RESEARCH ARTICLE

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Received: 04.02.2023
Acceptance: 20.06.2023
DOI: 10.18521/ktd.1247746

Konuralp Medical Journal
e-ISSN1309–3878
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www.konuralptipdergi.duzce.edu.tr

Investigation of Subcarinal Angle and Tracheobronchial Morphology in Patients with COVID 19: A Retrospective Computed Tomography Study

ABSTRACT

Objective: Morphological features of the trachea are very important in choosing the correct endotracheal tube size for intubation. In this study, it was proposed to reveal the effect of SARS-CoV-2 on tracheobronchial morphology and subcarinal angle.

Methods: 56 (26 female, 30 male) COVID-19 and 48 (24 female, 24 male) healthy individuals aged 40 and over were included in the study. The mean age of female patients with COVID-19 was 51.30±12.78 years, while the women in the control group were 45.00±11.89 years. The mean age of male patients with COVID-19 was 48.73±13.99 years, while the mean age of men in the control group was 43.76±8.45 years. The trachea length (TL), proximal, middle and distal levels anteroposterior (AP) and transverse (TR) trachea diameters (TD), subcarinal angle (SA), proximal right main bronchus (RMB) and left main bronchus (LMB) diameters were also measured on computed tomography (CT) images.

Results: The RMB angle was higher in men with COVID-19 than in the control group (p=0.005). TL was lower in women with COVID-19 than in the control group (p=0.030). Proximal AP-TD was higher in men with COVID-19 than in the control group (p=0.006). Proximal TR-TD was lower in men with COVID-19 than in the control group (p=0.029). TL, proximal, middle, and distal levels of AP and TR-TD, SA, RMB, and LMB angles, and proximal RMB and LMB diameters were found to be lower in women with COVID-19 than in men with COVID-19 (p=0.001).

Conclusions: It was deduced that tracheobronchial morphology might change in patients infected with SARS-CoV-2. It is clinically important that this situation should not be overlooked, especially in the indication of endotracheal intubation.

Keywords: Bronchi, COVID 19, CT, Morphology, SARS-CoV-2, Subcarinal Angle, Trachea.

COVID 19'lu Hastalarda Subkarinal Açı ve Trakeobronşiyal Morfolojinin İncelenmesi: Retrospektif Bilgisayarlı Tomografi Çalışması

ÖZET

Amaç: Trakeanın morfolojik özellikleri, entübasyonda doğru endotrakeal tüp boyutunu seçmede oldukça önemlidir. Çalışmada SARS-CoV-2'nin trakeobronşiyal morfolojiye ve subkarinal açıya olan etkisinin ortaya konulması amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya 40 yaş ve üstü 56 (26 kadın, 30 erkek) COVID-19 ve 48 (24 kadın, 24 erkek) sağlıklı birey dahil edilmiştir. COVID-19'lu kadın hastaların yaş ortalaması 51,30±12,78 yıl iken, kontrol grubundaki kadınların yaş ortalaması 45,00±11,89 yıldır. COVID-19'lu erkek hastaların yaş ortalaması 48,73±13,99 yıl iken, kontrol grubundaki erkeklerin yaş ortalaması 43,76±8,45 yıldır. Bilgisayarlı tomografi (BT) görüntüleri üzerinde trakea uzunluğu (TU), proximal, orta ve distal seviyelerde anteroposterior (AP) ve transvers (TR) trakea çapları (TÇ), subkarinal açı (SA), proximalden bronkus prinsipalis dekster (BPD) ve sinister (BPS) çapları ayrıca açıları da ölçülmüştür.

Bulgular: Çalışmaya katılan hasta ve kontrol grupları arasında her iki cinsiyette de yaş farkı istatistiksel olarak anlamlı değildi (kadınlarda p=0,051, erkeklerde p=0,126). BPD açısı COVID-19'lu erkeklerde kontrol grubuna göre daha yüksekti (p=0,005). TU COVID-19'lu kadınlarda kontrol grubuna göre daha düşüktü (p=0,030). Proksimal AP-TÇ COVID-19'lu erkeklerde kontrol grubuna göre daha yüksekti (p=0,006). Proksimal TR-TÇ COVID-19'lu erkeklerde kontrol grubuna göre daha düşüktü (p=0,029). TU, proksimal, orta ve distal seviyelerde AP ve TR-TÇ, SA, BPD ve BPS açıları, proksimalden ölçülen BPD ve BPS çapları COVID-19'lu kadınlarda COVID-19'lu erkeklerden daha düşük bulunmuştur (p=0,001).

Sonuç: SARS-CoV-2 ile enfekte olan hastalarda trakeabronşiyal morfolojinin değişebileceği sonucuna varılmıştır. Özellikle endotrakeal entübasyon endikasyonunda bu durumun gözardı edilmemesi klinik olarak önemlidir.

Anahtar Kelimeler: Bronkus, COVID 19, CT, Morfoloji, SARS-CoV-2, Subkarinal Açı, Trakea.

INTRODUCTION

The trachea is a channel that ensures the connection between the outside world and the parenchyma of the lungs. The trachea, which plays a major role in respiration, has a cartilaginous tubular structure, which is connected to the main bronches below and with the larynx above (1). Recent studies show that tracheobronchial morphology may be associated with chronic diseases (2). Tracheobronchial angles can vary according to age, race, and person, as well as affect the results of angle measurement (3). In a study using computed tomography (CT) in the Asian population, it was reported that the right main bronchus (RMB) angle was 35° and the left main bronchus (LMB) angle was 43° (4). It is known that the tracheal bifurcation angle can expand due to cardiac diseases and mediastinal abnormalities (3,5). It is also affected by the patient's age, gender, body structure, and the size of the chest cavity (6).

COVID-19 droplet infection can be transmitted by direct contact or fecal-oral way and be examined in three different phases, the first 2-14 days of clinical course asymptomatic phase, then the upper and lower airway response lasting for a few days, followed by hypoxia, frosted glass opacities in the lung, acute respiratory distress syndrome (ARDS) (7). SARS-CoV-2 enters the cell with ACE-2 receptors. ACE-2 receptors are expressed in the airway epithelium, especially in the lung, distal airways, glottis and supraglottic space, and trachea (8). In COVID-19, type 2 pneumocytes are activated, diffuse alveolar damage, hyaline membrane formation, and fibrin storage occur (9). Respiratory system uptake is correlated with type 2 pneumocytes uptake. In lung uptake cough, shortness of breath, and fever are typically seen. Radiologically, bilateral peripheral ground-glass areas and consolidation are seen (10). When analyzed histopathologically, interstitial mononuclear infiltrates dominated by lymphocytes and multinucleated and overgrown pneumocytes in intra-alveolar areas can be seen. Pulmonary edema, diffuse alveolar damage, and hyaline membrane formation can be observed (11).

The SARS-CoV-2 target receptor ACE-2 is most commonly found in the lungs, and small intestine and is expressed in endothelial cells and smooth muscle cells of vital organs. Endotheliitis occurs in virus-infected cells (12). Lymphocytic endotheliitis was observed in liver, kidney, heart, and lung examinations of patients who decedent from COVID-19 (13). For this reason, there is not only respiratory system involvement but also the central nervous system, circulatory system, and gastrointestinal system involvement (14). Although the findings related to COVID-19 are generally related to the respiratory system, the cardiovascular features of the disease started to be taken into consideration after a significant part of the patients showed signs of cardiac damage (15). It is a fact that has come up over time that the group most affected by the epidemic and with the highest mortality rate is the elderly with known cardiovascular diseases. Due to cardiac damage, tracheobronchial angles may also be affected. The conducive virus of COVID-19 causes serious consequences because it affects the trachea and tracheobronchial structures by first causing respiratory system involvement devastation.

Computed tomography (CT) is a non-invasive imaging method that is frequently preferred in the anatomical evaluation of the tracheobronchial tree, in determining the location of pathological changes and in monitoring the treatment process (16,17).

In our literature research, there are not enough studies indicating the effect of COVID-19 on the morphology of the subcarinal angle (SA) and other tracheal structures. This study aimed to propound the morphological changes caused by COVID-19 in the SA, trachea, and bronchi.

MATERIAL AND METHODS

Study Design and Patients: Ethics committee approval was obtained from the ethics committee of Malatya Hasan Çalık State Hospital with protocol number 2021/29 in this cross-sectional descriptive study. The study was implemented retrospectively in a total of 104 patients (56 COVID-19 and 48 control groups) aged 40 years and older, who were diagnosed with COVID-19 and had computed tomography (CT) scans taken at the Radiology Department of Malatya Hasan Çalık State Hospital. The measurements were performed in a single center in the relevant institution by an expert radiologist with 12 years of experience in thoracic and neuroradiology.

CT Scanning: Radiological images of patients treated for COVID-19 in our hospital were examined through the PACS system between March 2019 and December 2021. 56 patients diagnosed with COVID-19 who underwent thoracic CT were included in the study. The other group was generated from 48 patients who underwent thoracic CT for different reasons but did not have a history of COVID-19. After age and sex were recorded in both groups, (from three levels: proximal, middle and distal) transverse (TR) and anteroposterior (AP) tracheal diameter (TD), SA, tracheal length (TL), RMB and LMB diameters and angles were measured. Besides, the group with COVID-19 was evaluated in terms of the number of lobes retained in the lung. In both groups, those with lung masses and lung surgery were excluded from the study.

Moreover, those with a diagnosis of Chronic Obstructive Pulmonary Disease (COPD) were excluded from the study, as it may change the measurements in the non-COPD-19 group.

Measurement: SA was measured at the tracheal bifurcation level on coronal reformatted CT images (Fig 1a). The tracheobronchial angle was acquired by measuring the angle on coronal reformatted CT images where a perpendicular line to the RMB axis intersects a perpendicular line to the tracheal lumen (Fig 1b). The same method was used in the LMB (Fig 1c).

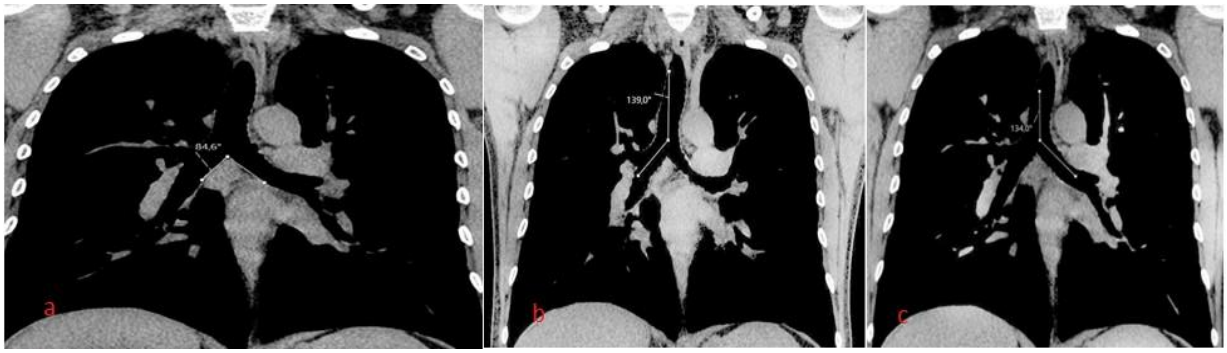

Figure 1. a-Left tracheobronchial angle measurement from CT images in coronal plane (Left main bronchus angle), b- Subcarinal angle measurement from CT images in the coronal plane, c- Right tracheobronchial angle measurement from CT images in coronal plane (Right main bronchus angle).

By examining the TL multiplanar reformat images, the proximal and distal trachea were designated, and measurements were made from the sagittal plane. The proximal trachea was determined as the lower level of the cricoid cartilage, and the distal trachea was specified as the carina level, and the distance was measured (Fig 2).

TD was measured as TR diameter and AP diameter in the axial plane from the proximal, distal, and mid-level (Fig 3a). RMB and LMB diameter measurements were measured in the most distal axial plane (Fig 3b).

Statistical Analysis: For statistical analysis of the data, IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) package program was used. The conformity of the data to the normal distribution was tested with Kolmogorov Smirnov test. Mean and standard deviation were used for numerical data, number and percentage values were used for categorical data, and independent t test and Mann Whitney U test was used for group comparisons. In evaluating the level of significance in the analysis, a p-value equal to and less than 0.05 was considered statistically significant.

Figure 2. Trachea length measurement in sagittal plane by determining proximal and distal trachea from multiplanar reformat images.

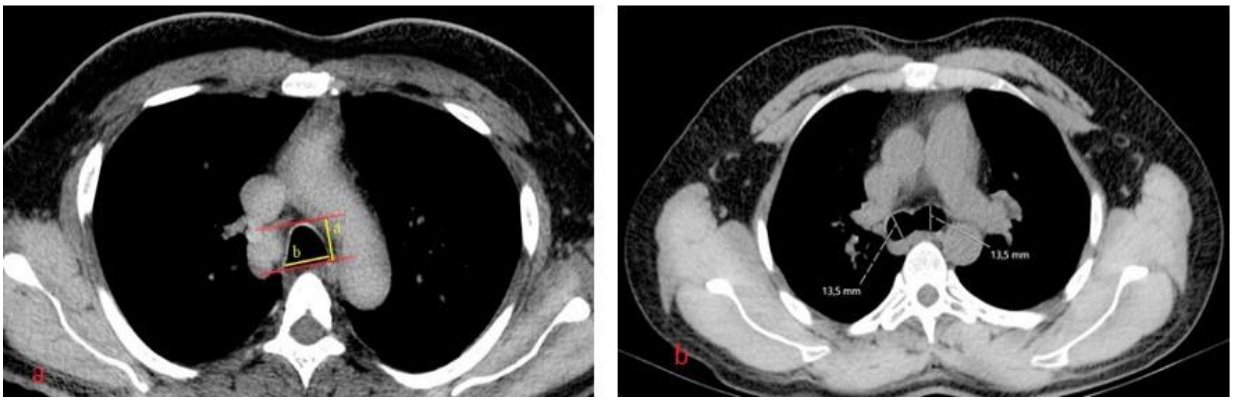

Figure 3. a- Anteroposterior (a) and transverse (b) trachea diameter measurements in the distal trachea from the axial plane CT image, b- Diameter measurements of right main bronchus and left main bronchus from CT image in axial plane.

RESULTS

46.4% were female and 53.6% were male of the 56 COVID-19 patients included in the study. The mean age of women in the COVID-19 group was 51.30±12.78 years, while the mean age of men was 48.73±13.99 years, and the difference was not statistically significant (p=0.478). A statistically significant difference was found between men and women in the diameters of RMB, and LMB, proximal, distal, and intermediate levels of AP and TR-TD, TL in patients with COVID-19 (p<0.05). The results of tracheobronchial morphological measurements acquired from COVID-19 patients are given in Table 1.

Table 1. Distribution of tracheobronchial morphological measurements of COVID-19 patients by gender.

	COVID-19 Groups		
Parameters	**Female**	**Male**	**p**
Age	51.30±12.78	48.73±13.99	0.478
SA	91.92±14.60	87.33±14.08	0.194
RMB angle	139.42±8.06	137.68±6.86	0.132
LMB angle	126.03±7.49	125.89±8.64	0.928
TL	82.09±7.32	93.37±10.17	0.001
Proximal AP-TD	16.19±2.34	21.13±2.90	0.001
Proximal TR-TD	14.18±1.68	17.07±2.26	0.001
Middle AP-TD	14.73±1.98	19.62±2.54	0.001
Middle TR-TD	14.69±1.33	17.48±2.12	0.001
Distal AP-TD	15.28±1.81	18.88±2.65	0.001
Distal TR-TD	16.95±2.66	20.58±2.37	0.001
RMB diameter	12.23±1.49	14.84±1.84	0.001
LMB diameter	11.52±1.41	13.58±1.50	0.001

SA: Subcarinal angle, RMB angle: Right main bronchus angle, LMB angle: Left main bronchus angle, TL:Trachea length, Proximal AP-TD:Proximal anteroposterior trachea diameter, Proximal TR-TD:Proximal tranverse trachea diameter, Middle AP-TD: Middle anteroposterior trachea diameter, Middle TR-TD: Middle tranverse trachea diameter, Distal AP-TD:Distal anteroposterior trachea diameter, Distal TR-TD: Distal tranverse trachea diameter, RMB diameter: Right main bronchus diameter, LMB diameter: Left main bronchus diameter.

The mean age of female patients with COVID-19 was 51.30±12.78 years, while the women in the control group were 45.00±11.89 years, and there was no statistically significant difference between them (p=0.051). The mean age of male patients with COVID-19 was 48.73±13.99 years, while the mean age of men in the control group was 43.76±8.45 years, and the difference was not statistically significant (p=0.126). TL was statistically lower in female patients with COVID-19 according to females in the control group (p<0.05). It was determined that the RMB angle and the TR-TD measured from the proximal level were statistically significantly lower in men with COVID-19 than in the control group (p<0.05). AP-TD measured from the proximal in male patients with COVID-19 was found to be significantly higher than those in the control group (p<0.05) (Table 2).

Table 2. Comparison of tracheabronchial morphometric measurements of COVID19 and control groups by gender

Parameters	***Female***			***Male***		
	COVID 19 Group	**Control Group**	**p**	**COVID 19 Group**	**Control Group**	**p**
Age	51.30±12.78	45.00±11.89	0.051	48.73±13.99	43.76±8.45	0.126
SA	91.92±14.60	88.20±9.57	0.509	87.33±14.08	85.18±12.76	0.754
RMB angle	139.42±8.06	142.48±6.33	0.238	137.68±6.86	142.24±5.10	0.005
LMB angle	126.03±7.49	128.28±7.19	0.455	125.89±8.64	127.48±5.22	0.520
TL	82.09±7.32	87.12±8.67	0.030	93.37±10.17	95.95±12.68	0.407
Proximal AP-TD	16.19±2.34	15.34±1.87	0.159	21.13±2.90	19.06±2.39	0.006
Proximal TR-TD	14.18±1.68	14.02±1.51	.0924	17.07±2.26	18.05.1.68	0.029
Middle AP-TD	14.73±1.98	14.54±2.08	0.740	19.62±2.54	18.81±2.98	0.286
Middle TR-TD	14.69±1.33	15.40±1.50	0.95	17.48. ±2.12	22.18±26.37	0.866
Distal AP-TD	15.28±1.81	14.82±1.54	0.289	18.88±2.65	17.83±1.92	0.168
Distal TR-TD	16.95±2.66	16.96±2.17	0.988	20.58±2.37	20.11±2.48	0.477
RMB diameter	12.23±1.49	12.90±1.39	0.061	14.84±1.84	15.08±1.95	0.594
LMB diameter	11.52±1.41	11.69±1.22	0.713	13.58±1.50	13.91±1.76	0.493

SA: Subcarinal angle, RMB angle: Right main bronchus angle, LMB angle: Left main bronchus angle, TL:Trachea length, Proximal AP-TD:Proximal anteroposterior trachea diameter, Proximal TR-TD:Proximal tranverse trachea diameter, Middle AP-TD: Middle anteroposterior trachea diameter, Middle TR-TD: Middle tranverse trachea diameter, Distal AP-TD:Distal anteroposterior trachea diameter, Distal TR-TD: Distal tranverse trachea diameter, RMB diameter: Right main bronchus diameter, LMB diameter: Left main bronchus diameter.

When we look at the lung lobe involvements in patients with COVID-19, it was observed that the upper lobe of the right lung 65.4%, middle lobe of the right lung 92.3%, lower lobe of the right lung 100% and lower lobe of the left lung 100% in women. In the case of men, upper lobe of the right lung 76.7%, middle lobe of the right lung 86.7%, lower lobe of the right lung 96.7%, and upper lobe of the left lung 80%, lower lobe of the left lung 100%.

DISCUSSION

The effect of COVID-19 pneumonia caused by the SARS-CoV-2 virus, which was declared a pandemic by the (World Health Organization) WHO, is now better known on the lung parenchyma and vascular structures (18). It is seen that conditions such as diffuse alveolar damage and related acute respiratory distress syndrome, ventilation/perfusion mismatch, thrombosis formation, and consequently raised risk of pulmonary embolism lend to existing hypoxia in patients. In patients with a high degree of hypoxia, it is frequently ventilated mechanically by endotracheal intubation. Here in, the decision is made by considering gas exchange and hemodynamic parameters. In these patients, surgical interventions such as endotracheal intubation and tracheostomy cause an increased risk of complications in the trachea and main bronchi. For this reason, respiratory tract morphology and morphometry are important in COVID-19 patients (19).

It was determined that TL was statistically higher in men with COVID-19 than in women in our study. In the study of Kamel et al., it was observed that the TL was 105.1 mm in men and 98.3 mm in women, and the difference was statistically significant (20). In the study conducted by Mi et al., on the Chinese population, the TL was found to be 107.8±13.2 mm in men and 101.4±12.8 mm in women, and the difference was statistically significant (4). It was reported in another study, that it was 116.21 mm in men and 105.67 mm in women (21). The findings of our study support the literature. However, although there is no data to state that the Sars-CoV-2 virus causes the difference, we can only say that it is due to the gender difference. In our study, while there was no difference in TL in men with COVID-19 according to the healthy group, it was found that it was lower in women with COVID-19 than in the healthy group. With ciliary activity in respiration, the particles descending into the lower respiratory tract are cleared from the trachea and bronchi through the epithelium. Within this process, some of the immunological reactions and some inhaled particles can cause inflammation (22). If there is a discomposed immune system, immune cells are piled in the lung and a large amount of pro-inflammatory substance cytokine is released (23). Cytokines normally regulate immunity, inflammation, and hematopoiesis. But, in some patients, excessive cytokine secretion can lead to a cytokine storm and lead to capillary leakage, tissue damage, thrombus formation, and even organ failure (24). The uncontrolled and increased cytokine release caused by COVID-19 is called a cytokine storm (23). As a result of cytokine storm and damage directly caused by the virus, widespread alveolar damage, hyaline membrane formation, and pulmonary edema take place (25), and multi-organ damage occurs. Because of the chronic inflammation that occurs, the tracheal cartilages can change and the patient becomes more prone to tracheomalacia (26). This may explain the TL change in the COVID-19 group.

In the current study, proximal AP-TD was found to be higher in men with COVID-19 compared to the control group. In a study, it was procured that the AP-TD length was 22.3 mm in patients with COPD and 19.4 mm in the control group, and the difference was statistically significant (2). In a study committed on patients with COVID-19, patients were divided into four groups upon lung involvement, and they found that the mean AP-TR diameter at the thyroid level was statistically higher in the fourth group, where the disease was most severe, compared to other groups. They indicated that severe inflammation may cause edema in the trachea, and as a result, this would set forward an increase in tracheal diameter (27). The findings of our study were found to be compatible with the literature. Taking into account the involvement of both lungs in our patient group, it is obvious that especially the upper lobes are more involved in men than in women, but we consider that the inflammation may cause edema in the trachea and lead to an increase in the AP-TD measured at the level of the thyroid gland.

It was defined in our study, that the proximal, middle and distal TR-TD was statistically significantly longer in men with COVID-19 than in women. In another study, it was established that there was no statistical difference in TR-TD between COPD patients and the control group (2). Similar to this study, it was determined in our study that TR-TD measured in the middle and distal segments was not different between the COVID-19 and control groups in both genders. However, it was determined that there was a reduction in the proximal TR-TD measured at the thyroid level in men with COVID-19 according to the control group. In a study, it was shown that this diameter increased in patients with COVID-19, who were divided into four groups, in contrast to our results, especially in the severe group compared to other groups (27). In a study (28), hard and inflammatory tissues in the paratracheal region were notified as well as areas containing coagulation necrosis during airway reconstruction to correct tracheal stenosis caused by COVID-19. These findings support the inflammation and edema process in the trachea. Edema and inflammation in the trachea engender an increase in the diameter of the trachea and narrowing of the tracheal lumen, that is, stenosis may also occur (27). We believe that cartilage tissue inflammation that may develop due to the symptoms of the disease in severe and long-term multisystemic infections such as COVID-19 may cause changes in tracheal diameters.

The SA was found to be lower in women than in men in a study executed on patients who applied to the hospital with various complaints and had thoracic CT scans (6). Kamel et al., determined that SA did not differ between men and women in their study of adult healthy individuals (20). In another study that was conducted on COPD patients, it was observed that there was no difference in intrabronchial angle measurement compared to the control group (2). Similar to previous studies, in the present study, no difference was found in the measurement of SA in both genders, both between male and female patients with COVID-19 and between the patient and control groups. Consequently, SA has an extensive range in normal individuals, and essential measurements of SA have little diagnostic value. At the same time, the patient's gender, body habits, and left atrium dimensions are also affected by the position of the carina (6).

In a study committed to patients with COPD, no significant difference was found between the right and left tracheobronchial angle values when evaluated according to the control group (2). In the current study, there was no difference between the COVID-19 and control group in terms of LMB, but it was found that the RMB angle was lower in men with COVID-19 compared to the control group. Studies have shown that edema and inflammation caused by COVID-19 in the tracheobronchial lumen can cause narrowing of the lumen and changes in diameter (27).

CONCLUSION

COVID-19 is a multisystem disease that can affect all systems in the body. Conceiving that it is transmitted through the respiratory tract, it is also very important to exhibit the situations in which the respiratory system organs are affected. Changes in tracheal morphology caused by COVID-19 were revealed in our study. It is significant for clinicians to consider these changes, especially in patients with endotracheal intubation indication, in the follow-up of patients with COVID-19 in clinics or intensive care units. The most important limitation of our study is that we cannot follow up whether our findings have changed or not, since the patients did not have long-term follow-up tomography. Comprehensive studies with larger series on the subject are needed.

REFERENCES

1. Minnich DJ, Mathisen DJ. Anatomy of the trachea, carina, and bronchi. Thoracic Surgery Clinics. 2007;17(4):571-85.
2. Küpeli A, Ünver E: Evaluation of Tracheobronchial Changes in Chronic Obstructive Pulmonary Disease with Computed Tomography. Sakarya Tıp Dergisi. 2019;9(4):687-92.
3. Daroszewski M, Szpinda M, Wiśniewski M, Flisiński P, Szpinda A, WoŸniak A, et al. Tracheo-bronchial angles in the human fetus–an anatomical, digital, and statistical study. Medical Science Monitor Basic Research. 2013;19:194.

4. Mi W, Zhang C, Wang H, Cao J, Li C, Yang L, et al. Measurement and analysis of the tracheobronchial tree in Chinese population using computed tomography. PLoS One. 2015;10(4):e0123177.
5. Taskin V, Bates MC, Chillag SA. Tracheal carinal angle and left atrial size. Archives Of Internal Medicine. 1991;151(2):307-8.
6. Karabulut N. CT assessment of tracheal carinal angle and its determinants. The British Journal of Radiology. 2005;78(933):787-90.
7. Mason RJ. Pathogenesis of COVID-19 from a cell biology perspective. European Respiratory Journal. 2020;55(4):2000607.
8. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020;181(2):271-80. e278.
9. To K, Lo AW. Exploring the pathogenesis of severe acute respiratory syndrome (SARS): the tissue distribution of the coronavirus (SARS-CoV) and its putative receptor, angiotensin-converting enzyme 2 (ACE2). The Journal of Pathology. 2004; 203(3):740-3.
10. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiology. 2020; 5(7):831-40.
11. Kumar S, Nyodu R, Maurya VK, Saxena SK: Morphology, genome organization, replication, and pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In Coronavirus Disease 2019 (COVID-19). Springer. 2020; 23-31.
12. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, et al. Endothelial cell infection and endotheliitis in COVID-19. The Lancet. 2020; 395(10234):1417-8.
13. Cevik M, Kuppalli K, Kindrachuk J, Peiris M: Virology, transmission, and pathogenesis of SARS-CoV-2. BMJ. 2020;371
14. Zhang Y, Geng X, Tan Y, Li Q, Xu C, Xu J, et al. New understanding of the damage of SARS-CoV-2 infection outside the respiratory system. Biomedicine & Pharmacotherapy. 2020;127:110195.
15. Hill RD, Vaidya PN. Angiotensin II Receptor Blockers (ARB). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; March 28, 2022.
16. Kligerman S, Sharma A. Radiologic evaluation of the trachea. Semin Thorac Cardiovasc Surg. 2009;21:246-54.
17. Acar T, Bayraktaroğlu S, Ceylan N, Savaş R. Computed tomography findings of tracheobronchial system diseases: A pictorial essay. Jpn J Radiol. 2015;33:51-8.
18. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. Jama. 2020;324(8):782-93.
19. Anwar A, Ramos-Bascon N, Crerar-Gilbert AA, Barnes N, Madden B. A specialised cardiorespiratory team approach in the intensive care management of COVID-19 patients: benefit on mortality, diagnosis and management. Clinical Medicine. 2021;21(2):101.
20. Kamel KS, Lau G, Stringer MD. In vivo and in vitro morphometry of the human trachea. Clinical Anatomy. 2009;22(5):571-9.
21. Khade BA, Yadav N, Divan C, Khade BA. Morphometry of human trachea in male and female using computerized tomography-a comparative study. Indian Journal of Clinical Anatomy and Physiology. 2016;3(4):526-30.
22. Miller K, Chang A. Acute inhalation injury. Emergency Medicine Clinics. 2003;21(2):533-57.
23. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020; 395(10223):497-506.
24. Mangalmurti N, Hunter CA. Cytokine storms: understanding COVID-19. Immunity. 2020;53(1):19-25.
25. Xu Z SL, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;(4):420-2.
26. Hoppe H, Dinkel H-P, Walder B, von Allmen G, Gugger M, Vock P. Grading airway stenosis down to the segmental level using virtual bronchoscopy. Chest. 2004; 125(2):704-11.
27. Ünlü S, Ilgar M, Akçiçek M. The evaluation of the trachea as a new parameter in determining the prognosis of COVID-19: First pilot study. Eur Rer Med Pharmacol Sci. 2021;25:4835-40.
28. Rendina EA, Maurizi G. Commentary: Coronavirus disease 2019 (COVID-19) and the airway: How can surgery help?. JTCVS Techniques. 2020;4:365.