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RESEARCH ARTICLE

# Doppler Ultrasound Vascularity Patterns in Morpho-radiological and Pathological Evaluation of Thyroid Nodules

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**ABSTRACT**

**Objective:** We aimed to evaluate Doppler ultrasound (US) vascularity patterns compared to morphological, radiological, and pathological thyroid nodule features to predict malignancy.

**Materials and Methods:** A total of 257 thyroid nodules (173 in women and 84 in men) were examined. The blood supply patterns of the nodules were categorized with color Doppler US. as (-); no vascularity (+); intranodular microvascular punctuate, (++); rod, or fine branching peripheral, (+++); intense intranodular and peripheral vascular blood supply.

**Results:** The data indicated a tendency for higher TI-RADS categories to exhibit higher Bethesda results, which are indicative of a higher risk of malignancy. TI-RADS 5 had the highest percentage in Beth-6. A statistically significant difference was found between vascularity and nodule diameter. Among those nodules with (+) and (++) vascularity, the percentage of nodule diameters between 11 mm and 20 mm was the highest, while among those with (+++), the percentage of those >20 mm was the highest. The data indicated that even nodules with low vascularization (negative) could belong to higher TI-RADS categories. TI-RADS 5 nodules were evident in intranodular vascularity group. The percentage of those in the Bethesda 2 group according to vascularity was the highest. Bethesda 6 nodules had prominent intranodular vascularity among others. A statistically significant difference was found in all groups compared to vascularity ($p<0.05$).

**Conclusion:** Along with other radiological findings, using Dopper US vascularity patterns in some nodule groups might elaborate the algorithm in predicting malignancy. This can accurately translate into better management planning, whether conservative, surgery, or invasive.

**Keywords:** Doppler flow imaging, malignant, thyroid nodule, ultrasound

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## INTRODUCTION

Ultrasound (US) is the primary modality utilized in diagnosing and following thyroid nodules.[1] Gray-scale US features are primarily used to differentiate malignant and benign nodules. Assorted reporting systems have been developed in recent years; of these, the American College of Radiology (ACR) thyroid imaging reporting and data system (TI-RADS) has found a wide range of implementation.[2–4] It categorizes the thyroid nodules based on the probability of malignancy, provides recommendations, and aims to avoid unnecessary biopsies and surveillance. On the other hand, the classification systems may vastly vary, and some problems still exist in differentiating benign and malignant nodules. Although it is not considered in TI-RADS, some studies demonstrated that color Doppler US might also help distinguish between malignant and benign nodules.[5–7] In this study, we investigated whether the blood supply pattern in Doppler US could contribute to morpho-radiological and pathological features of thyroid nodules to differentiate benign and malignant nodules.

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## MATERIALS and METHODS

A total of 257 thyroid nodules (173 in women and 84 in men) were examined in 220 patients (150 women and 70 men) who applied to our clinic between May 2018 and January 2023 and underwent a biopsy with indications according to ACR TI-RADS. Twenty-six nodules in which blood supply was not optimally evaluated with Doppler US and eight nodules where insufficient thyrocytes were detected in the pathology evaluation (Bethesda 1) were excluded from the study. Thus, 223 nodules (153 women and 70 men) were included in the study. This study was conducted according to the ethical standards of the Helsinki Declaration and approved by the Anadolu Medical Center Ethics Committee (ASM-EK-23/250).

All nodules were examined with 12 and 18 MHz probes (SIEMENS Healthineers Medical Solution, Acuson Sequoia) by two radiologists, who also performed the biopsy thereafter, independently and peer-review was only obtained in dubious cases. In the grayscale examination, the nodules were examined in the multi-planar sections in detail. ACR TI-RADS classifications were made after the dimensions of the nodules, their internal components (solid and cystic), the echogenicity of the solid components, their borders, and the presence of micro-macro calcification were noted. Then, the blood supply patterns of the nodules, which will be mentioned as vascularity later in this text, were evaluated and categorized with color Doppler US. In the first group (-), the nodules did not show vascularity on imaging (negative type). In the second group (+), intranodular microvascular punctuate, rod, or fine branching blood supply (Fig. 1); in the third group (++), peripheral vascular blood supply (Fig. 2); and in the fourth group (+++), intense intranodular and peripheral vascular blood supply (Fig. 3) were observed.

### Statistics

Variables belonging to all categories are presented in frequency tables and layers. A chi-square test was used to make comparisons; $p<0.05$ was considered significant. Cramer's V Test statistical values were calculated for effect size. All analyses were performed using R software's personal Jamovi 2.4.8.

## RESULTS

Accordingly, out of a total of 223 nodules that were biopsied, 79 were evaluated as TI-RADS 5, 104 as TI-RADS 4, 39 as TI-RADS 3, and one as TI-RADS 2. A draining procedure was performed on the nodule, which was evaluated as TI-RADS 2 due to pressure, and its pathology was evaluated. One nodule (TI-RADS 3 and 19 mm) was detected as malignant in the total thyroidectomy performed due to the TI-RADS 5 nodule detected on the opposite side and the Bethesda 6 structure nodule detected in the pathology (multifocal papillary cancer). Biopsy results revealed Bethesda 2 in 141, Bethesda 3 in 23, Bethesda 4 in 15, Bethesda 5 in 6, and Bethesda 6 in 38 nodules. The relationship between TI-RADS scores and Bethesda classification is given in Table 1.

The data indicates a tendency for higher TI-RADS categories to exhibit higher Bethesda results, which are indicative of a higher risk of malignancy. TI-RADS 5 had the highest percentage in Bethesda 6. A statistically significant difference was found between TI-RADS compared to Bethesda $X^2$ (4, N=200) =81.1, $p<0.05$ (effect size =0.46). When we look at the total percentages, according to Bethesda, the percentage of those in the TI-RADS 4 group is the highest.

The nodules divided into four categories based on their vascular patterns are shown in Table 2.

### Nodule Size & Vascularity

A statistically significant difference was found between vascularity and nodule diameter, $X^2$ (4, N=209) =20.3, $p<0.05$ (effect size =0.22). Among those nodules with (+) and (++) vascularity, the percentage of nodule diameters between 11 mm and 20 mm is the highest, while among those with (+++), the percentage of those >20 mm is the highest. When we look at the total percentages, the percentage of the group with nodule diameter between 11 mm and 20 mm according to vascularity is the highest, vascularity in groups decreased when the nodule size <11 mm. The data shows that size alone is not a reliable indicator of malignancy risk, as nodules of varying sizes exist across all TI-RADS and Bethesda categories.

### TI-RADS & Vascularity

The data indicates that even nodules with low vascularization (negative) could belong to higher TI-RADS categories. TI-RADS 5 nodules were evident in intranodular vascularity group. A statistically significant difference was found between vascularity and TI-RADS, $X^2$ (4, N=209) =35.0, $p<0.05$ (effect size =0.29). When we look at the total percentages, the percentage of those in the TI-RADS 4 group according to vascularity is the highest.

### Bethesta & Vascularity

The Bethesda system offers another layer of stratification.[8] Its correlation with TI-RADS and vascularization can be more thoroughly examined to predict malignancy and determine the need for surgery. A statistically significant difference was found between vascularity and Bethesda, $X^2$ (4, N=188)

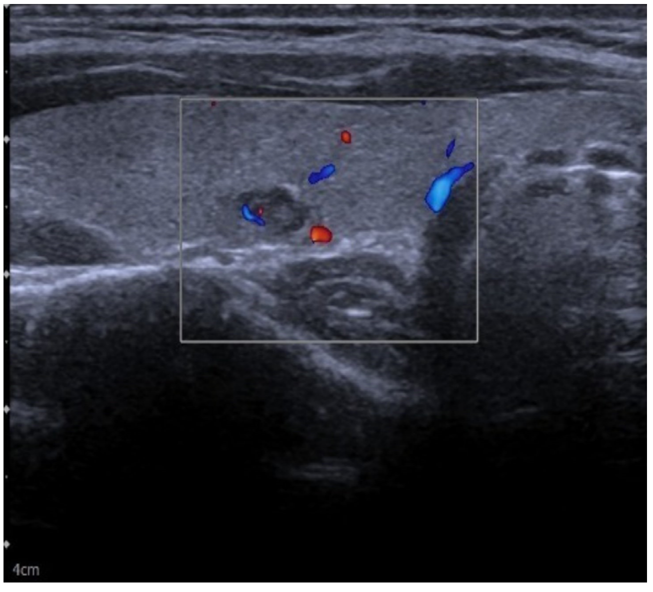


**Figure 1.** Color Doppler ultrasound image showing (+) vascularization. Intranodular microvascular punctuate, rod, or fine branching blood supply in a 24-year-old male, biopsy revealed Bethesda 2 findings

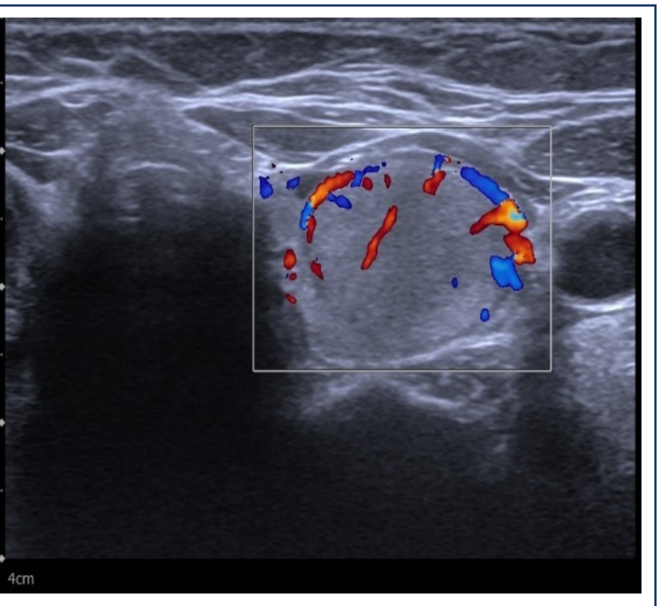


**Figure 2.** Color Doppler ultrasound image showing (++) vascularization. Color Doppler ultrasound image showing (++) vascularization. Peripheral vascular blood supply in 56-year-old female, biopsy yielded Bethesda 2 findings

= 37.8, $p<0.05$ (effect size =0.32). When we look at the total percentages, the percentage of those in the Bethesda 2 group according to vascularity was the highest. Bethesda 6 nodules had prominent intranodular vascularity, among others.

The relationship between the TI-RADS scores and Bethesda classification; nodule size and vascularity; TI-RADS scores and vascularity; Bethesda classification and vascularity are shown in Figure 4.

## DISCUSSION

In many previous studies, a US feature individually failed to differentiate between benign and malignant nodules.[9] On the other hand, utilizing multiple suspicious features correlated better with an increased risk of malignancy, as in TI-RADS, which has been implemented in recent years.[2–4] Similarly, vascularity can suggest an increased risk of malignancy, significantly when correlated with other suspicious findings.[10] In this study, TI-RADS findings correlated significantly with Bethesda classification after biopsy. We also investigated how the vascularity pattern of nodules in Doppler US correlates to morpho-radiological and pathological features of thyroid nodules to differentiate benign and malignant nodules. Intranodular vascularity was significantly prominent in nodules <11 mm, whereas peripheral vascularity with or without intranodular vascularity seemed to increase in larger nodules. On the other hand, TI-RADS 5 and Bethesda 6 nodules were significantly higher in the intranodular vascularity group.

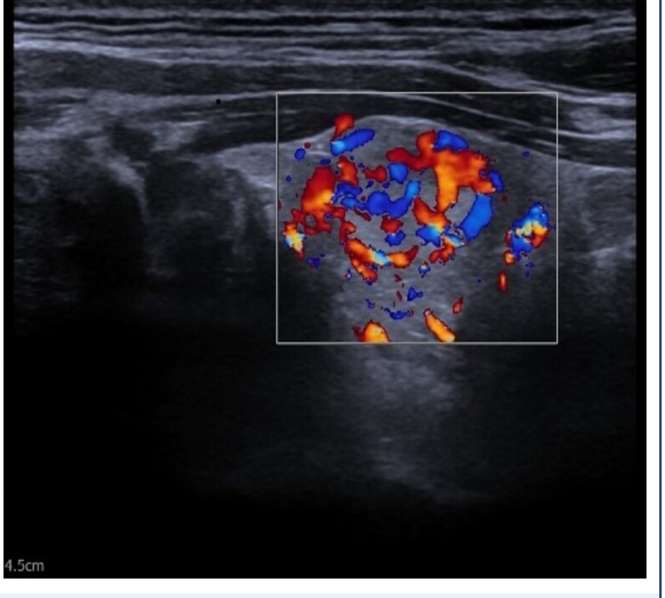


**Figure 3.** Color Doppler ultrasound image showing (+++) vascularization. Intense intranodular and peripheral vascular blood supply in a 36-year-old female, biopsy showed Bethesda 2 findings

Table 1. The relationship between TI-RADS scores and Bethesda classification

| | Bethesda 6 | Bethesda 5 | Bethesda 4 | Bethesda 3 | Bethesda 2 | Total |
|---|---|---|---|---|---|---|
| TI-RADS 5 | 36 | 6 | 8 | 10 | 19 | 67 |
| TI-RADS 4 | 2 | 0 | 7 | 12 | 83 | 97 |
| TI-RADS 3 | 0 | 0 | 0 | 1 | 38 | 35 |
| TI-RADS 2 | 0 | 0 | 0 | 0 | 1 | 1 |
| TI-RADS 1 | 0 | 0 | 0 | 0 | 0 | 0 |

TI-RADS: Thyroid imaging reporting and data system

Table 2. Distribution of thyroid nodules according to vascularization characteristics

| | - vascularity | + vascularity | ++ vascularity | +++ vascularity | Total |
|---|---|---|---|---|---|
| <11 mm | 7 | 32 | 10 | 7 | 56 |
| 11–20 mm | 6 | 40 | 40 | 16 | 102 |
| >20 mm | 3 | 15 | 32 | 15 | 65 |
| Bethesda 2 | 9 | 42 | 64 | 31 | 146 |
| Bethesda 3 | 1 | 7 | 12 | 4 | 24 |
| Bethesda 4 | 0 | 3 | 5 | 5 | 13 |
| Bethesda 5 | 2 | 4 | 0 | 0 | 6 |
| Bethesda 6 | 4 | 28 | 2 | 1 | 35 |
| TI-RADS 2 | 1 | – | – | – | 1 |
| TI-RADS 3 | – | 39 | – | – | 39 |
| TI-RADS 4 | – | – | 104 | – | 104 |
| TI-RADS 5 | – | – | – | 79 | 79 |

TI-RADS: Thyroid imaging reporting and data system

In a large meta-analysis including heterogeneous studies, it has been reported that vascular flow utilization on color Doppler US may not accurately predict malignancy in thyroid nodules.[10] Besides other known suspicious radio-morphologic features, intranodular vascularity could predict malignancy, although there might be overlaps between benign and malignant nodules.[5,6,11] These findings parallel ours, showing higher TI-RADS scores and Bethesda 6 classification correlated with intranodular vascularity. Internal vascularity vs. peripheral vascularity was investigated in other studies; the latter was related to benign nodules.[12,13] No flow, intranodular flow, and peripheral flow were reported to be vastly diverse in different studies, ranging from 0%, 0%, and 6% to 56%, 69, and 76%, respectively.[12,14,15] Our study noted that the vascularity patterns might also be related to nodule size. Several other studies have also detailed objective quantitative measurements to diagnose malignancy; however, this technique is out of our scope.[13,16]

The study's main limitation was the natural lack of some groups, such as TI-RADS 1 and TI-RADS 2 nodules, as we performed the biopsy according to the TI-RADS recommendations. We also had to exclude Bethesda 4 and Bethesda 5 nodules because of the small sample size in these groups. On the other hand, this enabled us to increase the power of the statistics. Another limitation could be the variability of the US examination due to vendors, device settings and operators. Although it might also be reflected in the other studies mentioned above, measuring variability was out of scope of our study.

## CONCLUSION

A more elaborate algorithm might be introduced using Dopper US vascularity patterns in selected conditions. This can accurately translate into better management planning, whether conservative, surgery, or invasive. Similarly to previous studies, our study demonstrated that vascularity in thyroid nodules may contribute to predicting malignancy, especially when it is intranodular. Our findings also showed vascularity patterns also depend on the thyroid nodule size. Further, well-designed studies are necessary to determine how the vascularity patterns are associated with thyroid malignancies.

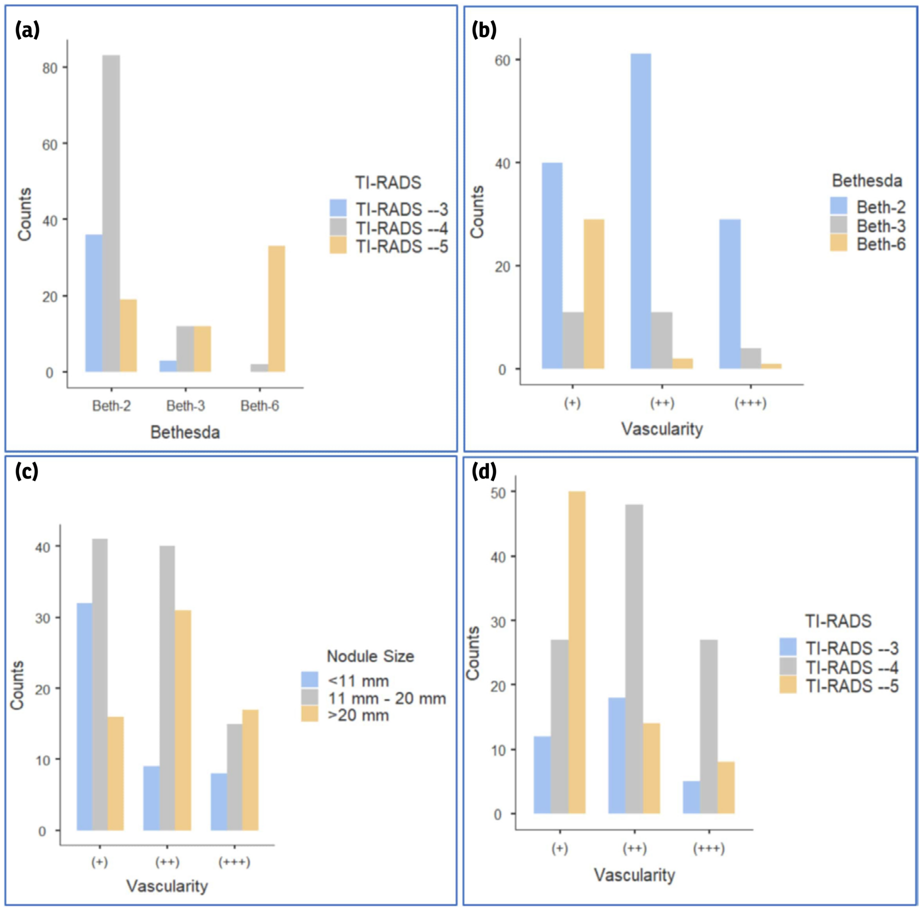


**Figure 4.** Bar charts comparing the features of nodules. **(a)** TI-RADS scores vs. Bethesda classification, **(b)** nodule size vs. vascularity, **(c)** TI-RADS scores vs. vascularity; **(d)** Bethesda classification vs. vascularity

## Disclosures

**Ethics Committee Approval:** The study was approved by the Anadolu Medical Center Ethics Committee (No: 23/250, Date: 12/10/2023).

**Authorship Contributions:** Concept: A.Y.; Design: A.Y.; Supervision: A.Y., M.D.; Data Collection or Processing: A.Y., A.A.; Analysis or Interpretation: O.D.; Literature Search: A.Y., A.A.; Writing: A.Y.; Critical review: A.Y., M.D., A.A.

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