Research Article

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Title: Illuminating the thymus mystery in pediatric CT studies.

Short title: CT assessment of the pediatric thymus.

Abstract

Purpose: This study aims to provide a comprehensive assessment of thymic morphology, attenuation, and anatomical variations in pediatric patients using modern multi-detector computed tomography (MDCT). Additionally, it seeks to establish reference values and analyze the factors influencing thymic density.

Materials and methods: A retrospective analysis was conducted on 622 pediatric chest CT scans obtained between 2017 and 2024. Thymic shape, contour, density, and size parameters were evaluated. Thymic attenuation was graded using a standardized scoring system, and measurements of thymic dimensions were recorded. Statistical analyses were performed to assess correlations between thymic density, age, gender, and morphological characteristics.

Results: Thymic morphology exhibited significant variation, with quadrilateral shape being the most common (42.1%), followed by round-oval (29.7%) and triangular (28.1%). Thymic attenuation showed no significant correlation with age (p=0.156) or gender (p=0.191). Regression analysis revealed a negative association between anteroposterior diameter and thymic density (β=-0.4019, p=0.015), while transverse diameter was positively correlated with thymic density (β=0.5465, p<0.001). No significant association was found between thymic shape, contour, localization, and thymic attenuation.

Conclusion: This study provides a detailed evaluation of normal thymic imaging characteristics in pediatric patients, offering reference values for radiologists. Recognizing thymic variability across different age groups is essential to avoid misdiagnosis and unnecessary interventions. Future research should focus on longitudinal studies and advanced imaging techniques to refine diagnostic criteria.

Keywords: Thymus, pediatric imaging, MDCT, thymic density, thymic morphology.

Makale başlığı: Pediatrik BT çalışmalarında timusun gizemini aydınlatmak.

Kısa başlık: Pediatrik timusun BT değerlendirmesi.

Öz

Amaç: Bu çalışma, modern çok kesitli bilgisayarlı tomografi (MDCT) kullanarak pediatrik hastalarda timusun morfolojisi, dansitesi ve anatomik varyasyonlarını kapsamlı bir şekilde değerlendirmeyi amaçlamaktadır. Ayrıca, referans değerler belirlemeyi ve timus dansitesini etkileyen faktörleri analiz etmeyi hedeflemektedir.

Gereç ve yöntem: 2017 ile 2024 yılları arasında elde edilen 622 pediatrik göğüs BT taraması retrospektif olarak analiz edildi. Timusun şekli, konturu, dansitesi ve boyut parametreleri değerlendirildi. Timus dansitesi standart bir skorlama sistemi kullanılarak sınıflandırıldı ve timusun boyutsal ölçümleri kaydedildi. Timus dansitesi ile yaş, cinsiyet ve morfolojik özellikler arasındaki ilişkileri değerlendirmek için istatistiksel analizler yapıldı.

Bulgular: Timus morfolojisinde belirgin farklılıklar gözlendi; en yaygın şekil dörtgen (%42,1) olup, bunu yuvarlak-oval (%29,7) ve üçgen (%28,1) şekiller takip etti. Timus dansitesi ile yaş ($p=0.156$) veya cinsiyet ($p=0.191$) arasında anlamlı bir korelasyon saptanmadı. Regresyon analizinde, ön-arka çap ile timus dansitesi arasında negatif bir ilişki ($\beta=-0.4019$, $p=0.015$) bulunurken, transvers çap ile timus dansitesi arasında pozitif bir ilişki ($\beta=0.5465$, $p<0.001$) gözlendi. Timus şekli, konturu ve lokalizasyonu ile timus dansitesi arasında anlamlı bir ilişki bulunmadı.

Sonuç: Bu çalışma, pediatrik hastalarda normal timus görüntüleme özelliklerini ayrıntılı olarak değerlendirerek radyologlar için referans değerler sunmaktadır. Farklı yaş gruplarındaki timus varyasyonlarının tanınması, yanlış tanıların ve gereksiz girişimlerin önlenmesi açısından kritiktir. Gelecekteki araştırmaların, uzunlamasına çalışmalar ve ileri görüntüleme tekniklerini içerecek şekilde tanı kriterlerini daha da geliştirmeye odaklanması gerekmektedir.

Anahtar kelimeler: Timus, pediatrik görüntüleme, MDCT, timus dansitesi, timus morfolojisi.

Introduction

The thymus is a key endocrine organ located in the mediastinum, primarily involved in T-cell development and immune function. Its appearance on computed tomography (CT) varies significantly with age, posing a challenge in distinguishing normal from pathological thymic characteristics. However, evaluating a normal thymus via CT can be challenging, as its morphology and size can vary significantly, even among children of the same age. The thymus is a bilobed structure encapsulated in connective tissue and positioned anterior to the ascending aorta, pulmonary outflow tract, and superior vena cava, while posterior to the sternum [1-4]. Initially presenting as a soft-tissue density with quadrilateral contours, it gradually transitions into a triangular configuration with concave or straight borders as age progresses [5].

It is the first lymphoid organ to form and grows significantly during infancy [6]. The thymus reaches its peak size during adolescence, weighing between 20-50 grams, before undergoing physiological involution, where fat replaces thymic parenchyma, reducing its size to 5-15 grams in adulthood [7]. The density of the thymus on computed tomography (CT), measured in Hounsfield Units (HU), has also been noted to decrease with age, from 80 HU to 56 HU, probably as a result of fat infiltration and cellular regression [8]. This involution is more pronounced in males than females but remains a dynamic process, as the thymus retains its regenerative capacity across all ages [9, 10]. Stress-related factors, such as chemotherapy, can lead to thymic rebound hyperplasia, where the gland temporarily enlarges beyond expected limits [11, 12].

The thymic shape shows significant variation even within the same age group [10]. Due to the dynamic changes the thymus undergoes in pediatric patients, a thorough understanding of its anatomy is crucial for radiologists to achieve accurate diagnoses [5]. Despite advancements in imaging, radiologists often misinterpret normal thymic variations, leading to unnecessary interventions such as biopsies or thymectomy [13, 14].

Currently, no standardized guidelines exist for pediatric thymic evaluation via CT, leaving interpretation reliant on expert consensus. Previous studies have examined thymic morphology and attenuation using earlier-generation CT scanners or limited sample sizes [8, 15-17]. Our study, leveraging modern multi-detector CT (MDCT) and a larger cohort, provides a comprehensive assessment of thymic imaging characteristics in children.

Methods

Study population and data collection

Permission was obtained from Pamukkale University Non-Interventional Clinical Research Ethics Committee for the study (Dated: 21.01.2025/ Approval No: E-60116787-020-643305).

Pediatric chest CT scans from January 2017 to October 2024 were reviewed using the hospital's electronic Picture Archiving and Communication System (PACS).

Among 1666 initial chest CT scans, 570 were non-contrast, 42 were repeat scans, and 99 were excluded due to poor image quality. After excluding cases with congenital or acquired thoracic pathology, malignancies, or trauma, 622 patients (226 girls, mean age 9.97±5.16 years; 396 boys, mean age 10.86±5.16 years) were included in the final analysis. Patients were categorized into six age groups: 0-12 months, 1-3 years, 4-6 years, 7-10 years, 11-14 years, and 15-18 years.

CT protocol

All CT scans were acquired using a 64-slice MDCT scanner (Philips Ingenuity 128, Philips Healthcare, Amsterdam, the Netherlands) with parameters optimized for pediatric imaging, including the following: matrix, 512x512; field of view, 250 mm; gantry rotation time, 0.625 s; slice collimation 0.625 mm; pitch, 1; interslice gap, 0 mm. Scans were performed at 80-120 kV, tube currents of 20-150 mA, and a slice thickness of 0.5 mm. Intravenous contrast media (1–2mL/kg) was administered in applicable cases. Two radiologists (G.G. and N.P., with 13 and 2 years of experience) independently reviewed the scans on PACS.

Evaluation of the imaging findings of thymus

Thymic fat content was graded using the Ackman et al. [18] scoring system (0-3 scale), and CT attenuation values were measured using a region of interest (ROI) covering the maximum thymic area. In this system, grade 0 represents complete fatty replacement of the thymus, with no visible soft tissue. Grade 1 indicates a predominantly fatty thymus. Grade 2 signifies a thymus with approximately equal amounts of fatty and soft tissue attenuation. Grade 3 is characterized by the thymus having an attenuation similar to that of muscle and soft tissue. Efforts were made to avoid measurements from areas with streak or beam hardening artifacts or other tissues such as surrounding mediastinal fat or large blood vessels to prevent a false decrease or increase in the ROI.

The thymus shape was classified as round-oval, quadrilateral, or triangular, while its lateral borders were described as convex, concave, or straight. When the thymic border showed a combination of these contours, it was labeled as "mixed. Thymic lateral dominance was also recorded as right-sided, left-sided, or midline (Figure 1).

The thymus's maximum anteroposterior (AP) diameter was recorded at the thickest section along the midline, marking the division between the right and left lobes. The maximum thickness of each thymus lobe at the level of the mid-gland was measured as previously recommended by Baron et al. [1] The thymus's maximum transverse diameter was calculated by measuring the greatest distance between the external boundaries of its lobes. Each lobe's maximum thickness was assessed by taking a perpendicular measurement from its long axis to the most lateral edge of the gland (Figure 2).

Statistical analysis

A priori power analysis was conducted to determine the adequacy of the sample size. The required sample sizes for different effect sizes were calculated based on an alpha level of 0.05 and a desired power of 0.80. For an independent samples t-test, the necessary sample sizes were 788 for a small effect (Cohen's d=0.2), 128 for a medium effect (Cohen's d=0.5), and 52 for a large effect (Cohen's d=0.8). For ANOVA comparisons, the required sample sizes were 392 for a small effect, 78 for a medium effect, and 32 for a large effect. Given that our study included 622 participants, the sample size was sufficient to detect medium and large effect sizes with a power of at least 0.80.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Normally distributed data were presented as mean ± standard deviation (SD) and compared using the independent samples t-test for two-group comparisons and one-way analysis of variance (ANOVA) for multiple-group comparisons, followed by post hoc analyses when necessary. Non-normally distributed data were expressed as median [interquartile range (IQR)] and analyzed using the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for multiple-group comparisons.

Correlations between continuous variables were assessed using Spearman's rank correlation test. The association between categorical variables was evaluated using the Chi-square test and reported as frequencies and percentages. To identify independent predictors of thymic density, multiple linear regression analysis was performed, adjusting for age, sex, and thymic size parameters. A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 622 pediatric patients were included in the study, consisting of 322 males (51.8%) and 300 females (48.2%). The mean age of the study population was 8.4±3.2 years.

Thymic density and visual scoring

There was no significant correlation between thymic density and visual thymic scoring (Spearman's rho=0.010, p=0.802). Although mean thymic density increased with higher thymic scores (Table 1), one-way ANOVA did not show a statistically significant difference among the groups (F=0.471, p=0.703).

Age and gender-related variations

Thymic density was slightly higher in males (42.1±9.8 HU) than in females (40.3±8.9 HU), but this difference was not statistically significant (p=0.191, independent samples t-test). Age-related trends were also not significant (p=0.157, Kruskal-Wallis test), suggesting thymic density does not decline uniformly across pediatric populations (Table 2).

Size-related parameters and their association with thymic density

Regression analysis demonstrated a significant association between thymic density and some anatomical dimensions of the gland. AP diameter was negatively correlated with thymic density (β=-0.4248, p=0.010). Transverse diameter showed a positive correlation with thymic density (β = 0.5450, p=0.001). Right lobe thickness (β=0.5984, p=0.073) showed a trend towards significance but did not reach statistical significance. Left lobe thickness (β=-0.0731, p=0.847) was not significantly associated with thymic density (Table 3).

Thymic shape, contour, and localization

The thymic shape, contour, and localization were assessed for their potential impact on thymic density. No significant association was found between thymic shape and thymic density (χ^2=3.62, p=0.727). Although thymic contour types did not significantly affect thymic density (χ^2=19.61, p=0.075), the trend suggests a potential association that may warrant further investigation. Thymic localization was not significantly associated with thymic density (χ^2=15.06, p=0.238). These findings suggest that thymic density is primarily influenced by gland size rather than its morphological characteristics, age, or sex differences. Among these factors, thymic contour showed the closest trend toward significance, suggesting a potential relationship (Table 4).

Discussion

Our findings highlight considerable variability in thymic morphology and density across pediatric age groups.

Thymic morphology and age-related changes

The most common thymic shape was quadrilateral (42.1%), followed by round-oval (29.7%) and triangular (28.1%). Younger children predominantly exhibited round-oval and quadrilateral thymuses, whereas older children more frequently displayed triangular configurations. These findings align with previous research indicating progressive thymic involution with age. Thymic margins also showed notable variability. Mixed margins were the most common (31.9%), followed by biconvex (30.8%) and straight (21.4%) margins, whereas biconcave borders were relatively rare (15.9%). The presence of biconvex margins in younger children and the predominance of straight margins in older individuals are consistent with the established pattern of thymic involution leading to glandular flattening and contour changes during adolescence [19].

Thymic position and gender differences

The thymus was predominantly located in a right-sided position (44.5%), followed by a left-sided position (36.5%) and midline placement (19.0%). Younger children (0–12 months) were more likely to have a right or left-sided thymus, whereas older children, particularly those over 15 years, exhibited more frequent midline positioning. These findings emphasize the importance of recognizing positional variations to avoid misinterpreting normal anatomy as mediastinal pathology.

Contrary to some previous studies, our findings did not reveal a statistically significant difference in thymic attenuation between male and female participants (p=0.191). Although hormonal influences have been suggested as a factor in thymic involution, our results indicate that sex may not be a primary determinant of thymic attenuation values [20]. Additionally, thymic scoring results did not show a significant difference between sexes, contradicting earlier reports that proposed a higher thymic attenuation and slower fat infiltration in females. This discrepancy may be due to differences in study populations, imaging protocols, or interobserver variability in thymic scoring.

Thymic attenuation and involution

Although thymic involution is a well-documented phenomenon, our study did not demonstrate a significant correlation between age and thymic density (p=0.156, Spearman correlation). This finding contrasts with previous literature that describes a steady decline in thymic attenuation with increasing age [8,17]. One possible explanation for this discrepancy is the relatively narrow age range of our study population, which may not fully capture the complete spectrum of thymic involution observed in older individuals. Additionally, external factors such as physiological stress, chronic illness, or hydration status may contribute to individual variability in thymic density.

Size-related variations and their ımpact on thymic density

Regression analysis showed significant associations between thymic density and anatomical dimensions: AP diameter was inversely correlated with thymic density (beta=-0.4019, p=0.015), suggesting that larger thymuses exhibit more fat infiltration. Transverse diameter was positively correlated (beta=0.5465, p<0.001), indicating that wider thymuses retain more soft tissue. Right and left lobe thicknesses showed no significant associations (p>0.05).

These results highlight the importance of considering thymic shape and volumetric changes in radiological assessments. While traditional metrics such as thymic scoring and attenuation values provide useful information, our findings suggest that size-related parameters may be more reliable indicators of thymic composition than previously assumed.

Clinical implications and comparison with previous studies

This study highlights the importance of recognizing normal thymic variations in pediatric imaging to avoid misdiagnosis and unnecessary interventions. Our findings provide a reference for radiologists in differentiating typical thymic morphology from pathology. Future research should explore longitudinal changes and the impact of physiological stressors on thymic development.

Limitations and future directions

Despite the strengths of a large sample size and advanced MDCT technology, this study has limitations. As a retrospective analysis, selection bias may be present. Additionally, while known thymic abnormalities were excluded, subclinical variations cannot be ruled out. The lack of longitudinal follow-up limits understanding of progressive thymic changes. Future studies should establish standardized reference values and explore advanced imaging techniques such as dual-energy CT or MRI for better characterization of thymic composition.

In conclusion this study provides a comprehensive evaluation of thymic morphology and density in pediatric patients using MDCT. Age-related changes in thymic shape and attenuation were observed, with size-related parameters influencing density. These findings serve as a valuable reference for radiologists, aiding in accurate assessment and reducing unnecessary interventions. Understanding the expected variations in thymic appearance across pediatric age groups is essential to prevent diagnostic errors. Future studies should refine these findings with longitudinal data and advanced imaging approaches to improve clinical interpretations.

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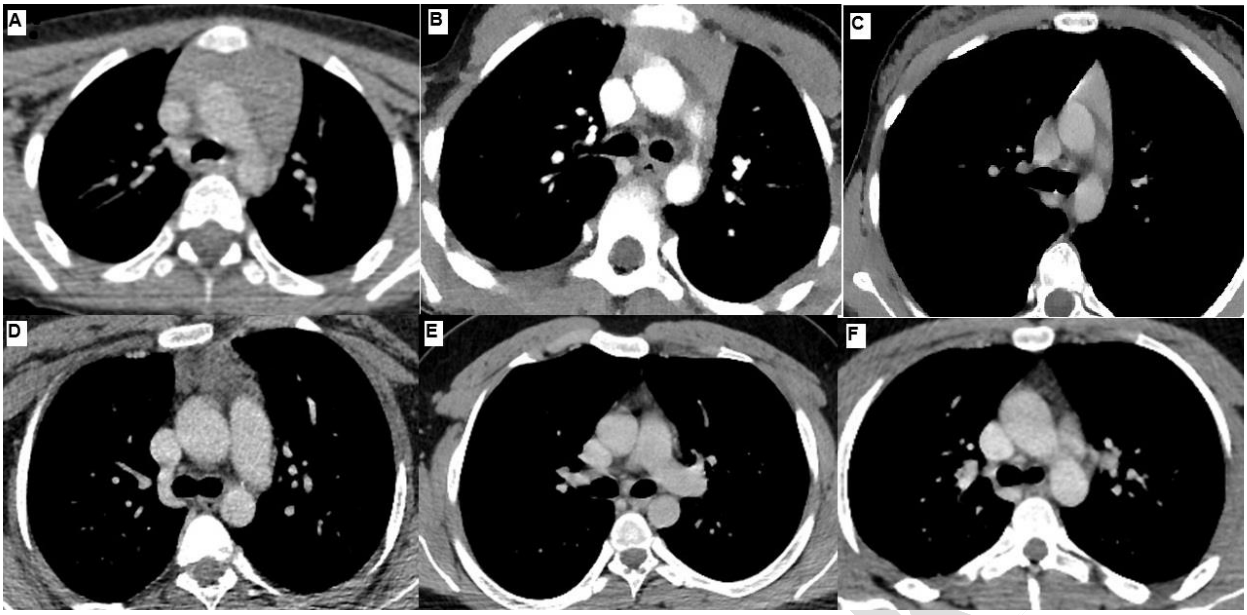

Figure 1. Axial contrast-enhanced thoracic CT images demonstrating different thymic morphologies in pediatric patients. (A) A 1-year-old girl with a round-oval thymus, biconvex margins, is predominantly left-sided; Score 3 indicates a primarily soft-tissue attenuated thymus. (B) A 7-year-old boy presented with a quadrilateral thymic shape, straight margins, and central positioning; Score 3, reflecting a soft-tissue dominant thymic composition. (C) 11-year-old girl with a triangular thymic structure, straight contours, predominantly left-sided placement; Score 3, representing a mostly soft-tissue attenuated thymus. (D) 14-year-old girl exhibiting a quadrilateral thymus with mixt margins (right straight, left convex), centrally located; Score 2, displaying an approximately equal mix of fatty and soft-tissue attenuation. (E) 16-year-old boy with a triangular thymus, straight margins, centrally positioned; Score 1, characterized by a predominantly fatty thymus. (F) 17-year-old boy featuring a triangular thymus, straight contours, centrally located; Score 0, denoting complete fatty replacement of the thymus.

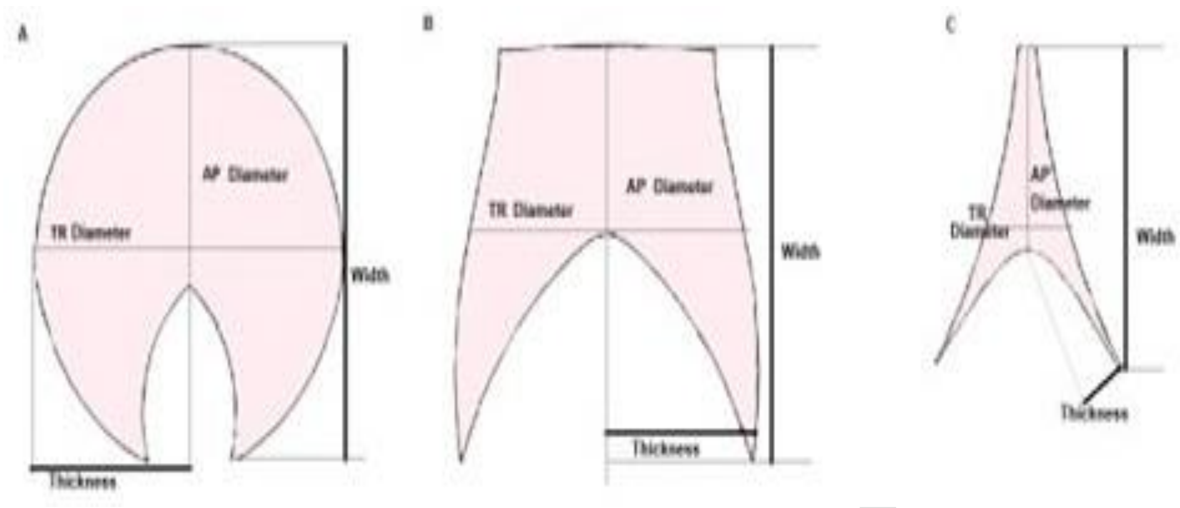

Figure 2. The diagram illustrates the measurements of various thymic configurations, including (A) round-oval, (B) quadrilateral, and (C) triangular shapes. It highlights the maximum anteroposterior (AP) and transverse (TR) diameters, as well as the greatest width and thickness of the thymic lobes for each morphological variant.

Table 1. Thymic density and visual scoring

	Thymic score	**Mean Density (HU)**	**Std Dev**	**ANOVA F-value**	***p*-value (ANOVA)**
1	0	30.2	7.9	0.471	0.703
2	1	35.6	8.3	0.471	0.703
3	2	40.8	9.7	0.471	0.703
4	3	45.2	10.5	0.471	0.703

Spearman’s correlation analysis was used to evaluate the relationship between thymic density and visual scoring (rho=0.010, *p*=0.802), while *p*-values in the table were derived from Spearman’s correlation and one-way ANOVA

Table 2. Thymic density across age groups

	Age Group	Mean Density (HU)	Std Dev	H value	*p* value
1	0-12 months	59.93	32.68	7.986	0.157
2	1-3 years	64.39	27.14		
3	4-6 years	69.67	26.00		
4	7-10 years	68.28	29.57		
5	11-14 years	69.16	24.06		
6	15-18 years	62.86	26.98		

p-values are derived from the Kruskal-Wallis test. No statistically significant difference was found among the age groups (p=0.157)

Table 3. Regression analysis results

Variable	Beta Coefficient (β)	Standard Error	t-value	*p* value	95% CI Lower	95% CI Upper
AP diamater	-0.4248	0.1647	-2.5789	*0.015	-0.7483	-0.1013
Transverse diamater	0.5450	0.1559	3.4941	< 0.001	0.2387	0.8513
RL Thickness	0.5984	0.3329	1.7974	0.097	-0.0554	1.2522
LL Thickness	-0.0730	0.3780	-0.1933	0.876	-0.8154	0.6692

Multiple linear regression analysis was conducted to determine independent predictors of thymic density. AP: Anteroposterior, RL: Right lobe, LL: Left lobe

Table 4. Shape, contour, and localization analysis

	Variable	Chi-square (χ^2)	Degrees of Freedom	*p* value
1	**Thymic Shape**	3.62	6	0.727
2	**Thymic Contour**	19.61	12	0.075
3	**Thymic Localization**	15.06	12	0.238

Chi-square test was used to evaluate the association between thymic shape, contour, localization, and thymic density

Güngör G, Piri N. Illuminating the thymus mystery in pediatric CT studies. Pam Med J 2025;18:…-…

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