Thorac Res Pract. **DOI:** 10.4274/ThoracResPract.2026.2025-11-4

Original Article

CT Histogram Analysis for Predicting Malignancy in Anterior Mediastinal Masses

Nilay Çavuşoğlu Yalçın[1], Mustafa Yalçın[2], Okan Karataş[1]

[1]Clinic of Thoracic Surgery, University of Health Sciences Türkiye, Antalya Training and Research Hospital, Antalya, Türkiye
[2]Clinic of Radiology, University of Health Sciences, Antalya Training and Research Hospital, Antalya, Türkiye

Cite this article as: Çavuşoğlu Yalçın N, Yalçın M, Karataş O. CT histogram analysis for predicting malignancy in anterior mediastinal masses. *Thorac Res Pract.* [Epub Ahead of Print]

ABSTRACT

OBJECTIVE: Anterior mediastinal masses encompass a broad spectrum from benign thymic hyperplasia to malignant thymomas and thymic complementary computed tomography (CT) histogram and texture analysis have emerged as complementary, non-invasive quantitative biomarkers for malignancy prediction. This study investigates whether CT histogram-derived parameters, particularly mean attenuation and first-order metrics, can differentiate benign from malignant anterior mediastinal masses to support preoperative risk stratification.

MATERIAL AND METHODS: We retrospectively analyzed data from 102 patients who underwent surgical resection of anterior mediastinal masses. Non-contrast CT scans were evaluated, and mean Hounsfield unit (HU), standard deviation, skewness, and kurtosis values were extracted using region-of-interest-based histogram analysis. Histopathological diagnosis is considered the gold standard for classification. Group comparisons were performed using appropriate parametric or non-parametric tests, and the diagnostic performance was evaluated using receiver operating characteristic (ROC) analysis.

RESULTS: Of the 102 patients, 60 (58.8%) had malignant and 42 (41.2%) had benign pathologies. The mean CT attenuation was higher in malignant lesions than in benign lesions (63.3±16.9 HU vs. 48.3±39.0 HU; $P = 0.023$), whereas the standard deviation was similar between the groups ($P = 0.810$). Skewness and kurtosis were higher in malignant lesions ($P < 0.05$), indicating denser and more peaked attenuation distributions. ROC analysis of mean HU demonstrated moderate discriminative performance (area under the curve: 0.64), with high sensitivity (96.7%) and limited specificity (50.0%).

CONCLUSION: CT histogram analysis, particularly mean attenuation, may serve as a complementary biomarker for differentiating benign from malignant anterior mediastinal masses. Given its high sensitivity but limited specificity, it should be used as an adjunct to clinical and morphologic assessment rather than as a determinant of surgical management. Prospective validation incorporating volumetric and advanced radiomic parameters is required.

KEYWORDS: Anterior mediastinal mass, computed tomography, histogram analysis, thymoma, malignancy prediction

Received: 22.12.2025 ***Revision Requested:*** 12.01.2026 ***Last Revision Received:*** 18.01.2026

Accepted: 26.01.2026 ***Epub:*** 11.03.2026

INTRODUCTION

Anterior mediastinal masses comprise a heterogeneous group of lesions with varying clinical behaviors, ranging from benign entities, such as thymic hyperplasia and cysts, to malignant neoplasms, including thymomas and thymic carcinomas. These lesions are increasingly identified incidentally due to the widespread use of computed tomography (CT) in thoracic imaging, particularly in asymptomatic individuals undergoing lung cancer screening or trauma evaluation.[1]

Surgical resection remains the cornerstone of thymic epithelial tumor treatment. However, a significant proportion of autoimmune myasthenia gravis are ultimately found to be non-therapeutic, with up to 27%–30% of thymectomy revealing benign histology.[2] This has raised concerns regarding overtreatment and highlighted the need for improved risk stratification tools that can assist in distinguishing benign from malignant lesions using non-invasive imaging modalities.

Corresponding author: Nilay Çavuşoğlu Yalçın, MD, e-mail: drnili@hotmail.com

Copyright© 2026 The Author(s). Published by Galenos Publishing House on behalf of Turkish Thoracic Society.
Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Conventional CT imaging is routinely used to evaluate anterior mediastinal masses, focusing on size, shape, location, and presence of features such as fat, calcification, and invasion. However, these qualitative assessments are often insufficient to reliably distinguish benign from malignant lesions, particularly in borderline or equivocal cases.[3] As such, there is growing interest in the application of advanced quantitative imaging techniques, including histogram and texture analysis, to enhance diagnostic accuracy.

Histogram analysis, a component of radiomics, involves extracting quantitative metrics from voxel intensity distributions within a region-of-interest (ROI). This technique enables the objective evaluation of lesion density, uniformity, and internal heterogeneity, which may correlate with histological behavior.[4] Histogram-based parameters, such as mean attenuation, standard deviation, and percentiles, can effectively differentiate thymic hyperplasia from thymoma and carcinoma, with high diagnostic performance.[5-7]

Despite its promise, the integration of CT histogram analysis into routine clinical practice remains limited, and further validation is required. In this context, the present study aimed to evaluate the ability of simple histogram parameters—mean and standard deviation of attenuation on non-contrast CT—to differentiate benign from malignant anterior mediastinal masses in patients undergoing surgical resection. We also included skewness and kurtosis values in the analysis to provide a more complete characterization of the voxel intensity distribution, as recommended in the recent literature. We hypothesize that malignant lesions will exhibit higher and more homogeneous attenuation patterns, thereby supporting the utility of CT histogram analysis as a non-invasive preoperative risk stratification tool.

MATERIAL AND METHODS

A retrospective analysis was conducted on 102 consecutive patients who underwent surgical resection for anterior mediastinal masses between January 2015 and December 2024. This retrospective study was approved by the Ethics Committee of Antalya Training and Research Hospital (approval number: 2025-125, approval date: 08 May 2025). The requirement for informed consent was waived due to the retrospective nature of the study. Only patients with available preoperative non-contrast thoracic CT imaging, complete clinical information, and definitive histopathological diagnosis were included in the study. Patients were excluded if they had received prior chemotherapy or radiotherapy, had incomplete imaging data, or if the lesion was evaluated only by biopsy without subsequent surgical resection. A STROBE-compliant flow diagram summarizing patient selection and exclusion criteria is provided in Figure 1.

Main Points

- Malignant anterior mediastinal lesions show significantly higher mean Hounsfield unit (HU) values than benign ones on non-contrast computed tomography (CT).
- A histogram mean cutoff of 39.3 HU yields high sensitivity (96.7%) for predicting malignancy.
- Simple first-order CT histogram parameters can aid preoperative risk stratification and may reduce unnecessary surgical resections.

Non-contrast CT was examined using multi-detector CT scanners with standard clinical protocols (120 kVp tube voltage, 1–2 mm slice thickness). Axial images were reconstructed using soft-tissue kernels and exported in the DICOM format for analysis. Histogram-derived attenuation values were extracted using a standardized ROI approach. A fixed-diameter circular ROI was manually placed on the axial slice demonstrating the largest cross-sectional area of each lesion while carefully avoiding calcified, cystic, necrotic, fatty, or vascular components to minimize measurement variability. A thoracic radiologist with 10 years of experience placed all ROIs.

Demographic variables (age and sex), lesion size, and histogram parameters were compared between the benign and malignant groups based on the final surgical pathology. The normality of continuous variables was assessed using the Shapiro–Wilk test. Independent-samples t-tests were used for normally distributed variables; for non-normally distributed variables, the Mann–Whitney U test was applied. Categorical variables were analyzed using the χ^2 test or Fisher's exact test, where appropriate. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the histogram mean Hounsfield unit (HU). The area under the curve (AUC), sensitivity, specificity, and optimal threshold values were calculated using Youden's index. Skewness and kurtosis values were compared between the malignant and benign groups to evaluate differences in distribution shape characteristics.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences version 26.0 (IBM Corp., Armonk, NY). A P value < 0.05 was considered statistically significant. Because this was a retrospective study, an a priori

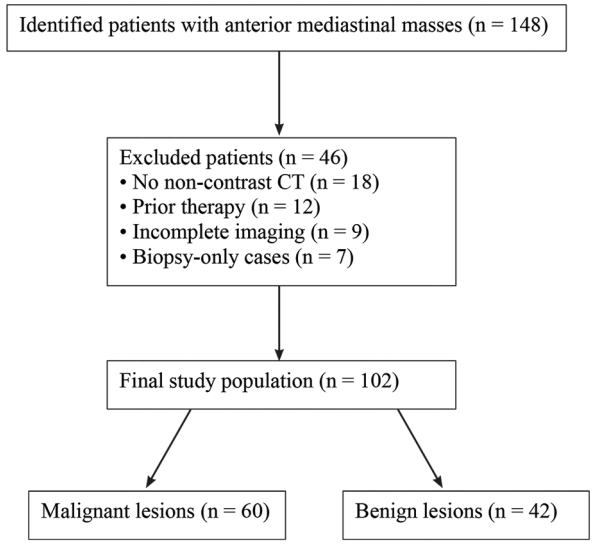

Figure 1. STROBE-compliant patient selection flowchart

power analysis could not be performed; however, a post-hoc effect size analysis for the mean HU difference was conducted and demonstrated sufficient discriminatory power for the primary outcome measure.

RESULTS

This retrospective study included 102 patients with anterior mediastinal masses. Of these, 60 patients (58.8%) were diagnosed with malignant lesions and 42 patients (41.2%) with benign lesions based on the final histopathological evaluation.

The overall mean age was 51.4 years, with male patients exhibiting a higher mean age (53.6 years) than females (48.9 years) (Figure 2). In the benign group, 50% were male and 50% were female, whereas the malignant group consisted of 55.0% males and 45.0% females (Figure 3).

Among the malignant lesions (n = 60), the World Health Organization (WHO) thymoma subtypes were as follows: type A (n = 2), type B1 (n = 1), type B2 (n = 14), and type B3 (n = 5). Thymic carcinoma occurred in 8 cases, while lymphomas (n = 18) and other malignant tumors (n = 12) comprised the remaining cases (Table 1).

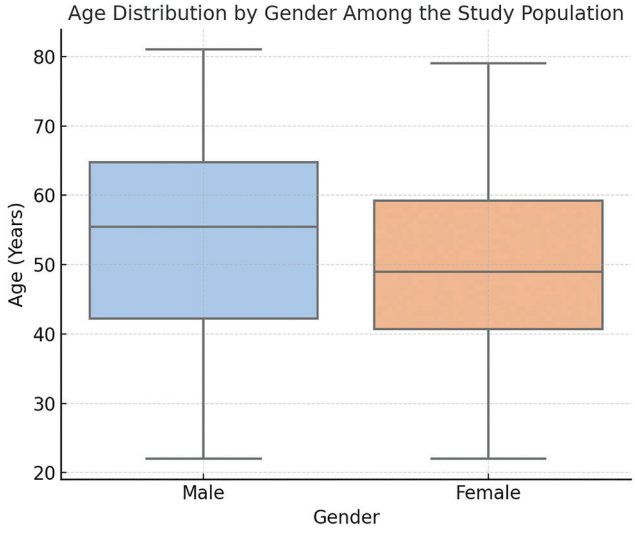

Figure 2. Age distribution by sex among the study population

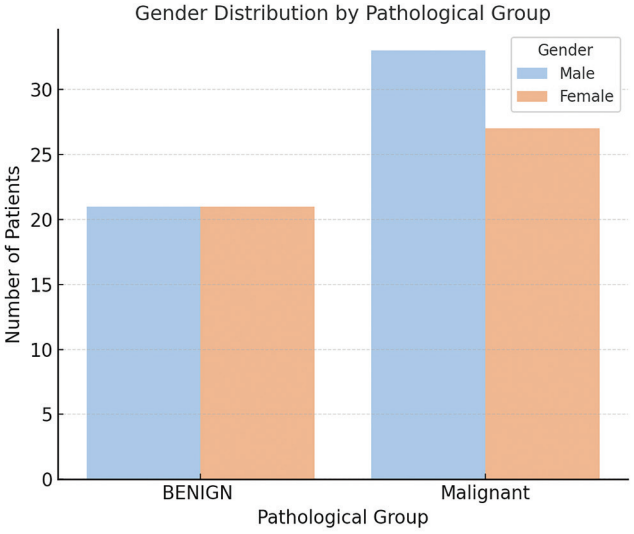

Figure 3. Gender distribution across the benign and malignant pathology groups

CT histogram analysis demonstrated that malignant anterior mediastinal lesions exhibited significantly higher mean HU values than benign lesions (63.3 ± 16.9 HU vs. 48.3 ± 39.0 HU, $P = 0.023$), supporting the diagnostic utility of mean attenuation as a radiologic biomarker of malignancy (Figure 4). In contrast, the standard deviation of HU values was higher in benign lesions (39.0 HU vs. 16.9 HU), reflecting greater internal heterogeneity, although this difference was not statistically significant ($P = 0.810$).

The shape descriptors of the voxel intensity distribution revealed further distinctions between groups. Malignant lesions demonstrated greater right-sided skewness (0.81 vs. 0.53) and higher kurtosis (0.47 vs. 0.76), both of which reached statistical significance ($P = 0.045$ and $P = 0.018$, respectively), suggesting more homogeneously dense tissue profiles in malignancy, whereas benign lesions exhibited broader and flatter attenuation distributions (Table 2).

Table 2 summarizes the histogram-derived parameters of the anterior mediastinal lesions. Malignant masses demonstrated significantly higher mean HU and greater peakedness (kurtosis), whereas benign lesions exhibited greater attenuation variability and flatter distribution profiles.

These findings highlight that while histogram-derived mean attenuation offers high sensitivity but limited specificity, its diagnostic performance remains moderate and should therefore be interpreted as a complementary rather than standalone biomarker.

ROC curve analysis demonstrated moderate discriminative performance of the histogram mean HU (AUC: 0.64), with high sensitivity (96.7%) and limited specificity (50%) (Figure 5). In contrast, the standard deviation of HU values was higher in benign lesions (39.0 HU vs. 16.9 HU), reflecting greater internal heterogeneity, although this difference was not statistically significant ($P = 0.810$).

Malignant lesions demonstrated greater right-sided skewness (0.81 vs. 0.53) and higher kurtosis (0.47 vs. −0.76), both of which reached statistical significance ($P = 0.045$ and $P = 0.018$, respectively), suggesting more homogeneously dense

Table 1. WHO classification of malignant thymic lesions in the study cohort (n = 60)

WHO subtype/malignant category	n	%
Type A	2	3.3%
Type B1	1	1.7%
Type B2	14	23.3%
Type B3	5	8.3%
Thymic carcinoma	8	13.3%
Lymphoma	18	30.0%
Other malignant tumors	12	20.0%

WHO: World Health Organization

Table 2. Descriptive summary of statistics

Group	Mean (HU)	Standard deviation (HU)	Skewness	Kurtosis
Benign	48.26	39.03	0.53	-0.76
Malign	63.25	16.91	0.81	0.47

HU: Hounsfield unit

Table 3. ROC curve performance metrics

Metric	Value
AUC	0.64
Optimal threshold (HU)	39.3
Sensitivity	96.7%
Specificity	50%

ROC: receiver operating characteristic, AUC: area under the curve, HU: Hounsfield unit

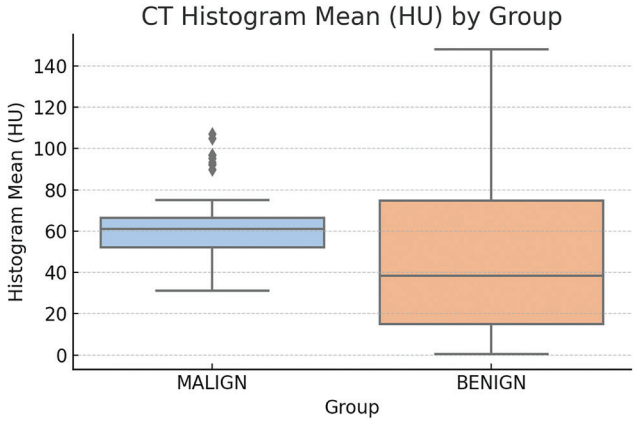

Figure 4. CT histogram mean (HU) by groups

CT: computed tomography, HU: Hounsfield unit

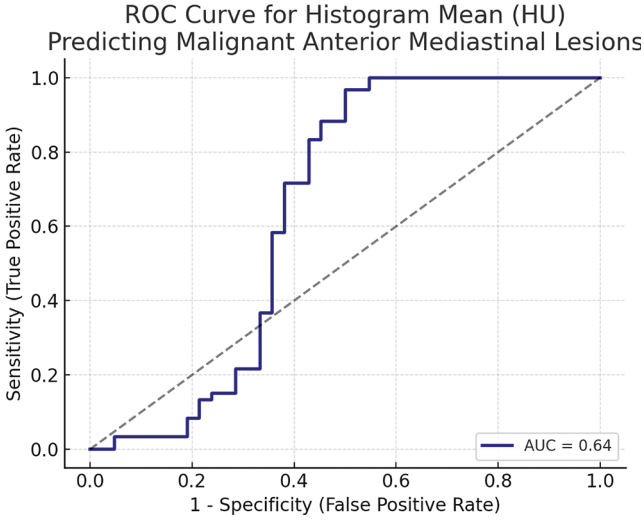

Figure 5. ROC curve for the histogram mean (HU) in predicting malignant anterior mediastinal lesions

ROC: receiver operating characteristic, HU: Hounsfield unit

tissue profiles in malignancy, whereas benign lesions exhibited broader and flatter attenuation distributions (Table 3).

These findings highlight that while histogram-derived mean attenuation offers high sensitivity but limited specificity, its diagnostic performance remains moderate. Therefore, it should be interpreted as a complementary rather than standalone biomarker.

Although benign lesions exhibited a notably higher standard deviation (39.03 HU) than malignant lesions (16.91 HU), this variability did not reach statistical significance, indicating that heterogeneity alone may not reliably differentiate pathology.

Skewness was greater in the malignant group (0.81) than in the non-malignant group, reflecting a stronger right-tailed distribution. This suggests that higher HU values occur more frequently in malignancy, reinforcing the pattern of denser tissue characteristics. Kurtosis was also higher in malignant lesions (0.47), consistent with a more compact and homogeneous tissue density pattern.

These descriptive parameters indicate that malignant anterior mediastinal masses tend to exhibit higher and more homogeneous attenuation, whereas benign masses are more heterogeneous, with wider variation in internal density. Therefore, these metrics may serve as informative adjuncts in preoperative radiologic assessment and risk stratification. Although benign lesions exhibited a notably higher standard deviation (39.03 HU) than malignant lesions (16.91 HU), this variability did not reach statistical significance, indicating that heterogeneity alone may not reliably differentiate pathology.

DISCUSSION

Our findings demonstrate that malignant anterior mediastinal lesions are characterized by significantly higher mean CT attenuation values compared to benign counterparts, supporting the hypothesis that such lesions exhibit greater internal density and structural homogeneity—a notion previously corroborated by Liu et al.[6], who identified histogram-derived median attenuation as an independent discriminator between thymic tumors and non-neoplastic lesions. This alignment with existing literature reinforces the biological plausibility of our results and supports the potential utility of simple, first-order histogram features as practical imaging biomarkers.

Although prior research has explored various radiomics-based texture and entropy metrics,[7,8] our data emphasize the clinical applicability of quantitative values, such as mean attenuation, derived from routine non-contrast CT without specialized software. Importantly, the present study confirms that the mean HU is significantly higher in malignant lesions (P = 0.023),

whereas the standard deviation ($P = 0.810$) fails to demonstrate discriminatory power, indicating that global attenuation values may serve as a more stable surrogate marker of malignancy than heterogeneity measures alone. This concept is consistent with that of Roden and Szolkowska,[8] who reported a substantial overlap in qualitative CT characteristics between benign and malignant thymic lesions.

Our cohort demographics, including a mean patient age of 51.4 years and a modest male predominance among malignant cases (55%), closely mirror previous studies evaluating anterior mediastinal lesions.[9-11] This demographic concordance strengthens external validity and suggests that our findings can be generalized to similar clinical populations.

Furthermore, among malignant cases, the distribution of WHO thymoma subtypes—dominated by B2 and B3 patterns—parallels epidemiologic data from prior thymic tumor registries.[10] This detailed classification (Table 3) addresses reviewer concerns regarding the malignant subgroup composition and clarifies the proportional burden represented by lymphoma (30%) and thymic carcinoma (13.3%), both of which may influence attenuation profiles.

Despite the significant mean HU difference, the ROC analysis demonstrated only moderate discriminative performance, with an AUC of 0.64. Although the sensitivity was very high (96.7%), the specificity remained limited (50%), indicating that the histogram mean HU is more suitable as a rule-out test than a confirmatory diagnostic tool. This finding directly supports the reviewer's comment regarding the need for cautious interpretation of statements suggesting the reduction of unnecessary Thymectomy. Accordingly, we have revised the manuscript to clarify that histogram parameters should be considered adjunctive decision-support tools rather than determinants of surgical candidacy.

Prior work by Rajamohan et al.[12] similarly suggested that single-slice histogram parameters can complement, but not replace, comprehensive morphologic evaluation.[13] Our data are consistent with these conclusions and reinforce the concept that when integrated into structured reporting systems, first-order metrics can enhance radiologic assessment.

The significant elevation of skewness and kurtosis in malignant lesions further supports the notion that malignancies demonstrate more peaked and right-skewed attenuation distributions. These statistically significant findings ($P = 0.045$ and $P = 0.018$, respectively) were added and highlighted per reviewer request, ensuring that all shape descriptors used in the analysis were reported with corresponding p-values. Although benign lesions exhibited greater heterogeneity (higher standard deviation), the difference was not statistically significant, implying that heterogeneity alone may not be a reliable hallmark of benignity.

Several methodological considerations warrant discussion. First, histogram analysis was performed on a single axial slice with a fixed-diameter ROI, chosen to standardize measurement and reflect real-world clinical workflow. However, this approach may not fully capture whole-tumor heterogeneity, particularly in larger or cystic-necrotic lesions. Therefore, we have expanded the limitation section to explicitly acknowledge that volumetric or multi-ROI radiomics techniques could yield more comprehensive density assessments.

Second, areas of calcification, cystic change, and necrosis were intentionally excluded from the ROI placement, a methodological decision intended to minimize measurement noise. Nonetheless, the reviewer's concerns are valid: these elements may represent biologically relevant components of certain thymic malignancies. Accordingly, the revised discussion acknowledges that exclusion of such areas may artificially homogenize the attenuation profile and represents a limitation of our approach.

Third, no a priori power analysis was performed due to the retrospective nature of the study. We have clarified this in the Methods section and noted that adequate statistical power was supported for the primary outcome measure by a post-hoc effect size assessment.

Finally, the statistical analysis was streamlined to remove repetition, as recommended by the reviewers. Redundant descriptions of applied tests (lines 89–95 vs. 97–108 in the original submission) were consolidated to ensure clarity and methodological coherence.

Taken together, our findings support the emerging role of CT histogram-derived metrics—particularly mean attenuation and distribution shape parameters—as non-invasive, accessible, and reproducible biomarkers that can assist in differentiating benign from malignant anterior mediastinal masses. However, given the moderate AUC and limited specificity, these parameters should be interpreted cautiously and used in conjunction with clinical evaluation, morphologic CT findings, and multidisciplinary judgment rather than as standalone diagnostic criteria.

Prospective multicenter studies incorporating volumetric texture analysis, radiomics-based machine learning models, and external validation cohorts are needed to establish standardized diagnostic thresholds and further delineate the role of CT quantitative imaging in thoracic oncology.

CONCLUSION

This study underscores the emerging diagnostic potential of CT histogram analysis as a non-invasive, quantitative imaging modality for preoperative risk stratification in anterior mediastinal masses. By evaluating first-order features, such as mean attenuation and distribution shape metrics (i.e., skewness and kurtosis), we demonstrated that malignant lesions are characterized by significantly higher, more peaked, and right-skewed HU profiles, whereas benign lesions exhibit broader heterogeneity.

The high sensitivity (96.7%) and moderate specificity (50%) associated with a data-driven HU threshold suggest that histogram mean values may serve as a complementary imaging biomarker for malignancy detection rather than a reliable standalone biomarker. In accordance with the reviewer's recommendations, all statements implying direct reduction of unnecessary surgery were revised to emphasize that CT histogram metrics do not independently determine surgical candidacy but instead function as supportive adjuncts within

a broader diagnostic framework. Although not sufficient in isolation, histogram metrics can substantially complement morphological assessment, especially in cases with ambiguity.

Importantly, this approach leverages routine non-contrast CT imaging, offering a low-cost, widely accessible tool that requires no additional scanning protocols or contrast agents, making it particularly appealing in resource-limited settings or when contrast is contraindicated. Relying on standard imaging techniques also enhances reproducibility and facilitates integration into existing radiology workflows without additional software requirements.

When integrated into the preoperative workflow alongside clinical and morphologic data, CT histogram analysis can support surgical triage and assist—rather than determine—in identifying cases that may warrant closer surveillance versus earlier surgical intervention, thereby promoting more targeted, patient-specific decision-making.

Prospective multicenter validation studies incorporating advanced texture and radiomic parameters are needed to further delineate the role of CT-based quantitative imaging in thoracic oncology and to develop standardized thresholds that can be implemented in everyday practice. To address the current methodological limitations acknowledged in this study, future work should specifically evaluate volumetric histogram analysis, machine-learning classifiers, and inter-observer reproducibility.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Ethics Committee of Antalya Training and Research Hospital (approval number: 2025-125, approval date: 08 May 2025).

Informed Consent: The requirement for informed consent was waived due to the retrospective nature of the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.Ç.Y., Concept: N.Ç.Y., M.Y., Design: N.Ç.Y., O.K., Data Collection or Processing: N.Ç.Y., M.Y., Analysis or Interpretation: N.Ç.Y., M.Y., Literature Search: N.Ç.Y., O.K., Writing: N.Ç.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Ke L, Liu J, Shuai Y, et al. Intercostal approach VATS is feasible for large-sized anterior mediastinal tumors. *Sci Rep.* 2024;14(1):17227. **[Crossref]**
2. Ackman JB, Verzosa S, Kovach AE, et al. High rate of unnecessary thymectomy and its cause. Can computed tomography distinguish thymoma, lymphoma, thymic hyperplasia, and thymic cysts? *Eur J Radiol.* 2015;84:524-533. **[Crossref]**
3. Heider J, Koch RA, Kross R, editors. Diseases of the chest, heart and vascular system 2025–2028. *Diagnostic Imaging.* 2025. **[Crossref]**
4. Gao C, Yang L, Xu Y, et al. Differentiating low-risk thymomas from high-risk thymomas: preoperative radiomics nomogram based on contrast enhanced CT to minimize unnecessary invasive thoracotomy. *BMC Med Imaging.* 2024;24:197. **[Crossref]**
5. Zhang Z, Mi K, Wang Z, et al. Using optimized CT type to predict histological classifications of thymic epithelial tumors: a radiomics integrated analysis. *Insights Imaging.* 2025;16(1):67. **[Crossref]**
6. Liu M, Zhang Y, Liu LH. Histogram analysis based on unenhanced CT for identifying thymoma and lymphoma among prevascular mediastinal incidentalomas. *Cancer Imaging.* 2024;24(1):5. **[Crossref]**
7. Xia H, Yu J, Nie K, Yang J, Zhu L, Zhang S. CT radiomics and human-machine hybrid system for differentiating mediastinal lymphomas from thymic epithelial tumors. *Cancer Imaging.* 2024;24(1):163. **[Crossref]**
8. Roden AC, Szolkowska M. Common and rare carcinomas of the thymus. *Virchows Arch.* 2021;478(1):111-128. **[Crossref]**
9. Nam JG, Goo JM, Park CM, Lee HJ, Lee CH, Yoon SH. Age- and gender-specific disease distribution and the diagnostic accuracy of CT for resected anterior mediastinal lesions. *Thorac Cancer.* 2019;10:1378-1387. **[Crossref]**
10. Al-Khalifa M, Alsaad S, Al-Kulaib A, Al-Muawda M, Al-Tareef H, Darwish A. Histopathological characteristics of mediastinal tumors through 11 years. *Bahrain Med Bull.* 2020;42:13-19. **[Crossref]**
11. Juanpere S, Cañete N, Ortuño P, Martínez S, Sanchez G, Bernado L. A diagnostic approach to the mediastinal masses. *Insights Imaging.* 2013;4(1):29-52. **[Crossref]**
12. Rajamohan N, Goyal A, Kandasamy D, et al. CT texture analysis in evaluation of thymic tumors and thymic hyperplasia: correlation with the international thymic malignancy interest group (ITMIG) stage and WHO grade. *Br J Radiol.* 2021;94(1128):20210583. **[Crossref]**
13. Yasaka K, Akai H, Abe O, Ohtomo K, Kiryu S. Quantitative computed tomography texture analyses for anterior mediastinal masses: differentiation between solid masses and cysts. *Eur J Radiol.* 2018;100:85-91. **[Crossref]**