Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2024;49(3):570-579
DOI: 10.17826/cumj.1434628

RESEARCH

Can lung anatomy predict the development of COVID-19 pneumonia in RT-PCR positive cases?

COVID-19 RT-PCR pozitif olgularda akciğer anatomisi pnömoni gelişimini öngörebilir mi?

Türker Acar[1], Raşit Eren Büyüktoka[1], Elif Aylin Yüce Yörük[2], Hülya Özkan Özdemir[1], Ali Murat Koç[3], Levent Altın[1], Mahmut Öksüzler[1], Mete Ertürk[4]

[1]Bozyaka Training and Research Hospital, İzmir, Türkiye
[2]Ministry of Health, Muğla, Türkiye
[3]İzmir Katip Celebi University, İzmir, Türkiye
[4]Ege University, İzmir, Türkiye

Abstract

Purpose: The objective of this study was to investigate the relationship between Coronavirus disease 2019 (COVID-19) pneumonia and anatomical characteristics, including tracheobronchial and fissure variations, right/left main bronchus angle, carina angle, and large airway diameter, in patients who tested positive for the virus via reverse transcription-polymerase chain reaction (RT-PCR) at the outset of the pandemic.
Materials and Methods: This cross-sectional study included 165 cases with positive RT-PCR tests who were admitted between March and June 2020 and subsequently scanned with thin-section unenhanced chest computed tomography (CT). They were divided into two groups according to the presence of pneumonia based on the chest CT images.
Results: In our study, a total of 165 cases were analyzed, pneumonia was found in 35 of 76 (46.05%) female patients and 51 of 89 (57.30%) male patients. COVID-19 pneumonia was observed in older age groups. Anatomical variations and the presence of incomplete fissures were statistically higher in the pneumonia-positive group, while the difference was not statistically significant for accessory fissures. Mean tracheal area and right main bronchus angle were statistically higher in the pneumonia-positive group compared to the negative patients. The right lung was more involved than the left in terms of both zonal and total lung involvement. When the presence of comorbidity was assessed, 59 patients (35.75%) were found to have comorbidity. Hypertension, diabetes mellitus and cardiovascular disease were significantly higher among comorbidities in the pneumonia-positive group. The

Öz

Amaç: COVID-19 pandemisi süreci başlangıcında ters transkripsiyon-polimeraz zincir reaksiyonu (RT-PCR) pozitif olan hastalarda, trakeobronşiyal ve fissür varyasyonları, sağ/sol ana bronş açısı, karina açısı, geniş hava yolu çapı gibi anatomik işaretlerle COVID-19 pnömonisinin ilişkisini belirlemek amaçlanmıştır.
Gereç ve Yöntem: Bu kesitsel çalışmada Mart- Haziran 2020 tarihleri arasında hastanemize başvuran ve ardından ince kesit kontrastsız thoraks bilgisayarlı tomografisi (BT) ile taranan, RT-PCR testleri pozitif olan 165 vaka incelenmiştir. Thoraks BT görüntüleri değerlendirilen vakalar pnömoni varlığına göre iki gruba ayrıldı.
Bulgular: Toplam 165 olgunun incelendiği çalışmamızda 76 kadın hastanın 35'inde (%46,05) ve 89 erkek hastanın 51'inde (%57,30) pnömoni saptandı. İleri yaş gruplarında COVID-19 pnömonisi daha fazla görüldü. Anatomik varyasyonlar ve inkomplet fissür varlığı pnömoni pozitif grupta istatistiksel olarak daha yüksekti, aksesuar fissürlerde ise fark istatistiksel olarak anlamlı değildi. Ortalama trakeal alan ve sağ ana bronş açısı pnömoni pozitif grupta negatif hastalara göre istatistiksel olarak daha yüksekti. Hem zonal hem de total akciğer tutulumu açısından sağ akciğer sola göre daha fazla tutulmuştu. Ek hastalık varlığı değerlendirildiğinde 59 hastada (%35,75) ek hastalık olduğu görüldü. Pnömoni pozitif grupta eşlik eden hastalıklar arasında hipertansiyon, diyabet ve kardiyovasküler hastalık anlamlı derecede yüksekti. Regresyon modeli, hipertansiyonun RT-PCR pozitif vakalarda COVID-19 pnömonisinde 3,75 kat artışla ilişkili bulundu.

Address for Correspondence: Elif Aylin Yüce Yörük, Ministry of Health, Provincial Health Directorate, Muğla, Türkiye.
E-mail: elfaylinyuce@hotmail.com.
Received: 09.02.2024 Accepted: 06.07.2024

regression model showed that hypertension was associated with a 3.75-fold increase in COVID-19 pneumonia in test positive cases.
Conclusion: Anatomical lung variations and incomplete fissures were observed more frequently in the COVID-19 pneumonia cases, independent of other comorbidities. We believe that there are anatomical variables that can be used to identify those predisposed to pneumonia in RT-PCR test positive cases.
Keywords:. SARS-COV-2, COVID-19, pneumonia, thorax, lung, anatomic variation, multidetector computed tomography, comorbidity

Sonuç: COVID-19 pnömonisi vakalarında diğer komorbiditelerden bağımsız olarak anatomik akciğer varyasyonları ve tamamlanmamış fissürler daha sık gözlendi. RT-PCR testi pozitif olan olgularda pnömoniye yatkınlığı belirlemede kullanılabilecek anatomik değişkenlerin mevcut olduğunu düşünüyoruz.

Anahtar kelimeler: SARS-COV-2, COVID-19, pnömoni, toraks, akciğer, anatomik varyasyon, çok dedektörlü bilgisayarlı tomografi, komorbidite.

INTRODUCTION

In the COVID-19 pandemic, which has caused many deaths around the world, the need to diagnose cases in the shortest time and with the most accurate method has become very important. Chest radiography can be used as the first imaging modality in the diagnosis of COVID-19 pneumonia due to its accessibility and low radiation exposure. However, because low-density lesions such as ground-glass opacities are difficult to see and may be normal in the early stages, the sensitivity of chest radiography is lower than that of computed tomography (CT)[1,2]. In addition, the findings on a CT scan may be positive even before the onset of symptoms[3,4].

Although real-time reverse transcription-polymerase chain reaction (RT-PCR) for viral nucleic acids is the gold standard method of choice for the diagnosis of COVID-19, the use of CT has increased due to its lower false negative rates[5]. The most common pattern of involvement in COVID-19 pneumonia on chest CT is bilateral, peripheral ground-glass infiltration(s). It has been shown in the literature that the right lower lobe segments of the lung are more frequently involved[6]. Tracheal and cardiac accessory bronchi, accessory fissure are developmental anomalies of the tracheobronchial tree and are characterized by recurrent lung infections in both childhood and adulthood[7–9].

It has previously been shown that some comorbidities may increase the likelihood of pneumonic infiltration or worsening of underlying pneumonia in RT-PCR test positive cases. In addition to demographic variables such as age, comorbidities that may worsen COVID-19 pneumonia include hypertension, diabetes mellitus, chronic renal failure, malignancy and cardiovascular disease[10–15].

Prior to commencing the study, we postulated that cases exhibiting positive RT-PCR results and displaying anatomical landmarks would exhibit a higher prevalence of lung involvement. This relationship, which has not been examined before in the literature, constitutes the unique aspect of our research. This situation reveals the originality of our study. Therefore, in this study we aimed to investigate the relationship between pneumonic involvement, anatomical variations and measurable variables such as right/left main bronchus angle, carina angle, large airway diameter and lung parenchymal involvement in patients diagnosed with COVID-19 by RT-PCR.

MATERIALS AND METHODS

Study design sample

A total of 313 patients who applied to the Turkish Ministry of Health University Bozyaka Training and Research Hospital between March and June 2020, underwent RT-PCR testing for clinical suspicion of COVID-19, were positive and underwent thin-section lung CT without contrast were included in the study. After excluding cases retrospectively classified as having 'poor' CT image quality due to respiratory or metallic artifacts, analysis was performed on 165 patients. The patients were PCR test positive cases at the beginning of the COVID-19 pandemic and were excluded from the study because it was not possible to evaluate fine structures such as fissures in patients with movement artifacts due to tachypnea.

A post-hoc analysis was performed on the 165 cases in the study using the G Power 3.1.9.4 program, and the power of the study was calculated to be 99.99%.

According to the standardized reporting table recommended by the 'Radiological Society of North America (RSNA), American College of Radiology

(ACR) and Society of Thoracic Radiology (STR)' [15]; two groups, positive and negative, were created according to the presence of pneumonia on chest CT images. Major anatomical variations of the lung were defined as tracheal bronchus, cardiac accessory bronchus, accessory fissure, superior and inferior accessory fissure, incomplete fissure, azygos lobe, lung isomerism (Figure 1a, b and c), (Figure 2).

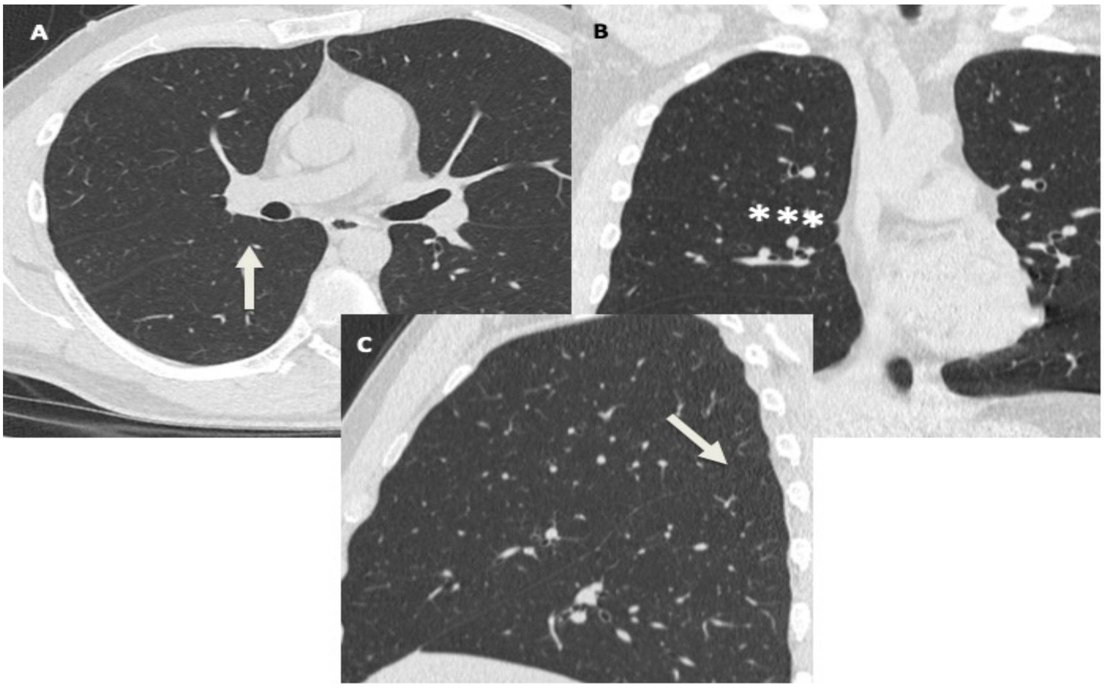

Figure 1. 46-year-old male patient. In the reformatted axial (a), coronal (b) and sagittal (c) images, the right oblique fissure (arrows) and the horizontal fissure (asterisk) are incomplete.

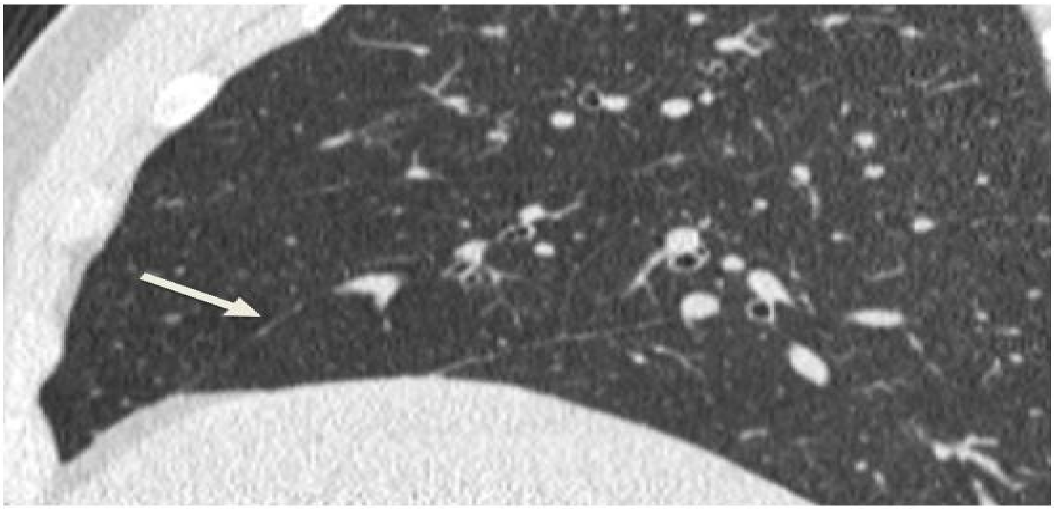

Figure 2. 27-year-old male. The sagittal reformatted image shows an accessory fissure in the middle lobe of the right lung (arrow).

Comorbidities (hypertension, diabetes mellitus (DM), history of cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD), asthma, malignancy, autoimmune endocrine disorders and chronic renal failure), which are common risk factors that can cause or exacerbate COVID-19 pneumonia, were noted in each case.

The manuscript was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cohort, case-control, and cross-sectional studies. For this retrospective cross-sectional study, ethics committee approval was received from the Ministry of Health Bozyaka University Training and Research Hospital Clinical Research Ethics Committee dated 29/6/2020 and numbered 2020-242.

The research was conducted at the Ministry of Health Bozyaka University Training and Research Hospital, which is a tertiary-level training hospital and is provided by experts in their field. Each researcher in the research team is competent and experienced in their field. The CT images of these patients were evaluated in a retrospective manner by three different radiologists.

Tomographic data acquisition

Each case was scanned with a 16-detector multidetector CT scanner (Alexion, Toshiba Medical Systems Co Ltd, Otowara, Japan) during deep inspiration, including all thoracic slices and caudal adrenal glands and the entire diaphragm. The following standard parameters were used during the examination Cross section thickness: 1 mm; kV: 120; mAs: 150; effective mAs: 120; rotation time: 0.75 sec. Intravenous iodinated contrast was not used during the examination.

Image acquisition and evaluation

Images were evaluated in the mediastinal and lung windows in standard axial, sagittal and coronal reformatted images. The standard window width (WW) and window level (WL) used for mediastinal evaluation were COVID: 400; WL: 40; and for lung evaluation WW: 1600; WL: -550. To improve parenchymal assessment and increase the visibility of possible lesions, WW and WL values were manually manipulated when necessary. Maximum and minimum intensity projection (MIP and MinIP) reconstruction images were analysed in detail when required for a more detailed assessment of lung fissure variations and airways. Cases were evaluated simultaneously by three different radiologists experienced in thoracic radiology.

Following assessment of COVID-19 involvement, images from 165 cases were uploaded to a MacOS-based computer and quantitative data were obtained using Horos software (www.horosproject.org). Using double-oblique multiplanar reconstruction images in the lung window setting, the areas of the trachea, right main bronchus and left main bronchus were measured for each case (Figure 3a, b and c). The minimum intensity projection method was used to determine the carinal angle and the right and left main bronchial angles in the coronal plane (Figures 4a, b and c). In addition to these quantitative variables, the right main bronchus/trachea and left main bronchus/trachea area ratios were added to the data table for each case.

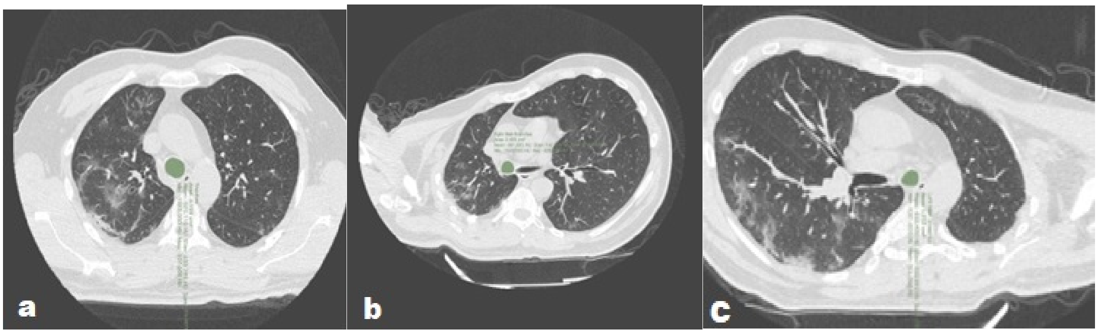

Figure 3. Double oblique multiplanar reconstruction images showing the trachea (a), right (b), and left (c) main bronchus with the largest area.

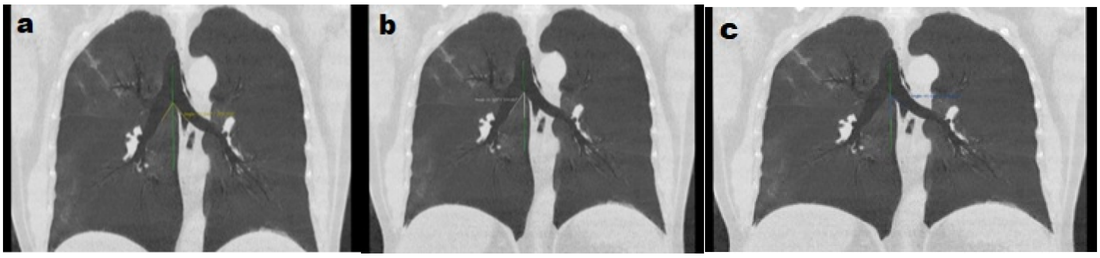

Figure 4. Using the minimum intensity projection method, coronal reformatted images showing the measurements of the carinal angle (a) and the right (b) and left (c) main bronchial angles.

Image analysis

COVID-19 infiltration characteristics (ground glass uptake, consolidation, cobblestone appearance, etc.) were scored according to the relevant literature. A severity score based on the percentage of CT involvement was used for evaluation. Each of the five lung lobes was scored visually on a scale of 0 to 5, with 0 indicating no involvement; 1, less than 5% involvement; 2, 5%-25% involvement; 3, 26%-49% involvement; 4, 50%-75% involvement; and 5, more than 75% involvement[4]. Both lungs were segmented into upper, middle and lower zones and the above scoring was applied to all three zones. In all cases, the lung was segmented into three zones: the upper zone above the tracheal carina, the middle zone between the inferior pulmonary vein and the diaphragm, and the lower zone below the inferior pulmonary vein[16]. Major anatomical variations of the lungs were noted in each case.

Statistical analysis

All statistical tests were performed using SPSS for Windows, version 25.0 (SPSS Inc., Chicago, Ill., USA). Descriptive data were presented as numbers and percentages, minimum and maximum values. The Kolmogorov-Smirnov or Shapiro-Wilk test was used as a standard test of distribution suitability. For categorical data like sex, presence of comorbidities and pneumonia, a crosstabulation table was created and a chi-square test was performed. For numerical variables like age, anatomical measurements, the t-test was used to test the significance of the difference between the groups. The Mann-Whitney U test was used for comparison of numerical variables that did not have a normal distribution between groups like incomplete fissure presence. The Wilcoxon signed-rank test was performed for numerical variables that did not meet the normal distribution condition for repeated measurements in CT image evaluation. For right and left bronchial angles, Spearman correlation analysis was performed for numerical variables that were not normally distributed. Logistic regression analysis was performed to determine the variables influencing pneumonia. A p value less than 0.05 was considered statistically significant.

RESULTS

In our study, a total of 165 cases were analyzed, 76 women and 89 men. The age of the group ranged from 18 to 94 years. The mean age of the females was 48.00 ± 19.07 years and that of the males was 46.31 ± 18.02 years. There was no significant difference in age between the female and male groups ($p=0.561$). Female and male patient groups were evaluated for the incidence of pneumonia. Pneumonia was found in 35 of 76 (46.05%) female patients and 51 of 89 (57.30%) male patients. There was no statistically significant difference between sex and pneumonia ($p=0.149$).

The mean age of the patients with pneumonia was 54.76 ± 17.29 years, whereas the mean age of the group without pneumonia was 38.75 ± 16.02 years. Accordingly, pneumonia was observed at an older age and the difference was statistically significant ($p<0.001$).

When the presence of comorbidity was assessed, 59 patients (35.75%) were found to have comorbidity. A total of 44 patients had both lung involvement and comorbidity. A statistically significant difference was found between the presence of comorbidity and pneumonic involvement ($p<0.001$).

When analyzing common comorbidities alone, hypertension ($p=0.004$), DM ($p=0.001$) and concomitant CVD ($p=0.100$) were significantly different in patients with lung involvement compared to those without pneumonia. Other comorbidities in the study group included 5 patients with COPD, 3 with asthma, 5 with malignancy, 7 with autoimmune endocrine disorders and 4 with chronic renal failure. No statistically significant difference in pneumonia was found in any of these comorbidities.

Anatomical variations of the lung were mainly associated with pneumonia, and one or more variations were positive in 93 patients (56.36%). Seventy patients had both lung involvement and variation. When the association between variation and lung involvement was compared, the difference was statistically significant ($p<0.001$). When considered separately, there was no association between accessory fissure and pneumonic involvement ($p=0.679$). However, the presence of an incomplete fissure was more frequently associated with COVID-19 pneumonia in RT-PCR positive cases ($p<0.001$). Incomplete fissures and their locations are summarized in Table 1.

Table 1. The relationship between incomplete fissures and the presence of pneumonia

Incomplete Fissure		**Pneumonia Negative**	**Pneumonia Positive**	**Total**	**P value**
Incomplete Right Oblique Fissure	Absence	67	50	117	0.000*
	Presence	12	36	48	
Incomplete Left Oblique Fissure	Absence	68	50	118	0.000*
	Presence	11	36	47	
Incomplete Horizontal Fissure	Absence	66	33	99	0.000*
	Presence	13	53	66	

*p<0.05

Regarding quantitative data, the right main bronchus angle was statistically significantly smaller in pneumonia-positive cases than in those without pneumonia ($p=0.012$), and the tracheal area was statistically larger in the pneumonia group than in the group without pneumonia ($p=0.011$). No significant difference was found between the groups for other quantitative variables (Table 2).

Table 2. The relationship between anatomical measurements and the presence of pneumonia

Pneumonia		**N**	**Mean**	**Standard Deviation**	**P value**
Right main bronchus angle	Negative	79	34.95	10.46	*0.012**
	Positive	86	38.62	7.95	
Left main bronchus angle	Negative	79	41.23	8.56	0.259
	Positive	86	42.80	9.24	
Carinal angle	Negative	79	76.55	15.69	0.051
	Positive	86	81.21	14.76	
Left main bronchus area	Negative	79	1.34	0.34	0.118
	Positive	86	1.43	0.41	
Right main bronchus area	Negative	79	1.66	0.41	0.113
	Positive	86	1.76	0.45	
Tracheal area	Negative	79	2.37	0.58	*0.011**
	Positive	86	2.61	0.62	
Left main bronchus to trachea ratio	Negative	79	0.56	0.06	0.094
	Positive	86	0.54	0.08	
Right main bronchus to trachea ratio	Negative	79	0.70	0.08	0.062
	Positive	86	0.67	0.09	

*p<0.05

The severity of pneumonia was compared for the right and left lungs in terms of total, upper, middle, and lower zones. In this study, right lung involvement was statistically higher than left lung involvement ($p<0.001$).

Comorbidities that may affect pneumonia were assessed individually by regression analysis. When assessed by univariate logistic regression analysis, hypertension, diabetes mellitus, presence of cardiovascular disease, presence of variation and presence of incomplete fissure were among the factors that may affect pneumonia. P values and confidence intervals are shown in Table 3.

Variants that cause pneumonia are presented with multivariate logistic regression analysis when comorbidities are considered together in Table 4. The study revealed that only hypertension was found to be effective.

Table 3. Comorbidities that may affect pneumonia in univariate logistic regression analysis

Variable	P value*	Exp (B)	Confidence Interval %95	
			Lower limit	Upper limit
Sex	0.150	1.572	0.849	2.912
Hypertension	0.004	3.755	1.510	9.339
Diabetes Mellitus	0.009	15.167	1.945	118.272
Cardiovascular diseases	0.019	6.243	1.351	28.849
Anatomic variation	0.000	10.652	5.142	22.069
Incomplete fissure	0.000	10.489	5.106	21.550

*$p<0.05$, Exp B: Expected B.

Table 4. Comorbidities that may affect pneumonia in multivariate logistic regression analysis

Comorbidity	P value*	Exp (B)	Confidence Interval %95	
			Lower limit	Upper limit
Hypertension	0.011	4.032	1.385	11.731
Anatomic variation	0.053	3.971	0.985	16.006
Incomplete fissure	0.090	3.263	0.830	12.835

*$p<0.05$, Exp B: Expected B.

DISCUSSION

In this study, we aimed to investigate the relationship between COVID-19 involvement and anatomical variations of the lung and measurable variables of the tracheobronchial system. Other comorbidities that may exacerbate existing pneumonia were added to our research list, and regression analyses were performed for all variables.

One of the most important findings of our study is the significant association between the presence of anatomical variation and COVID-19 pneumonia. Accordingly, when comparing the association between the presence of variation and lung involvement, the difference was statistically significant. Tracheal and accessory cardiac bronchi are fetal developmental anomalies of the tracheobronchial tree and are characterized by recurrent lung infections in childhood and adulthood. In the literature, the prevalence of tracheobronchial anomalies in children ranges from 0.9-3% [7]. Similarly, accessory cardiac bronchus is a rare fetal anomaly with an incidence of 0.09-0.5% and an average prevalence of about 0.3% [8]. In this study, tracheal and accessory bronchus were not found as anatomical anomalies. In our research, we could not investigate the relationship between these two rare anomalies and COVID-19 pneumonia, as a total of 165 cases were included and the number of cases was relatively small. Accessory fissures were examined in all lobes and were found in 28 patients (16.96%), of which 3 were observed as superior accessory fissures. The prevalence of accessory fissures on CT scan has been reported to be between 0.7-8.7% [9]. In our recent study this rate was found to be higher (16.96%). This may be related to the fact that we assessed changes more accurately using thinner slices. A total of 16 patients had both pneumonic involvement and an accessory fissure. However no significant correlation was found between accessory fissure and lung involvement.

The presence of an incomplete fissure, another anatomical variation, was examined in detail in our study. One or more incomplete fissures were found in 83 cases (50.30%). Horizontal fissures were incomplete in 66 cases (40%), right oblique fissures in 48 cases (29.09%), and left oblique fissures in 47 cases (28.48%). Although the prevalence varies slightly in post-mortem and CT-based studies, incomplete fissures are present in approximately half of the individuals, and incomplete presentation is most commonly observed in the posteromedial, near hilus, part of the minor fissure [9,17,18]. In our study, similar to the literature, incomplete fissures were observed in about half of the cases (50.30%), but incomplete presentation was most commonly observed in the horizontal (small) fissure, especially in the medial part adjacent to the mediastinum. In this study, the odds of COVID-19 pneumonia were statistically significantly higher in RT-PCR-positive individuals regardless of location in the presence of incomplete fissures (each for right oblique, left oblique and horizontal fissures). Fissures are natural anatomical barriers that prevent the spread of infection within the lobes of the lungs. It has been previously reported in the literature that fungal and bacterial infectious agents such as Aspergillus, Actinomycetes and Nocardia facilitate the spread of infection in the presence of incomplete fissures in immunosuppressed patients [9,19,20]. To our knowledge, at least at the time of writing, there is no published literature on the relationship between COVID-19 pneumonia and incomplete lung fissures.

Carina angle and right/left main bronchus areas were quantitatively higher in patients with COVID-19 pneumonia compared to those with positive RT-PCT tests but no pneumonia. However, these variables were not statistically different (Table 2). We believe that studies with larger numbers of cases may show stronger associations in the future. In our current study, tracheal area was statistically significantly larger in subjects with positive pneumonia. We believe that as the size of the large airways increases, the SARS-CoV-2 viral particle load may increase and the risk of the pathogen causing pneumonia may increase. In the systematic review, increasing viral load may increase the severity of COVID-19, especially with increasing age [21]. Since an increase in tracheal diameter would mean that more viral particles would be inhaled, this may explain why larger tracheal areas were found in the COVID-19 group.

Our study observed that the right lung was more involved than the left lung when both zonal and total lung sections were evaluated, and right lung involvement was statistically significant in the COVID-19 pneumonia group compared to left lung involvement. Similarly, the higher degree of right lung involvement in COVID-19 pneumonia has been reported in the literature[22,23]. The original 2013 study, which looked at the radiological appearance of patients with H7N9 Influenza A pneumonia, reported that the right lung was more involved in Influenza A, as was COVID-19[24]. As the right main bronchus is thicker, shorter and more vertical, the SARS-CoV-2 agent has a predilection for this area, which may explain the higher rate of right lung involvement.

In our recent study, the right main bronchus angle was lower than the left main bronchus angle, as expected due to its more vertical course. In our study, the mean right main bronchial angle was significantly higher in the COVID-19 pneumonia-positive group compared with the non-pneumonia group. Left main bronchial angles were also found to be slightly higher in pneumonia-positive subjects compared to negative subjects, but the difference was not statistically significant. There were no similar studies in the literature on this topic, at least until this paper was written. We believe that the increased angle and horizontalization tendency in the right main bronchus may reduce the expiratory outflow of SARS-CoV-2 virus particles entering through the large airways, thus facilitating the development of pneumonia, but our interpretation of this issue is beyond speculation.

Important risk factors for severe COVID-19 disease include age, male gender, obesity, smoking history, hypertension and DM among comorbidities. In our current study, COVID-19 was more likely to cause pneumonia in RT-PCR positive individuals, even in the presence of comorbidities, and the difference was statistically significant. COVID-19 symptoms are mostly mild, but many studies from around the world have shown that the most important risk factor for severe COVID-19 pneumonia is advanced age and comorbidities associated with advanced age[25]. Our current study showed that positive RT-PCR cases led to pneumonia at an older age, in line with the literature.

Hypertensives are more sensitive to COVID-19 than normotensives. In a meta-analysis evaluating the association between HT and COVID-19, hypertensives were found to be 2.5 times more likely than normotensives to have a severe form of COVID-19 pneumonia [relative risk: 2.49], similar for mortality [relative risk: 2.42][26]. Hypertensive patients are more likely to develop severe COVID-19 pneumonia and fatal infections[26]. In our study, COVID-19 pneumonia in RT-PCR test positive individuals was more common in those with hypertension and the difference was statistically significant.

The presence of DM, another comorbidity, increases the probability of pneumonia in COVID-19 RT-PCR positive cases and the probability of severe disease in COVID-19 pneumonia cases[27]. Our study is consistent with the literature, and it was observed that RT-PCR test-positive individuals developed more COVID-19 pneumonia when DM was present as a comorbidity [13]. Although the relationship between CVD and COVID-19 is not well understood, the suppressed immune system in CVD and the increased number of ACE-2 receptors in the heart muscle may explain the increased morbidity and mortality [28].

The literature has reported that COVID-19 pneumonia increases the risk of severe disease more than fivefold in COPD patients[29]. Asthma has been previously reported to be associated with prolonged COVID-19 and asthma-related symptom exacerbation[26]. Similarly, in patients with underlying malignancies, increased hospitalization and the likelihood of severe forms of COVID-19 have been reported[30]. Frequent travel to and from hospitals and healthcare facilities for cancer treatment also increases the likelihood of COVID-19 transmission. Underlying chronic renal failure may exacerbate COVID-19 due to a compromised immune system and lead to a further deterioration in urea and creatinine levels. As chronic renal failure is usually associated with co-morbidities such as CVD and DM, mortality and morbidity during the COVID-19 infection process can be elevated [10]. In our study, no significant association was found between COVID-19 pneumonia and COPD, asthma, malignancy and chronic renal failure. This may be related to the small number of cases with these comorbidities in our cohort.

One of the main limitations of our study is its cross-sectional design and the relatively small number of cases for rare anatomical variants. In addition, because these variants were not studied during the design, but cases were identified in a short period of time and at the beginning of the pandemic, the association of variant SARS-CoV-2 types with lung variants could not be commented on. As some comorbidities (COPD, asthma, malignancy and chronic renal failure) were rare in our cohort, the effect of these variables could not be adequately assessed.

Anatomical lung variations and incomplete fissures were observed more frequently in COVID-19 pneumonia cases, independent of other comorbidities. The existence of anatomical variables that can be used to detect susceptibility to pneumonia in cases with test positive will provide us with a predictive facility. It has been posited in the scientific literature that the presence of structural differences in the lung will have an impact on the involvement of pneumonic disease and the severity of pneumonia in similar pandemics.

Author Contributions: Concept/Design : TA, ME; Data acquisition: TA, REB, EAYY, HÖÖ, AMK, LA, MÖ; Data analysis and interpretation: TA, EAYY, HÖÖ; Drafting manuscript: TA, REB, EAYY, MÖ; Critical revision of manuscript: TA, HÖÖ, MÖ, ME; Final approval and accountability: TA, REB, EAYY, HÖÖ, AMK, LA MÖ, ME; Technical or material support: TA, REB, HÖÖ, AMK, LA; Supervision: TA, EAYY, ME; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained from the Ethics Committee for Clinical Research of the Ministry of Health, University of Bozyaka Training and Research Hospital, dated 29/6/2020 and numbered 2020-242, prior to the study. The need for informed consent was waived by the ethics committee, because of the retrospective nature of the study.
Peer-review: Externally peer-reviewed.
Conflict of Interest: The authors have no relevant financial or non-financial interests to disclose.
Financial Disclosure: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

REFERENCES

1. Wong HYF, Lam HYS, Fong AHT, Leung ST, Chin TW, Lo CSY et al. Frequency and distribution of chest radiographic findings in patients positive for COVID-19. Radiology. 2020;296:72–8.
2. Yoon SH, Lee KH, Kim JY, Lee YK, Ko H, Kim KH et al. Chest radiographic and CT findings of the 2019 Novel coronavirus disease (COVID-19): analysis of nine patients treated in Korea. Korean J Radiol. 2020;21:494-500.
3. Kim JY, Choe PG, Oh Y, Oh KJ, Kim J, Park SJ et al. The first case of 2019 novel coronavirus pneumonia imported into Korea from Wuhan, China: implication for infection prevention and control measures. J Korean Med Sci. 2020;35:e61.
4. Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. Eur Radiol. 2020;30:3306-09.
5. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical coronavirus disease 2019

(COVID-19) pneumonia: relationship to negative RT-PCR testing. Radiology. 2020;296:41–5.
6. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W et al. Correlation of Chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology. 2020;296:32–40.
7. Al-Naimi A, Hamad S, Abushahin A. Tracheal bronchus and associated anomaly prevalence among children. Cureus 2021;13:15192.
8. Manolakis A, Bordei P, Dina C, Iliescu DM. Peculiar case of branching of the trachea together with both, main and lobar, bronchi into a fetal lung. ARS Medica Tomitana. 2015;21:112-15.
9. Bayter PA, Lee GM, Grage RA, Walker CM, Suster DI, Greene RE et al. Accessory and incomplete lung fissures: clinical and histopathologic implications. J Thorac Imaging. 2021;36:197-207.
10. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020;97:829-38.
11. Schiffrin EL, Flack JM, Ito S, Muntner P, Webb RC. Hypertension and COVID-19. Am J Hypertens. 2020;33:373-4.
12. Robilotti E V, Babady NE, Mead PA, Rolling T, Perez-Johnston R, Bernardes M et al. Determinants of COVID-19 disease severity in patients with cancer. Nat Med. 2020;26:1218-23.
13. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17:259-60.
14. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab. 2020;31:1068–77.
15. Zhu T, Wang Y, Zhou S, Zhang N, Xia L. A comparative study of chest computed tomography features in young and older adults with corona virus disease (COVID-19). J Thorac Imaging. 2020;35:W97-101.
16. Yun Y, Wang Y, Hao Y, Xu L, Cai Q. The time course of chest CT lung changes in COVID-19 patients from onset to discharge. Eur J Radiol Open. 2021;8:100305.
17. Aziz A, Ashizawa K, Nagaoki K, Hayashi K. High resolution CT anatomy of the pulmonary fissures. J Thorac Imaging. 2004;19:186-91.
18. Koster TD, Slebos DJ. The fissure: interlobar collateral ventilation and implications for endoscopic therapy in emphysema. Int J Chron Obstruct Pulmon Dis. 2016;11:765-73.
19. Meenakshi S, Manjunath KY, Balasubramanyam V. Morphological variations of the lung fissures and lobes. Indian J Chest Dis Allied Sci. 2004;46:179-182.
20. Tarver RD. How common are incomplete pulmonary fissures, and what is their clinical significance? AJR Am J Roentgenol. 1995;164:761.
21. Dadras O, Afsahi AM, Pashaei Z, Afroughi F, Dashti M, Khodaei S et al. The relationship between COVID-19 viral load and disease severity: A systematic review. Immun Inflamm Dis. 2021;10:e580.
22. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med. 2020;382:1199-207.
23. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis. 2020;20:425-34.
24. Wang Q, Zhang Z, Shi Y, Jiang Y. Emerging H7N9 influenza A (novel reassortant avian-origin) pneumonia: radiologic findings. Radiology. 2013;268:882-89.
25. Chen Y, Klein SL, Garibaldi BT, Li H, Wu C, Osevala NM et al. Aging in COVID-19: Vulnerability, immunity and intervention. Ageing Res Rev. 2021;65:101205.
26. Gasmi A, Peana M, Pivina L, Srinath S, Gasmi Benahmed A, Semenova Y et al. Interrelations between COVID-19 and other disorders. Clin Immunol. 2021;224:108651.
27. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R et al. Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. J Diabetes Sci Technol. 2020;14:813-21.
28. Yang R, Li X, Liu H, Zhen Y, Zhang X, Xiong Q et al. Chest CT severity score: an imaging tool for assessing severe COVID-19. Radiol Cardiothorac Imaging. 2020;2:e200047.
29. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). Respir Med. 2020;167:105941.
30. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA. 2020;323:1775-6.