic Profile and Overall Ultrasound-Doppler Characteristics (N = 120)

Variable	Benign (n = 83)	Malignant (n = 37)	Test of significance	Effect size (95% CI)	p-value
Age (years), Mean ± SD	44.1 ± 11.8	49.8 ± 12.4	Welch t = 2.36	Mean diff = +5.7 (0.9 to 10.5)	0.021
Female sex, n (%)	63 (75.9)	25 (67.6)	χ^2 = 0.91	RR = 0.76 (0.43-1.32)	0.340

Nodule size (mm), Mean ± SD	17.8 ± 8.4	21.7 ± 9.1	Welch t = 2.22	Mean diff = +3.9 (0.4 to 7.4)	0.030
Solitary nodule, n (%)	41 (49.4)	24 (64.9)	χ^2 = 2.47	RR = 1.56 (0.88-2.77)	0.116
Suspicious cervical LN, n (%)	3 (3.6)	9 (24.3)	χ^2 = 12.20	RR = 2.89 (1.83-4.57)	<0.001
TIRADS 4-5, n (%)	18 (21.7)	30 (81.1)	χ^2 = 37.62	RR = 6.43 (3.08-13.44)	<0.001
High-risk Doppler*, n (%)	16 (19.3)	27 (73.0)	χ^2 = 32.09	RR = 4.83 (2.60-9.01)	<0.001

*High-risk Doppler = central/mixed flow with RI ≥0.75 or chaotic vessels

Table 1 compares the clinicodemographic characteristics and overall ultrasound-Doppler findings between benign and malignant thyroid nodules. Patients with malignant nodules were significantly older than those with benign nodules, with a mean age of 49.8 ± 12.4 years compared to 44.1 ± 11.8 years, demonstrating a statistically significant mean difference of 5.7 years (95% CI: 0.9 to 10.5; p = 0.021). Although females constituted the majority in both groups, the proportion of female patients did not differ significantly between benign (75.9%) and malignant (67.6%) nodules (p = 0.340).

Malignant nodules were significantly larger in size, with a mean diameter of 21.7 ± 9.1 mm compared to 17.8 ± 8.4 mm in benign nodules (mean difference: 3.9 mm; 95% CI: 0.4 to 7.4; p = 0.030). Solitary nodules were more frequently observed in malignant cases (64.9%) than benign cases (49.4%); however, this difference did not reach statistical significance (p = 0.116).

The presence of suspicious cervical lymph nodes showed a strong association with malignancy, being observed in 24.3% of malignant nodules compared to only 3.6% of benign nodules (RR = 2.89; 95% CI: 1.83-4.57; p < 0.001). High-risk TIRADS categories (4-5) were significantly more common in malignant nodules (81.1%) than benign nodules (21.7%), demonstrating a markedly increased risk of malignancy (RR = 6.43; p < 0.001). Similarly, high-risk Doppler features were observed in 73.0% of malignant nodules compared to 19.3% of benign nodules, showing a strong and statistically significant association with malignancy (RR = 4.83; p < 0.001).

Table 2: Gray-Scale Ultrasound Features and Association with Malignancy (N = 120)

Gray-scale feature	**Benign n (%)**	**Malignant n (%)**	**Test of significance**	**Relative Risk (95% CI)**	**p-value**
Solid composition	39 (47.0)	31 (83.8)	χ^2 = 14.26	3.69 (1.67-8.17)	<0.001
Hypoechogenicity	24 (28.9)	29 (78.4)	χ^2 = 25.39	4.58 (2.29-9.18)	<0.001
Irregular margins	12 (14.5)	25 (67.6)	χ^2 = 33.85	4.67 (2.65-8.25)	<0.001
Microcalcifications	9 (10.8)	18 (48.6)	χ^2 = 20.98	3.26 (2.02-5.28)	<0.001
Taller-than-wide shape	7 (8.4)	16 (43.2)	χ^2 = 20.02	3.21 (2.02-5.12)	<0.001
Absent halo	26 (31.3)	28 (75.7)	χ^2 = 20.34	3.80 (1.97-7.35)	<0.001
Extrathyroidal extension	2 (2.4)	6 (16.2)	χ^2 = 7.84	2.71 (1.64-4.47)	0.005

Table 2 outlines the distribution of gray-scale ultrasound features among benign and malignant thyroid nodules. Solid composition was significantly more prevalent in malignant nodules (83.8%) compared to benign nodules (47.0%), with a relative risk of 3.69 (95% CI: 1.67-8.17; p < 0.001). Hypoechogenicity was also strongly associated with malignancy, being present in 78.4% of malignant nodules versus 28.9% of benign nodules (RR = 4.58; p < 0.001).

Irregular margins showed one of the strongest associations with malignancy, occurring in 67.6% of malignant nodules compared to only 14.5% of benign nodules (RR = 4.67; p < 0.001). Microcalcifications were significantly more common in malignant nodules (48.6%) than benign nodules (10.8%), indicating a threefold increased risk of malignancy (RR = 3.26; p < 0.001).

A taller-than-wide shape was observed in 43.2% of malignant nodules but only 8.4% of benign nodules, demonstrating a significant association with malignancy (RR = 3.21; p < 0.001). The absence of a peripheral halo was also significantly more frequent in malignant nodules (75.7%) compared to benign nodules (31.3%) (RR = 3.80; p < 0.001). Extrathyroidal extension, although less common overall, was significantly associated with malignancy, being present in 16.2% of malignant nodules compared to 2.4% of benign nodules (RR = 2.71; p = 0.005).

Table 3: Doppler Vascular Patterns and Indices with Pathological Correlation (N = 120)

A. Vascular Pattern

Vascularity pattern	Benign n (%)	Malignant n (%)	χ^2 (df)	Effect size	p-value
Peripheral	46 (55.4)	7 (18.9)			
Central	19 (22.9)	8 (21.6)	χ^2 = 21.98 (3)	Cramer's V = 0.43	<0.001
Mixed	4 (4.8)	1 (2.7)			
Absent	14 (16.9)	21 (56.8)			

B. Spectral Doppler Indices

Doppler index	Benign Mean ± SD	Malignant Mean ± SD	Test	Mean diff (95% CI)	p-value
Resistive Index (RI)	0.64 ± 0.11	0.78 ± 0.09	Welch t = 7.33	+0.14 (0.10-0.18)	<0.001
Pulsatility Index (PI)	1.08 ± 0.33	1.62 ± 0.38	Welch t = 7.48	+0.54 (0.40-0.68)	<0.001
PSV (cm/s)	19.7 ± 8.6	28.6 ± 10.4	Welch t = 4.56	+8.9 (5.0-12.8)	<0.001
Chaotic intranodular flow	10 (12.0)	20 (54.1)	χ^2 = 24.08	RR = 3.53 (2.15-5.80)	<0.001

Table 3 evaluates Doppler vascular patterns and spectral indices in benign and malignant thyroid nodules. Peripheral vascularity was the predominant pattern in benign nodules (55.4%), whereas malignant nodules more commonly demonstrated absent vascularity (56.8%). Central and mixed vascularity patterns were relatively more frequent in malignant nodules compared to benign nodules. Overall, the distribution of vascular patterns differed significantly between benign and malignant nodules (χ^2 = 21.98; p < 0.001), with a moderate effect size (Cramer's V = 0.43).

Spectral Doppler analysis revealed significantly higher resistive and pulsatility indices in malignant nodules. The mean resistive index was 0.78 ± 0.09 in malignant nodules compared to 0.64 ± 0.11 in benign nodules, with a statistically significant mean difference of 0.14 (95% CI: 0.10-0.18; p < 0.001). Similarly, the mean pulsatility index was significantly higher in malignant nodules (1.62 ± 0.38) than in benign nodules (1.08 ± 0.33), with a mean difference of 0.54 (95% CI: 0.40-0.68; p < 0.001).

Peak systolic velocity was also significantly elevated in malignant nodules (28.6 ± 10.4 cm/s) compared to benign nodules (19.7 ± 8.6 cm/s) (p < 0.001). Chaotic intranodular flow was observed in more than half of malignant nodules (54.1%) but only in 12.0% of benign nodules, indicating a strong association with malignancy (RR = 3.53; p < 0.001).

Table 4: Diagnostic Accuracy of Ultrasound, Doppler, and Combined Parameters (N = 120)

Modality	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV %	NPV %	Accuracy %	Test of significance	p-value
Gray-scale US alone	72.9 (55.9-85.4)	78.3 (68.0-86.4)	59.6	86.7	76.7	χ^2 vs reference	< 0.001

Doppler alone	78.4 (62.8-89.2)	80.7 (70.7-88.4)	63.8	89.3	80.0	χ^2 vs reference	< 0.001
Combined US + Doppler	**86.5 (71.2-94.9)**	**85.5 (76.0-92.3)**	**72.7**	**93.4**	**85.8**	McNemar vs US	**0.013**

Table 4 compares the diagnostic performance of gray-scale ultrasound, Doppler evaluation, and their combined use in differentiating benign from malignant thyroid nodules. Gray-scale ultrasound alone demonstrated a sensitivity of 72.9% and specificity of 78.3%, with an overall diagnostic accuracy of 76.7% ($p < 0.001$). Doppler evaluation alone showed improved sensitivity (78.4%) and specificity (80.7%), resulting in a higher diagnostic accuracy of 80.0% ($p < 0.001$).

The combined use of ultrasound and Doppler parameters yielded the highest diagnostic performance, with a sensitivity of 86.5% and specificity of 85.5%. This approach achieved a positive predictive value of 72.7%, a negative predictive value of 93.4%, and an overall accuracy of 85.8%. The improvement in diagnostic accuracy with combined assessment was statistically significant when compared with ultrasound alone (McNemar test, $p = 0.013$), highlighting the added value of Doppler parameters in thyroid nodule evaluation.

DISCUSSION

Clinicodemographic Profile and Overall Ultrasound-Doppler Characteristics: In the present study, malignant thyroid nodules were observed in an older age group compared to benign nodules, with a statistically significant mean age difference of 5.7 years. This finding is consistent with earlier studies demonstrating increasing malignancy risk with advancing age. Aghaghazvini L et al. (2020)[5] similarly reported that patients with malignant thyroid nodules were significantly older than those with benign lesions, suggesting that age remains an important clinical risk factor. However, female predominance was observed in both benign and malignant groups without a statistically significant difference, which aligns with epidemiological data indicating higher overall prevalence of thyroid nodules in women but no consistent sex-based difference in malignancy rates, as reported by Elsheikh H et al. (2021)[6].

Nodule size was significantly larger in malignant nodules in the present study, a finding supported by studies from Maddaloni E et al. (2021)[7], who demonstrated that increasing nodule size correlates with a higher probability of malignancy, particularly when associated with suspicious sonographic features. Although solitary nodules were more frequent among malignant cases, this difference did not reach statistical significance, echoing observations by Miao S et al. (2020)[1], who emphasized that solitary status alone is an unreliable discriminator of malignancy.

The presence of suspicious cervical lymphadenopathy showed a strong association with malignancy in the current study, consistent with findings by Wu Y et al. (2022)[2], who highlighted lymph node involvement as a highly specific indicator of thyroid cancer. High-risk TIRADS (4-5) categories were significantly more prevalent in malignant nodules, reinforcing the diagnostic validity of risk stratification systems, as also reported in multicentric studies by Alamdaran SA et al. (2024)[3]. Additionally, high-risk Doppler patterns were markedly associated with malignancy, corroborating evidence that vascular characteristics reflect tumor neoangiogenesis.

Gray-Scale Ultrasound Features and Malignancy Risk: The present study demonstrated that solid composition, hypoechogenicity, irregular margins, microcalcifications, taller-than-wide shape, and absent halo were significantly associated with malignant thyroid nodules. These findings are in strong agreement with the landmark work by Miao S et al. (2020)[1], who identified these features as independent predictors of malignancy. Hypoechogenicity and irregular margins, in particular, showed the highest relative risks, consistent with meta-analyses by Elsheikh H et al. (2021)[6].

Microcalcifications were observed in nearly half of malignant nodules but were uncommon in benign nodules, reflecting their known association with psammoma bodies in papillary thyroid carcinoma. This observation parallels results reported by Wu Y et al. (2022)[2], who described microcalcifications as one of the most specific ultrasound markers of malignancy. The taller-than-wide shape, although less frequent, showed a strong association with malignancy, supporting prior studies emphasizing its high specificity despite moderate sensitivity.

Extrathyroidal extension, though infrequent, demonstrated a significant association with malignancy, aligning with studies by Alamdaran SA et al. (2024)[3], which reported this feature as a marker of aggressive disease and advanced pathological stage.

Doppler Vascular Patterns and Spectral Indices: Doppler evaluation in the present study revealed significant differences in vascular patterns between benign and malignant nodules. Benign nodules predominantly exhibited peripheral vascularity, whereas malignant nodules frequently showed absent or central vascularity. This distribution was statistically significant with a moderate effect size, in concordance with studies by Maddaloni E et al. (2021)[7], who emphasized the role of abnormal intranodular vascular patterns in malignancy.

Spectral Doppler analysis showed significantly higher resistive index, pulsatility index, and peak systolic velocity in malignant nodules. These findings reflect increased vascular resistance and disorganized tumor vasculature, consistent with observations by Jiang L et al. (2023)[8]. Chaotic intranodular flow was strongly associated with malignancy in the present study, further supporting the role of Doppler indices as adjunctive diagnostic tools rather than standalone criteria.

Diagnostic Accuracy of Ultrasound, Doppler and Combined Assessment: Gray-scale ultrasound alone demonstrated moderate sensitivity and specificity in differentiating malignant from benign nodules, comparable to values reported in previous studies by Saade-Lemus SM et al. (2021)[9]. Doppler assessment alone modestly improved diagnostic accuracy, supporting the notion that vascular parameters provide incremental diagnostic information.

The combined use of gray-scale ultrasound and Doppler parameters yielded the highest sensitivity, specificity, and overall diagnostic accuracy in the present study, with a statistically significant improvement over ultrasound alone. This synergistic benefit has been consistently reported in literature, including studies by Chung J et al. (2020)[10] & Saito D et al. (2020)[11], which advocate for multiparametric ultrasound evaluation to optimize risk stratification and reduce unnecessary FNAC procedures.

CONCLUSION

This cross-sectional study demonstrates that high-resolution ultrasound, when combined with Doppler evaluation, plays a pivotal role in differentiating benign from malignant thyroid nodules. Malignant nodules were significantly associated with older age, larger nodule size, suspicious cervical lymphadenopathy, higher TIRADS categories, and high-risk Doppler features. Gray-scale ultrasound characteristics such as solid composition, hypoechogenicity, irregular margins, microcalcifications, taller-than-wide shape, absent halo and extrathyroidal extension showed strong and statistically significant associations with malignancy.

Doppler assessment further enhanced diagnostic confidence by revealing distinct vascular patterns and significantly elevated spectral indices including resistive index, pulsatility index, and peak systolic velocity in malignant nodules. The presence of chaotic intranodular flow emerged as a particularly strong indicator of malignancy. Importantly, the combined use of ultrasound and Doppler parameters achieved superior diagnostic accuracy compared to either modality alone, with high sensitivity, specificity, and negative predictive value.

These findings underscore the value of a multiparametric ultrasound approach in thyroid nodule evaluation. Integrating gray-scale and Doppler parameters can improve risk stratification, optimize selection of nodules for fine-needle aspiration cytology, reduce unnecessary invasive procedures, and facilitate early and appropriate clinical management. Ultrasound with Doppler thus remains an indispensable, non-invasive, and cost-effective tool in routine thyroid imaging practice.

LIMITATIONS OF THE STUDY

1. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other populations and healthcare settings.
2. The cross-sectional design precluded assessment of long-term outcomes, disease progression, and prognostic implications of ultrasound and Doppler features.
3. Although FNAC and histopathology were used as reference standards, a proportion of nodules relied on cytology alone, which may be subject to sampling errors and indeterminate results.
4. Inter-observer variability in ultrasound and Doppler interpretation was not formally assessed, which could influence reproducibility of findings.
5. Advanced ultrasound techniques such as elastography and contrast-enhanced ultrasound were not included, which might have further improved diagnostic performance.

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