Original Article

ANATOLIAN CURRENT MEDICAL

DOI: 10.38053/acmj.1206657

Anatolian Curr Med J 2023; 5(1); 24-28

Prognosis prediction of the mean tracheal air column area in COVID-19 patients

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Cite this article as: Çoraplı M, Çoraplı G. Prognosis prediction of the mean tracheal air column area in COVID-19 patients. Anatolian Curr Med J 2023; 5(1); 24-28.

ABSTRACT

Aim: SARS-CoV-2 infection frequently affects the lungs, it can also cause severe inflammation in the lower respiratory tract, leading to tracheal damage. We aimed to investigate the relationship between the mean tracheal air column and COVID-19.

Material and Method: Chest computed tomography scans of COVID-19 patients treated in an intensive care unit between June 1st, 2020 and October 1st 2022 were retrospectively evaluated. The air column area of the trachea was measured and the effect of the values obtained on mortality and length of stay in the intensive care unit for patients COVID-19 was examined.

Results: We found that an increase in the mean tracheal air column increased mortality by 1.218 times. We also determined that an increase in the mean area of the tracheal air column increased the length of stay in the intensive care unit. Furthermore, we showed that advanced age and an increase in the length of stay in the intensive care unit were factors that increased mortality.

Conclusion: Tracheomegaly is a poor prognostic factor in COVID-19 disease and is easily diagnosed with CT.

Keywords: COVID-19, computed tomography, trachea, prognosis

INTRODUCTION

COVID-19 is caused by the SARS-CoV-2 virus and mostly affects the respiratory system (1). This agent may be asymptomatic in patients or may cause mild, moderate,or severe infection, leading to acute respiratory syndrome and multisystem organ failure (2,3). The diagnosis of COVID-19 is made by real-time-reverse transcription polymerase chain reaction (RTR-PCR) amplification of a nasopharyngeal swab taken from individuals witha suspected disease (4). This virus binds to the angiotensin-converting enzyme 2 receptor, which is found specifically in the epithelium of the lungs, distal airways, and trachea. Therefore, COVID-19 is expected to cause more damage to these organs (5). Studies have shown that the SARS-CoV-2 virus can cause severe inflammation in the trachea (6).

Tracheomegaly is a rare and often missed diagnosis, and it is diagnosed when its diameter exceeds the upper limit in both males and females (7, 8). Chest radiography, computed tomography, and bronchoscopy methods are used for the diagnosis of tracheomegaly (9). Among these methods, computed tomography is the best noninvasive method that can show tracheal changes and is considered the gold standard (10). Tracheomegaly is frequently congenital but may also occur in connective tissue diseases, because of prolonged inflammation, and because of smoking or the use of mechanical ventilation (11, 12). Several studies in the literature (6, 13-16) have examined characteristics of tracheomegaly and COVID-19, such as their relationship to each other, incidence rate, and management. However, as far as we are aware, there is no existing study examining the effect of tracheal dilatation on prognosis in COVID-19 patients by measuring the tracheal air column area. Therefore, we believe that this study will make important contributions to the literature.

MATERIAL AND METHOD

Patient Selection

In our study, designed as a cross-sectional observational analysis, a retrospective evaluation of patients treated for SARS-CoV-2 infections in an intensive care unit in our hospital between June 1st, 2020 and October 1st, 2022 was performed. This study was approved by Adıyaman University Non-interventional Clinical Researches Ethics Committee (Date: 15.11.2022, Decision No: 2022/8-28).

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Received: 18.11.2022 **Accepted:** 19.12.2022

All procedures were carried out under the ethical rules and the principles of the Declaration of Helsinki. The effect of the mean tracheal air column area of the observed patients on prognosis of COVID-19 was examined. Patients over 18 years of age were included in the study; patients with positive RT-PCR for SARS-CoV-2 RNA and those whose test results showed compatibility with COVID-19 pneumonia on thorax CT imaging were also included in the study. Patients with negative RT-PCR for SARS-CoV-2 RNA and whose test results showed no compatibility with COVID on thorax CT examination were excluded from the study. Thoracic CT examinations comprised thoracic CT scans performed at the time of initial admission to the hospital. Patients with a history of intubation were excluded. Patients included in the study were those treated in the intensive care unit of our hospital. The criteria for treatment in the intensive care unit were based on criteria specified in the Republic of the Turkey Ministry of Health's COVID-19 adult patient treatment guideline (17).

Exclusion Criteria

- Chronic obstructive pulmonary disease,
- Tracheal compression lesion (thyroid nodule, enlarged lymph node, malignancy, vascular variations, and so on)
- Thoracic kyphoscoliosis
- Calcific trachea
- Not having been monitored properly (motion artifacts, images that do not include Level 1, and so on)
- Tracheas with dense secretions
- Intubated patients
- Poorly performed examinations

Imaging

All thorax CT images used in our study were performed using a 16-detector CT scanner (MX16, Philips Medical Systems, Koninklijke, The Netherlands). Images were acquired using parameters of 0.75's rotation time, 16 × 0.75-mm beam collimation, 1-mm slice thickness, 1-mm slice reconstructions, 90–120 kV tube voltage, and 50–110 mAs effective tube current. Thorax CT images were analyzed using the Oracle Database program, version 1.10.48.299, to measure the tracheal air column area. Axial and coronal reformat images were used for all measurements. To measure the mean tracheal air column area, two separate area measurements were made from the proximal and distal levels measured by Breysem et al. (18), and the mean value was subsequently obtained. For the proximal tracheal area, the tracheal air column area was measured at the cylindrical-shaped 1st tracheal level just below the larynx; for the distal tracheal area, the tracheal air column area was measured 6 mm above the tracheal bifurcation (Figure). The mean tracheal air column area was obtained by taking the arithmetic mean of the measured tracheal air area in both regions. All evaluations and measurements were performed by a radiology specialist (M.Ç.) with 12 years of experience in the field.

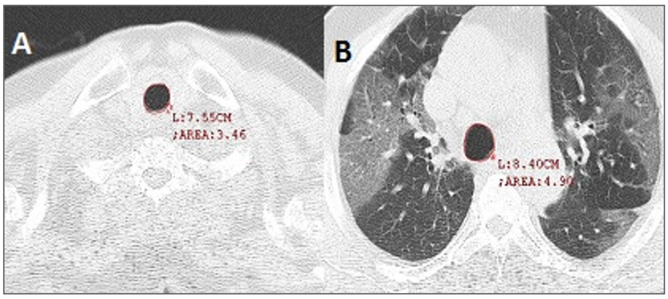

Figure. Axial thorax CT images of the measurements made from level 1 (A) and bifurcation superior (B) (mean tracheal air column area= (3.46+4.90)/2: 4.18 cm2).

Statistical Analysis

In the statistical analysis phase of the study, the effects of tracheal air column area on survival were examined. Frequency analysis of categorical variables and descriptive statistics of numerical variables were then performed. An independent samples t-test was used for independent group comparison tests, and a Pearson correlation test was applied to evaluate the direction and severity of the correlation between numerical measurements. The effect of the mean tracheal air column area on survival was examined in the survival analysis performed by applying the Cox regression model. The margin of error in the study was 5%, and the entire application was performed with the R-Project program (R Core Team, 2022) (19).

RESULTS

Among the patients included in the study, 59.9% were male and 40.1% were female. Approximately 63.6% of these patients died and 36.4% survived. The mean age of the patients was 64.44±12.26 years, the mean pneumonia severity score was 13.88±4.88, the mean length of stay in the intensive care unit (days) was 6.64±6.50, and the mean tracheal air column area was 2.76±0.79 (**Table 1**).

Table 1. Descriptive statistical values of the distribution of gender and living status of the patients and age, length of stay in the intensive care unit (days), and tracheal air column area variables.

Variable	n	%
Gender		
Male	290	59.9
Female	194	40.1
Living status		
No	308	63.6
Yes	176	36.4
	X±SD	**Median (min–max)**
Age	64.44±12.26	71.00 (27.00–95.00)
LSICU	6.64±6.50	4.00 (1.00–40.00)
MTACA	2.76±0.79	2.75 (1.26–5.50)

X±SD: mean±standard deviation, min: minimum, max: maximum, LSICU: length of stay in ICU (days), MTACA: mean tracheal air column area

Table 2. Comparison of each patient's age, length of stay in the intensive care unit (days), and mean tracheal air column area variables according to gender and living status.

Variable	Gender*				Living status*			
	Male	Female	t	p	No	Yes	t	p
Age	68.58±12.44	70.73±11.91	–1.897	0.058	71.14±11.48	66.48±13.04	4.085	<0.001
LSICU	6.21±5.50	7.28±7.74	–1.769	0.078	7.38±6.56	5.35±6.21	3.329	0.001
MTACA	3.13±0.69	2.21±0.60	15.135	<0.001	2.90±0.80	2.53±0.72	4.963	<0.001

*mean±standard deviation, LSICU: length of stay in ICU (days), MTACA: mean tracheal air column area

In **Table 2**, the t-test results of the age, length of stay in the intensive care unit (days), and average tracheal air column area variables of the patients participating in the study according to gender and living status are shown. It was observed that the variables related to age and length of stay in the intensive care unit (days) did not differ significantly according to gender (p>0.05). However, it was determined that the mean tracheal air column area of the patients differed significantly according to gender (p<0.05). The mean tracheal air column area of male patients was higher than that of female patients. It was determined that the variables of age, length of stay in the intensive care unit (days), and mean tracheal air column area of the patients differed significantly according to their living status (p<0.05). Age, length of stay in the intensive care unit (days), and the mean tracheal air column area values of the patients who survived were lower than those of the patients who died (**Table 2**).

In **Table 3**, the results of the Pearson correlation test showing the correlation between age, length of stay in the intensive care unit (days), and tracheal air column area variables of the patients included in the study are shown. It was determined that there was a low level of positive correlation between the length of stay in the intensive care unit (days) and age, respectively (r=0.173, p<0.05). There was a statistically significant positive correlation between the tracheal air column area and the length of stay in the intensive care unit (p<0.05) (**Table 3**).

Table 3. Correlation between age, length of stay in the intensive care unit (days), and mean tracheal air column area variables.

	1	2	3
Age	1		
LSICU	–0.119*	1	
MTACA	–0.012	0.001	1

*p<0.05; LSICU: length of stay in ICU (days); MTACA: mean tracheal air column area

The effects of the meantracheal air column area on survival time were statistically significant (p<0.05). A 1-unit increase in the mean tracheal air column area increases the probability of mortality by 1.218 (95% CI: 1.064–1.395) times (**Table 4**).

Table 4. Cox regression analysis performed on the effect of mean tracheal air column area on survival time

Variable	OR	95% CI		p
		Lower limit	Upper limit	
MTACA	1.218	1.064	1.395	0.004

OR: odds rate, CI: confidence interval

DISCUSSION

In this study, we revealed that an increase in the mean tracheal air column area increases mortality and length of stay in the intensive care unit in COVID-19 patients. We showed every 1unit increase in the mean tracheal air column increased mortality by 1.218 times. Our study showed that tracheal air column width is a poor prognostic factor in COVID-19 disease.

As far as we are aware, there is no existing study in the literature examining the prognosis prediction in COVID-19 patients by measuring the mean tracheal air column area. In a study conducted by Ünlü et al. (13), the anterior–posterior and transverse diameters of the trachea were measured and their effect on prognosis in patients with COVID-19 was examined. The tracheal diameter measurement method used in this study only considers the measurement of the length of the trachea in the linear direction in the axial section. Therefore, we believe it would be more accurate to examine the effect of tracheal dilation on prognosis by measuring the mean air column area. A study conducted by Ünlü et al. (13) similarly revealed that an increase in mean tracheal diameters resulted in poor prognosis in COVID-19 patients. However, our study also showed that the mean tracheal air column area increased the length of stay in an intensive care unit. Therefore, the present study is more comprehensive one compared to other studies because of its method and results.

Oliver et al. (20) revealed in their work that COVID-19 causes inflammation in the bronchi, trachea, and larynx, as well as in the lungs, causing damage to these tissues. Tissue destruction resulting from inflammation caused by the cytokine storm leads to organ deterioration (21). The membranous posterior part of the trachea, which is continuous with the cartilage component forming its anterior part, allows dilatation in the tracheal air column area because of tissue damage caused by inflammation (22). Therefore, we think that the dilatation of the tracheal air column area is directly proportional to the severity of inflammation in the lower respiratory tract as a result of COVID-19. According to the results of our study, we interpret this to mean that an increase in the mean tracheal air column area is an indirect indicator of an increase in inflammation due to COVID-19.

Tracheomegalyis divided into four groups according to its etiology. These groups are the following: patients with previous tracheal intervention; patients with recurrent infection and pulmonary fibrosis; patients with extrapulmonary elastolysis; and patients without a clear predisposing factor (23). It has been demonstrated in the literature that tracheomegaly develops in patients undergoing mechanical ventilation due to COVID-19 (16). It has also been hypothesized that high-pressure ventilation causes dilation of the trachea (14). In the study conducted by Tarle et al. (15), it was shown that tracheomegaly occurred due to severe damage to the trachea as a result of long-term mechanical ventilation in COVID-19 patients.

Although the diagnosis of tracheomegaly is initially made with chest radiographs, the method has its limitations (24,25). Tracheomegaly is often missed on chest radiography, leading to misdiagnosis and underdiagnosis. Tracheomegaly may not be visible on chest radiography until the trachea's diameter exceeds the vertebral column (26). Jaiswal et al. (27) showed that tracheal diameter measured above 30 mm on chest radiography was compatible with tracheomegaly. The gold standard method used in the diagnosis of tracheomegaly in other studies in the literature is CT (28,29). Smaller diameters are used as limit values for tracheomegaly for females, while higher values are used for males (9). The findings of our study also show that the mean air column area is higher in males than in females. Although the upper limit for tracheomegaly was above 30 mm in some studies (25, 27), Krustins et al. (30) found that 36.1 mm was the upper limit. The aim of our study was not to examine the presence of tracheomegaly in patients, but rather to investigate the effect of tracheal enlargement on prognosis. Therefore, a prognosis derived from grouping patients according to the presence or absence of tracheomegaly can be a useful subject for future studies.

In our study, instead of examining tracheomegaly, we thought we could make a more specific contribution to the literature using the mean tracheal air column, which we believed to be a better indicator of tracheal dilation. As far as we are aware, there is no existing study in the literature measuring the tracheal air column area. Therefore, we could not show the presence of tracheomegaly because the normal values were not known. Although this seems like a limitation, it makes our study unique because of its method, which has a unique structure. In our research, we believe the values obtained by CT images, accepted as the gold standard for the diagnosis of tracheomegaly, are more objective in demonstrating tracheal dilation. Moreover, biases were eliminated by measuring the area from the levels that Breysem et al. (18) measured to diagnose tracheomegaly.

Limitations

Our study had several limitations. First, it was a single-center study and was designed retrospectively. Other limitations include the patient's history of smoking and previous tracheal intervention; the presence of additional diseases, such as frequent recurrent infections and connective tissue disease; and the unknown status of the drug used for the previously mentioned ailments. Considering the findings in our study, more research is needed to evaluate the condition of the trachea in the long term after COVID-19 diagnosis. Will tracheomegaly develop because of relaxation in the elastic fibers that form the trachea, especially after inflammation—and damage the muscles? Will tracheal stenosis occur due to tracheal calcification as a result of inflammation? The answers to these questions will be obtained as a result of more comprehensive studies possibly carried out in the future.

CONCLUSION

COVID-19, a multisystemic disease, damages the trachea, as well as the lungs. An increase in the diameter of the air column in the trachea increases mortality and prolongs the length of stay in intensive care units. Our study revealed that the tracheal air column area, which can be easily evaluated with CT, can lead to better, more precise predictions of COVID-19.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Adıyaman University Non-interventional Clinical Researches Ethics Committee (Date: 15.11.2022, Decision No: 2022/8-28).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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