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Retrospective Study

Detection of Tracheal Branching with Computerized Tomography: The Relationship between the Angles and Age-Gender

Kahraman S *et al.* Tracheobronchial branching angles with MinIP technique

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Abstract

BACKGROUND

Our study is the first study in the literature to measure the angle values of the tracheobronchial system using the multislice CT and MinIP technique with the number of 1511 patients and to have the largest patient population including both pediatric and adult demographic data. In addition, unlike previous studies, we measured all branching angles of the tracheobronchial tree and assessed their relationship with age and gender.

We think that this study will be a guide for future studies in this way.

AIM

Our study will be a guide for future studies that measure the angle values of the tracheobronchial system in a large patient population.

METHODS

Our institutional review board gave its approval to this retrospective study. Ethics committee did not require informed consent, as our study was retrospective.

A total of 1511 patients, including 753 pediatrics and 758 adults, were included in our study. patients who do not obey breath commands enough to prevent image formation, tracheobronchial surgery or tracheal intubation history), patients with pneumothorax, pneumomediastinum as a result of trauma, patients with pathology that may cause mediastinal changes (mediastinal mass, mediastinal LAP, severe cardiomegaly), musculoskeletal deformity patients (scoliosis, kyphosis) and patients with diaphragmatic hernia were not included in the study. CT scanners today can scan the entire chest in a matter of seconds. Thin sections in multiple planes, including the axial, coronal, and sagittal planes, can be used to quickly reconstruct images. Coronal images taken off-axis are useful for imaging the trachea in a single plane.

RESULTS

Our study is the first study in the literature to measure the angle values of the tracheobronchial system using the multislice CT and MinIP technique with the number of 1511 patients and to have the largest patient population including both pediatric and adult demographic data. In addition, unlike previous studies, we measured all branching angles of the tracheobronchial tree and assessed their relationship with age and gender.

In our study, tracheal bifurcation angle was found to be $73.3^{\circ} \pm 13.7^{\circ}$ ($59.6-87^{\circ}$) in the whole population. The tracheal bifurcation angle and the angle of the right middle lobe bronchus and the right lower lobe bronchus in the coronal plane increase statistically with increasing age. We think that this study will be a guide for future studies in this way.

CONCLUSION

Our study will be a guide for future studies that measure the angle values of the tracheobronchial system in a large patient population.

Key Words: Tracheobronchial branching angles; Subcarinal angle; MinIP technique with multislice CT

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Core Tip: This study is one of the rare studies with the highest number of patient population and measurement values in the literature measuring the branching angles of the tracheobronchial tree using the MinIP technique with multislice CT in pediatric and adult populations. In this study, a wide variety of branching angles of the tracheal bronchial tree, which were not reported in the literature, were reported. Anatomical knowledge of the tracheobronchial system is essential during the use of interventional fiberoptic bronchoscopy during various airway devices, intubation, airway maneuvers. These results guide interventional procedures and offer new methods for future studies.

INTRODUCTION

Trachea is a cylindrical flexible tube that provides air passage between the larynx and the lung. Trachea bifurcation angle; It is measured by the interbronchial angle, which is the angle measured at the intersection of the central axes of the right and left main bronchus, or by the subcarinal angle, which is the angle at the intersection of the lower borders of the right and left main bronchus. Many cardiac and mediastinal pathologies can cause changes in tracheal bifurcation angle (1-4).

Examination of the tracheobronchial tree can be done with invasive and noninvasive methods such as bronchoscopy, bronchograms, computed tomography, magnetic resonance imaging (2, 3, 5). Most previous studies measured the subcarinal

angle on chest radiographs using a goniometer (6, 7). Helical computed tomography provides volumetric imaging of chest films and accurate measurement of the subcarinal angle at a workstation using the minimum intensity projection (MinIP) technique. Because the MinIP technique uses all the data in the volume of interest to create a one- and two-dimensional image, it is a technique that enables the visualization of structures of low density (e.g. air) at this level. This technique allows us to accurately measure the subcarinal angle compared to the coronal multiplane reconstructed image (3, 8).

Anatomical knowledge of the tracheobronchial system is essential when using interventional fiberoptic bronchoscopy during various airway devices (eg, double-lumen endobronchial tube), intubation, airway maneuvers, airway reconstruction, and tracheobronchial tumor resection (9, 10).

Previous studies were insufficient for the pediatric population (11-14).

In 2018, SF Fernandes *et al* found the mean subcarinal angle of $69.75^{\circ} \pm 3.38^{\circ}$ (range 66.37° - 73.13°) in the measurements made with thorax CT and MinIP technique on 193 patients aged 20-60 years (3). AH Parry *et al* in the measurements made with thorax CT and MinIP technique on 552 patients aged 9-85 years in 2019, they found the mean subcarinal angle to be statistically significantly larger in women than in men ($78.90 \pm 11.04^{\circ}$ vs $67.60 \pm 14.55^{\circ}$, $p < 0.05$) (5). In 2018, SF Fernandes *et al* and AH Parry *et al* although the measurement methods are similar in his studies in 2019, the number of patients and measurement parameters are limited. In addition, the relationship between age and gender and the subcarinal angle was not clarified.

The aim of our study is to determine the tracheobronchial branching angles in pediatric and adult individuals with a high sample size population by using the multislice CT and MinIP technique, which is a non-invasive method, and to eliminate the above-mentioned literature deficiencies.

MATERIALS AND METHODS

Our institutional review board gave its approval to this retrospective study. Ethics committee did not require informed consent, as our study was retrospective.

A- Study Population: A total of 1511 patients, including 753 pediatrics and 758 adults, were included in our study. patients who do not obey breath commands enough to prevent image formation, tracheobronchial surgery or tracheal intubation history), patients with pneumothorax, pneumomediastinum as a result of trauma, patients with pathology that may cause mediastinal changes (mediastinal mass, mediastinal LAP, severe cardiomegaly), musculoskeletal deformity patients (scoliosis, kyphosis) and patients with diaphragmatic hernia were not included in the study. CT scanners today can scan the entire chest in a matter of seconds. Thin sections in multiple planes, including the axial, coronal, and sagittal planes, can be used to quickly reconstruct images. Coronal images taken off-axis are useful for imaging the trachea in a single plane.

Patients who were unable to obtain good image quality (for example, those who were unable to hold their breath or who had motion artifacts) were excluded from the study. Thoracic CT scans were also performed in pediatric patients of all ages in order to produce the best image in the shortest amount of time. Images with poor image quality and coinciding with the expiratory phase were excluded from the study.

In our study, people with diseases that disrupt the anatomy and physiology of the tracheobronchial system, infective or inflammatory processes, lung cancer, significant pneumonia or collapse, and respiratory system diseases in all patient groups (adults and children) were not included in the study.

Inclusion criteria for the study; excluding the exclusion criteria, the tracheobronchial system and lung parenchyma images of the anatomically and pathophysiologically good quality were obtained in patients who underwent CT with or without contrast for any reason (**Figure 1**).

B- Imaging: This study consists of contrasted and non-contrast thoracic CT examinations with a double tube 256 slice Somatom Definition Flash device (Siemens Healthcare, Forchheim, Germany). The images of the patients were evaluated using the

Siemens Somatom Sensation-Syngo.via software program from the PACS (Picture Archiving Communication System) archive on coronal planes and using the MinIP technique.

Shooting parameters; Lung parenchyma images were obtained by adjusting tube voltage 120 kV, automatic tube current modulation 100-250 mAs, section thickness 1.25 mm, pitch 1.4, gantry rotation time 0.5-1 sec, FOV 455 mm. Images were acquired with adequate inspiration and in the supine position. In contrast-enhanced thorax shots, the dose was administered by administering a total of 100-120 mL of contrast material at a rate of 4 mL/sec.

Then, the images in the PACS system were measured in the coronal plane using the 25 mm MinIP technique in the Siemens (Syngo.via, Siemens Healthineers, Erlangen, Germany) software program.

Measurements were taken by 2 independent radiologists and verified by a partner radiologist. All radiologists then reviewed any discrepancies between the measurements. All investigators were blind to the age of the patients until the measurements were analysed.

At the same time, demographic data (age, gender) of the patients were recorded. Measurements were made using the 25 mm MinIP technique obtained in the lung parenchyma window in the coronal plane. *via* program. Right main bronchus-left main bronchus angle, right upper lobe bronchus-intermedius bronchus angle, right middle lobe bronchus-right lower lobe bronchus angle, left upper lobe bronchus-left lower lobe bronchus angle measurements were made in the coronal plane. It was measured as the angle at the junction of the line passing through the center of the bronchi on the long axis (Figure 2).

A data visualization technique called minimum intensity projection (MinIP) makes it possible to find low-density structures in a given volume. The algorithm projects the voxel with the lowest attenuation value across all views in the volume onto a 2D image, using all the data in the volume of interest to create a single bidimensional image.

Figure 2. A: Measurements of tracheobronchial angles with MinIP technique in coronal plane thoracic images of a 9-year-old male pediatric patient and B: a 25-year-old male adult patient.

- 1: Angle of right(R) and left(L) main bronchus in coronal plane
- 2: R upper-intermedius(coronal): It means the angle of the right upper lobe bronchus and the right intermedius bronchus in the coronal plane.
- 3: R middle-lower (coronal): It means the angle of the right middle lobe bronchus and the right lower lobe bronchus in the coronal plane.
- 4: L upper-lower (coronal): It means the angle of left upper lobe bronchus and left lower lobe bronchus in the coronal plane.

Right main bronchus-left main bronchus angle (interbronchial angle) right left main coronal, right upper lobe bronchi-intermedius bronchus angle right upper-intermedius (coronal), right middle lobe bronchus-right lower lobe bronchus angle right middle-lower (coronal) , left upper lobe bronchus-left lower lobe bronchial angle is abbreviated as left upper-lower (coronal).

C- Statistical Analysis: Statistical analyses of collected data were conducted using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). Determination of the normally distributed data was conducted using the Kolmogorov-Smirnov test. Numerical variables that had normal distribution were expressed as the mean \pm standard deviation, while those with non-normal distribution were expressed as the median (min-max). The categorical variables were expressed as numbers and percentages. For comparisons between groups, the Student T test or Mann-Whitney U test were used according to normality distribution. Categorical variables were expressed as numbers and percentages, and comparisons between groups were evaluated with Chi-square and Fisher's Exact tests. Spearman correlation analysis was used for the relationship between age and angels. $P < 0.05$ was taken as statistical significance.

RESULTS

² Our study is the first study in the literature to measure the angle values of the tracheobronchial system using the multislice CT and MinIP technique with the number of 1511 patients and to have the largest patient population including both pediatric and adult demographic data. In addition, unlike previous studies, we measured all branching angles of the tracheobronchial tree and assessed their relationship with age and gender.

In our study, tracheal bifurcation angle was found to be $73.3^{\circ} \pm 13.7^{\circ}$ ($59.6-87^{\circ}$) in the whole population. ³ The tracheal bifurcation angle and the angle of the right middle lobe bronchus and the right lower lobe bronchus in the coronal plane increase statistically with increasing age. ¹ We think that this study will be a guide for future studies in this way.

DISCUSSION

While there are many studies evaluating the tracheal bifurcation angle with cadaver studies and chest radiographs, there are limited studies evaluating using CT. However, it was not detected except in the study conducted by Fernandes *et al*, in which 193 patients reported using CT with the MinIP technique were examined (3). In addition, our study Weidong Mi *et al* except for the measurements made with thorax CT and MPR technique on 2107 patients aged 18-89 years in 2015, it has a larger patient population than previous studies in the literature measuring the angle values of the tracheobronchial system (9).

Our study is a study with the largest number of patient population in our country, which measures the angle values of the tracheobronchial system using multislice CT and MinIP technique, which is a noninvasive method, and includes both pediatric and adult demographic data.

⁸ Tracheal bifurcation angle ; it is measured by the interbronchial angle, which is the angle measured at the intersection of the central axes of the right and left main

bronchus, or by the subcarinal angle, which is the angle at the intersection of the lower borders of the right and left main bronchus (4). In our study, we measured the tracheal bifurcation angles by measuring the interbronchial angle. The normal values of the tracheal bifurcation angle range from 40° to 99°, with an average value of 60–65° (11). In our study, we found the tracheal bifurcation angle of $73.3^{\circ} \pm 13.7^{\circ}$ (range 59.6–87°).

Karabulut *et al* in 2005, found the mean interbronchial angle of $77^{\circ} \pm 13^{\circ}$ in a study that measured the tracheal bifurcation angle with helical CT performed on 120 patients aged 17–85 years (11).

The results of our study showed similar results with Karabulut *et al* study and literature. The tracheal bifurcation angle may widen due to various mediastinal and cardiac pathologies, for example (subcarinal mass, lobar collapse, left atrial enlargement, generalized cardiomegaly, pericardial effusion) (4, 15). Tracheal bifurcation angle may decrease after pulmonary lobectomy (16). Therefore, since the tracheal bifurcation angle is in a wide range and may change due to mediastinal and cardiac pathologies, diseases with mediastinal and cardiac pathologies and disrupting the anatomy and physiology of the tracheobronchial system were not included in our study. In our study, measurements were made during the inspiration phase because the tracheal bifurcation angle narrows due to the downward extension of the lungs in inspiration and expands with upward displacement of the lungs in expiration (3).

The first studies measuring the tracheal bifurcation angle (interbronchial angle) were made towards the end of the 19th century by Kobler *et al* on cadavers and found the average angle of 70° (10, 17). Adriani *et al* found the average tracheal bifurcation angle (interbronchial angle) of 110° in infantar (10). Kubota *et al* found the tracheal bifurcation angle of 80° on average using chest radiography in their study on infants and children aged 0–13 years (12). Alavi *et al* in their study of children up to 16 years of age, they found the tracheal bifurcation angle to range from 52° to 78° using chest radiography (13).

Ulusoy *et al* in their study using multislice CT, found that the right bronchial angle was smaller than the left in their study in the 0–18 age range. Ulusoy *et al* calculated the

mean right subcarinal angle as $34.5^{\circ} \pm 8.1^{\circ}$ degrees and the mean left subcarinal angle as $38.1^{\circ} \pm 8.9^{\circ}$. Although the mean right and left subcarinal angles were not significant in all age groups except the 0-18 age group, they were measured higher in women than in men (14). In our study, the tracheal bifurcation angle, which is the sum of the right subcarinal angle and the left subcarinal angle, was used and our method was similar. In our study, the tracheal bifurcation angle passing through the central axes of the right main bronchus and left main bronchus in the coronal plane was found to be statistically significantly higher in boys compared to girls in our study ($74.6^{\circ} \pm 12.9$ vs $71.2^{\circ} \pm 13.9$; $P = 0.001$). The high number of cases and measurement parameters in our study suggest that our study is more reliable. The angle of the right upper lobe bronchus and the right intermedius bronchus in the coronal plane, the angle of the left upper lobe bronchus and the left lower lobe bronchus in the coronal plane, and the angle values of the right middle lobe bronchus and the right lower lobe bronchus in the coronal plane are the first measurements in the literature using the MinIP technique. However, no significant differentiation was detected for these measurements.

Karabulut *et al* in 2005, the mean interbronchial angle was $77^{\circ} \pm 13^{\circ}$ and the mean subcarinal angle was $73^{\circ} \pm 16^{\circ}$ in the study of 120 patients aged 17-85 years, measuring the tracheal bifurcation angle with helical CT. They found an excellent correlation between the interbronchial angle and the subcarinal angle ($r = 0.88$, $p < 0.001$). They found that the interbronchial angle and subcarinal angle, which are tracheal bifurcation angles, were statistically significantly larger in females compared to males (11).

JG Murray *et al* reported higher interbronchial and subcarinal angles in female patients in the measurements made using chest radiography on 122 patients with an age range of 27-85 years, but they were not statistically significant (7). Karabulut *et al*'s study conducted in 2005 and our study contradicts previous studies measuring the tracheal bifurcation angle with chest radiography, which reported that the angle of tracheal bifurcation was independent of gender (13, 18, 19). Measurements with CT can be considered to be more reliable and accurate since it is possible to evaluate the

anatomy of the tracheobronchial system in multiplanar (axial, sagittal and coronal) planes.

Weidong Mi *et al* found the subcarinal angle, known as the sum of the right bronchial angle and the left bronchial angle, to be statistically significantly larger in women than in men, in the measurements made using thorax CT and MPR techniques on 2107 patients aged 18-89 years in 2015, similar to our study ($80.1^{\circ} \pm 13.4^{\circ}$ vs. $75.1^{\circ} \pm 13.4^{\circ}$) (9).

Khade *et al* in 2016, found the mean subcarinal angle of $79.92^{\circ} \pm 11.6^{\circ}$ (range 68.32° - 91.52°) in 110 patients aged 10-70 years, measuring the subcarinal angle with thorax CT. Khade *et al* in contrast to our study, found the subcarinal angle to be statistically insignificantly larger in men than in women ($80.01 \pm 12.53^{\circ}$ vs. $79.75 \pm 9.99^{\circ}$, $P = 0.902$) (2).

In 2018, SF Fernandes *et al* found the mean subcarinal angle of $69.75^{\circ} \pm 3.38^{\circ}$ (range 66.37° - 73.13°) in the measurements made with thorax CT and MinIP technique on 193 patients aged 20-60 years. Fernandes *et al* found the subcarinal angle to be statistically insignificantly larger in women than in men ($69.90 \pm 4.07^{\circ}$ vs. $69.63 \pm 2.75^{\circ}$, $P = 0.589$). Fernandes *et al* found the mean subcarinal angle to be statistically significantly greater in the 20-40 age group than in the 41-60 age group ($70.38 \pm 3.85^{\circ}$ vs. $69.25 \pm 2.88^{\circ}$, $P = 0.02$) (3).

In a study by Kamel KS *et al* in 2009 on tracheal morphology with CT and cadaver dissection, they found the mean subcarinal angle on thorax CT of 60 patients to be greater in women than in men ($81^{\circ} \pm 20^{\circ}$ vs. $76^{\circ} \pm 20^{\circ}$) (17).

AH Parry *et al* in the measurements made with thorax CT and MinIP technique on 552 patients aged 9-85 years in 2019, they found the mean subcarinal angle to be statistically significantly greater in women than in men, similar to our study ($78.90 \pm 11.04^{\circ}$ vs $67.60 \pm 14.55^{\circ}$, $p < 0.05$) (5).

In the current study, we measured the branching angles of the tracheobronchial tree (tracheal bifurcation angle passing through the central axes of the right main bronchus and left main bronchus in the coronal plane, the angle of the right upper lobe

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bronchus and the right intermedius bronchus in the coronal plane, the angle of the right middle lobe bronchus and the right lower lobe bronchus, the angle of the left upper lobe bronchus and the left lower lobe bronchus in the coronal plane) in both adult and pediatric patients. This study is one of the rare studies in the literature with the highest number of patient population and different measurement angles.

The data of other studies examining the relationship between age and tracheobronchial angle are contradictory. In 2018, SF Fernandes *et al* found the mean subcarinal angle in the 20-40 age group statistically significantly higher than the 41-60 age group in the measurements made with thorax CT and MinIP technique on 193 patients with an age range of 20-60 years ($70.38 \pm 3.85^\circ$ vs. $69.25 \pm 2.88^\circ$, $P = 0.02$) (3). Khade *et al* in 2016, in a study that measured the subcarinal angle with thorax CT on 110 patients with an age range of 10-70 years, they did not find any correlation with age and gender (2). Chunder *et al* in his study conducted in 2015 on 60 cadaver specimens, the mean subcarinal angles in the 0-15 years, 16-25 years, 26-40 years, 41-55 years, and >55 age groups were 61.4° , 52.9° , 49.2° , 48.2° and 48.2° in women, respectively; 54° , 64.3° , 56.4° , 58.4° , 57.1° and 59.5° found in males. They concluded that there was a decrease in the subcarinal angle with increasing age, except for patients aged >55 years (20). In our study, the trachea bifurcation angle passing through the central axes of the right main bronchus and the left main bronchus in the coronal plane, and the angle of the right middle lobe bronchus and right lower lobe bronchus in the coronal plane increase statistically with increasing age. It may have occurred due to the variability of the angle due to inspiration-expiration, various mediastinal and cardiac pathologies, measurement technique. In addition, the characteristics of the study populations such as age, gender and race may affect the results. There is a need for further studies measuring with similar methods in more standardized populations to clarify this issue.

CONCLUSION

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Our study is the first study in the literature to measure the angle values of the tracheobronchial system using the multislice CT and MinIP technique with the number

of 1511 patients and to have the largest patient population including both pediatric and adult demographic data. In addition, unlike previous studies, we measured all branching angles of the tracheobronchial tree and assessed their relationship with age and gender.

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ARTICLE HIGHLIGHTS

Research background

This study is one of the few in the literature that uses the MinIP technique with multislice CT to measure the branching angles of the tracheobronchial tree in pediatric and adult populations. This study reported a wide range of branching angles of the tracheal bronchial tree that had not previously been reported in the literature.

Our study's objectives are to fill the gaps in the literature by measuring the tracheobronchial branching angles in a large sample size population of pediatric and adult patients using the non-invasive multislice CT and MinIP technology.

Research motivation

Our study is the first study in the literature to measure the angle values of the tracheobronchial system using the multislice CT and MinIP technique with the number of 1511 patients and to have the largest patient population including both pediatric and adult demographic data. In addition, unlike previous studies, we measured all branching angles of the tracheobronchial tree and assessed their relationship with age and gender.

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with increasing age. ¹ We think that this study will be a guide for future studies in this way.

Research objectives

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In a study by Kamel KS *et al* in 2009 on tracheal morphology with CT and cadaver dissection, they found the mean subcarinal angle on thorax CT of 60 patients to be greater in women than in men ($81^{\circ} \pm 20^{\circ}$ vs. $76^{\circ} \pm 20^{\circ}$) (17).

AH Parry *et al* in the measurements made with thorax CT and MinIP technique on 552 patients aged 9-85 years in 2019, they found the mean subcarinal angle to be statistically significantly greater in women than in men, similar to our study ($78.90 \pm 11.04^{\circ}$ vs $67.60 \pm 14.55^{\circ}$, $p < 0.05$) (5).

In the current study, we measured the branching angles of the tracheobronchial tree (tracheal bifurcation angle passing through the central axes of the right main bronchus and left main bronchus in the coronal plane, the angle of the right upper lobe bronchus and the right intermedius bronchus in the coronal plane, the angle of the right middle lobe bronchus and the right lower lobe bronchus, the angle of the left upper lobe bronchus and the left lower lobe bronchus in the coronal plane) in both adult and pediatric patients. This study is one of the rare studies in the literature with the highest number of patient population and different measurement angles.

The data of other studies examining the relationship between age and tracheobronchial angle are contradictory. In 2018, SF Fernandes *et al* found the mean subcarinal angle in the 20-40 age group statistically significantly higher than the 41-60 age group in the measurements made with thorax CT and MinIP technique on 193 patients with an age range of 20-60 years ($70.38 \pm 3.85^{\circ}$ vs. $69.25 \pm 2.88^{\circ}$, $P = 0.02$) (3). Khade *et al* in 2016, in a study that measured the subcarinal angle with thorax CT on 110 patients with an age range of 10-70 years, they did not find any correlation with age and

gender (2). Chunder *et al*⁴ in his study conducted in 2015 on 60 cadaver specimens, the mean subcarinal angles in the 0–15 years, 16–25 years, 26–40 years, 41–55 years, and >55 age groups were 61.4°, 52.9°, 49.2°, 48.2° and 48.2° in women, respectively; 54°, 64.3°, 56.4°, 58.4°, 57.1° and 59.5° found in males. They concluded that there was a decrease in the subcarinal angle with increasing age, except for patients aged >55 years (20). In our study, the trachea bifurcation angle passing through the central axes of the right main bronchus and the left main bronchus in the coronal plane, and the angle of the right middle lobe bronchus and right lower lobe bronchus in the coronal plane increase statistically with increasing age. It may have occurred due to the variability of the angle due to inspiration-expiration, various mediastinal and cardiac pathologies, measurement technique. In addition, the characteristics of the study populations such as age, gender and race may affect the results. There is a need for further studies measuring with similar methods in more standardized populations to clarify this issue.

² Our study is the first study in the literature to measure the angle values of the tracheobronchial system using the multislice CT and MinIP technique with the number of 1511 patients and to have the largest patient population including both pediatric and adult demographic data. In addition, unlike previous studies, we measured all branching angles of the tracheobronchial tree and assessed their relationship with age and gender.

In our study, tracheal bifurcation angle was found to be $73.3^{\circ} \pm 13.7^{\circ}$ (59.6° – 87°) in the whole population.³ The tracheal bifurcation angle and the angle of the right middle lobe bronchus and the right lower lobe bronchus in the coronal plane increase statistically with increasing age.¹ We think that this study will be a guide for future studies in this way.

Research methods

Our institutional review board gave its approval to this retrospective study. Ethics committee did not require informed consent, as our study was retrospective.

Research results

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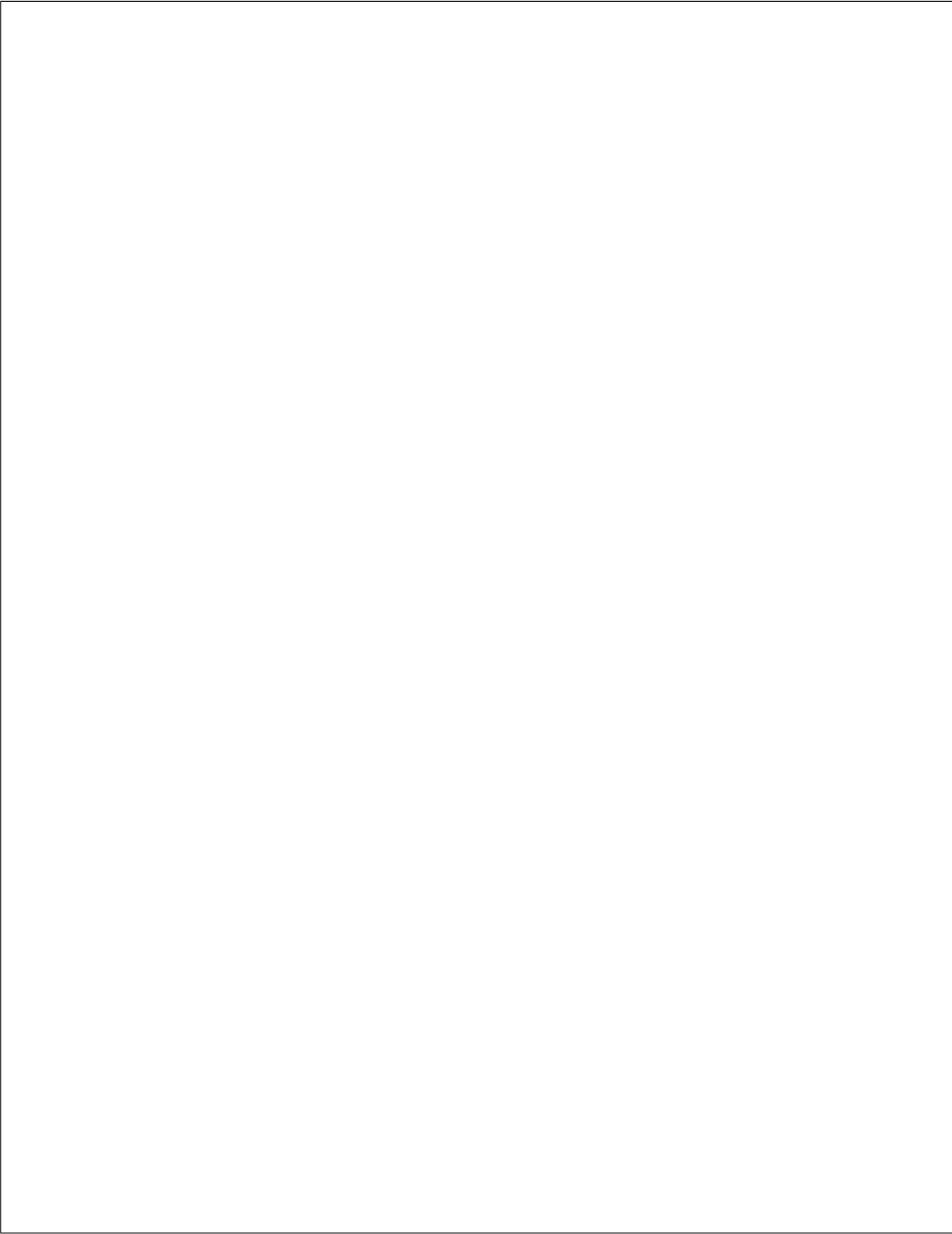
Research conclusions

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Research perspectives

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