Clinical and Experimental Health Sciences

Quantitative Evaluation of Lung Parenchyma Changes after Treatment in COVID-19 Pneumonia with Volumetric Study in Computed Tomography

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ABSTRACT

Objective: COVID-19 pandemic, causing approximately 3 million deaths over worldwide, still continues. Effect of COVID-19 pneumonia after treatment on the lungs still not know. Although widely using computed tomography (CT) for diagnosing COVID-19 pneumonia, there is not enough study to determine damage of lung after treatment in COVID-19 pneumonia. In this study, our aim was to evaluate lung parenchyma changes in COVID-19 pneumonia after treatment with volumetric study, quantitatively.

Methods: 25 patients, who has CT at the time of diagnosis (CT1) and after 28±2 days (CT2), and positive polymerase chain reaction test, were included in this retrospective single center study. Total lung volüme (TLV) and emphysematous lung (ELV) volume of CT1 and CT2 were calculated automatically by using Myrian® XP-Lung and Percentage of emphysematous area (PEA) was calculated by dividing ELV by TLV. Differences between CT1 and CT2 in PEA and in TLV and ELV was determined by Wilcoxon and Paired sample t test, respectively.

Results: Although higher TLV was found in CT2 (4216,43 ± 1048,99 cm3) than CT1 (3943,22 ± 1177,16 cm3), there was no statistical significance difference (p=0.052) between CT1 and CT2. ELV was statistically (p=0.017) higher in CT2 (937,22 ± 486,89 cm3) than CT1 (716,26 ± 471,65 cm3). There was a strong indication that the medians were significantly different in PEA (p=0,009).

Conclusion: Our study showed that there were emphysematous changes in lung parenchyma after COVID-19 pneumonia with CT, quantitatively and in our knowledge, this is the first study that evaluating lung changes quantitative after COVID-19 pneumonia.

Keywords: COVID-19, Emphysema, Pneumonia, Quantitative, Tomography

1. INTRODUCTION

Novel coronavirus disease (COVID-19), named by The World Health Organization (WHO), was first reported in Wuhan, China, in December 2019. It spread rapidly all over the World (1). WHO has declared the outbreak on March 11 2020, a public health emergency of international concern (2). As of April 2 2020, 130,400,220 cases have been documented globally and 3,357,988 cases in Turkey. 31,713 deaths also were reported in Turkey (3). With the epidemic, the burden of hospitals and healthcare workers has increased, and it has had many social, psychological and economic effects in terms of health professionals and society. (4). Coronaviruses, belonging to the Coronoviridea family, are single-stranded, non-segmented, positive-strand, enveloped Ribonucleic Acid (RNA) viruses (5). Quantitative polymerase chain reaction (Qpcr) for quantitative detection of nucleic acid was used to diagnose COVID-19 (6). However, there were some limitations as a sample collection and transportation, and depending on these limitations, the total positive rate of RT-PCR for nasal and pharyngeal swab samples was informed to be approximate 30%–60% at first admitted (7).

The main route of transmission of this disease is respiratory infection (8). Fever, cough, dyspnea, headache are the main symptoms (2). However, other viruses, such as İnfluenza A and B, can cause the same clinical symptoms as COVID-19 (9). COVID-19 demonstrated apparent destruction of the pulmonary parenchyma, interstitial inflammation and consolidation and caused lesions characteristic of interstitial pneumonia (10).

Imaging plays an essential role in diagnosing and treating COVID-19 pneumonia, Computed Tomography (CT) is the gold standard imaging examination in COVID-19 pneumonia, and imaging-based scoring systems have been developed for diagnosis (2,11). Various lung changes patterns such as

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ground-glass opacities, consolidation, the reticular pattern was seen on CT (12). CT was used for many years to diagnose emphysema qualitatively, but special software programs have been developed to analyse emphysematous lung volume quantitatively (13).

The effect of COVID-19 pneumonia after treatment on the lungs is still not known. Although widely used CT for diagnosing COVID-19 pneumonia, there is not enough study to determine lung damage after treatment in COVID-19 pneumonia. The primary target of our study was to determine lung parenchyma changes in COVID-19 pneumonia after treatment with a quantitative volumetric study using a threshold value. To the best of our knowledge, this is the first study that evaluates the role of CT in lung parenchyma changes of COVID-19 pneumonia after treatment, quantitatively.

2. MATERIAL AND METHODS

The study was conducted in adherence to the Declaration of Helsinki. It was reviewed and approved by the institutional review board, and protocol review committee (Approval No: 07.07.2020/2020-12-04) and patient consent was waived by committee decision.

2.1. Patients

1297 patients admitted to the emergency room with suspicion of COVID-19 disease were evaluated between March 23 and June 30 2020. Patient selection was consecutive for this study. Nasal and pharyngeal swab specimens were taken from all patients, and the diagnosis of 895 patients was confirmed by one positive result of real-time reverse transcriptase-polymerase chain reaction (rRT-PCR). Exclusion criteria were; no thorax CT examination at the time of diagnosis (625 patients), no thorax CT after 1 month from first CT (233 patients) and patients with cardiac, lung and other systemic disease affecting lung parenchyma (12 patients). 25 patients were included in this single-centre, retrospective study.

2.2. CT acquisition

All CT examinations were performed by a 64-slice multi-detector row CT scanner (Somatom Go Now, Siemens Healthcare, Erlangen, Germany). All images were acquired at full inspiration in the supine position. No intravenous contrast media was used. The scanning range was C3 vertebrae to L2 vertebrae, including the apex and base of the lung. 512x512 matrix size, 1.0 mm slice thickness, and a sharp reconstruction kernel (KernelBr64) were used. A window level of – 600 Hounsfield Unit (HU) and width level of 1200 HU were used for standard window settings.

2.3. Image analysis

One radiologist with 6 years of experience assessed all images who was blinded to the clinical information. All images were transferred to the workstation, and Myrian (version 2.7.6) software was used for advanced analysis of images. The consistency of intragroup correlation was not checked because the software analysed all measurements automatically.

2.4. CT visual, quantitative evaluation

Total lung volumes (TLV) of all patients were calculated automatically with Myrianâ XP-Lung application (Fig. 1). Healthy and pathological areas were identified automatically with the threshold method by the COVID-19 application. Emphysematous lung volume (ELV) with threshold values under – 950 HU and TLV were recorded for each patient (Fig. 2). The percentage of the emphysematous area (PEA) was calculated by dividing ELV by TLV. All calculations were done for both first (CT1) and second CT (CT2) separately.

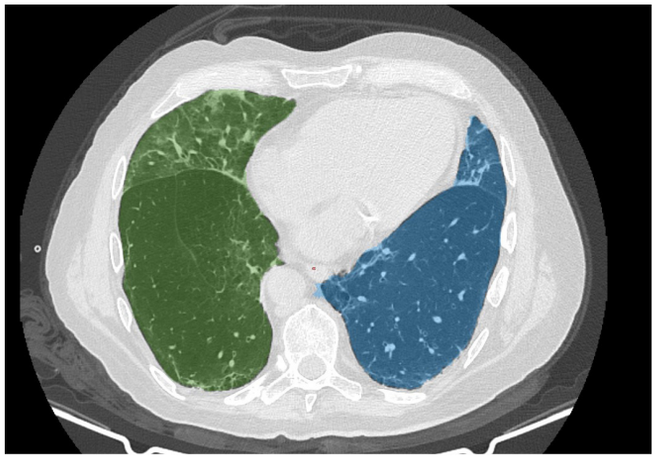

Figure 1. *60 years old men admitted to the emergency room with fever and cough. MyrianÒ software XP-Lung application calculates right and left lung volume separately from axial CT images.*

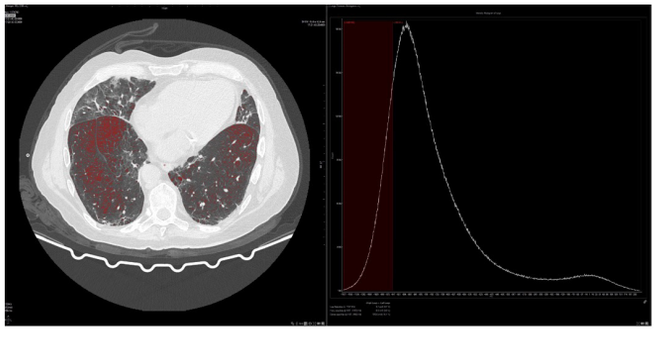

Figure 2. *The COVID-19 application evaluated the same patient. When threshold level choosing – 950 HU and under, the software calculated emphysematous lung volume automatically.*

2.5. Statistical analysis

IBM Statistical Package for the Social Sciences (SPSS version 25 for Mac OS) software was used for all statistical analysis. The Shapiro-Wilk test determined the fitness of the numeric

data set to the normal distribution. Descriptive analyses were determined for each data. Due to non-normal distribution, the Wilcoxon test was carried out to measure differences between PEA of patients. Paired sample t-test was used for measuring differences of TLV and ELV between CT1 and CT2. A p-value lower than 0.05 was considered statistically significant.

3. RESULTS

3.1. Patients demographics

13 patients (52%) were male, and 12 patients (48%) were female. The mean age and standard deviation was 51,31 ± 3,88 for male (range: 30-84 years) and 45,50 ± 4,97 for female (range: 24-73 years) (Fig. 3). During the study period, 5 males and 3 females were hospitalised, and no patient was died and required intensive care unit. 21 patients (84%) had a cough, 12 patients (48%) had a fever, 6 patients (24%) had dyspnea, and 4 (16%) patients had headaches. According to the COVID-19 treatment guideline of the Turkey health ministry, hydroxychloroquine sulfate 2x200 mg was taken by all patients for 5 days. 8 patients who were hospitalised took Favipiravir 2x600 mg for 5-7 days.

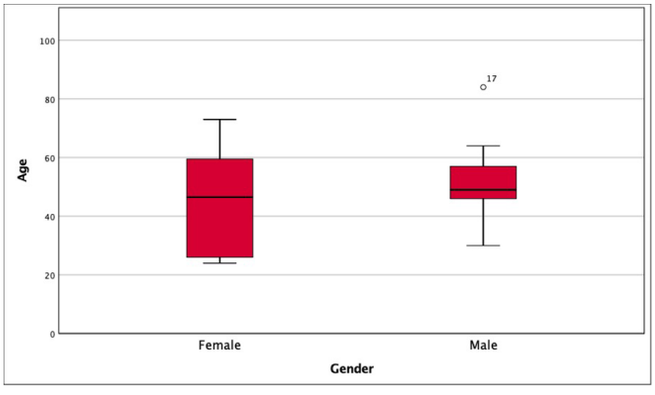

Figure 3. *The distribution of age according to gender.*

3.2. Radiological findings

The mean and standard deviation (SD) for TLV of CT1 was 3943,22 cm^3 ± 1177,16 cm^3 and 4216,43 cm^3 ± 1048,99 cm^3 for CT2. The mean of ELV for CT1 and CT2 were 716,26 cm^3 (SD; ± 471,65 cm^3) and 937,22 cm^3 (SD; ± 486,89 cm^3). According to gender, same measurements were summarized in table 1. PEA of CT1 and CT2 was showed non-normal distribution and median and interquartile range values were 16,51% (10,61% – 19,98%) and 22,14% (15,51% – 27,94%), respectively.

The mean value of TLV in CT2 was higher than CT1, but there were no statistically significant differences between the two measures. Nevertheless, p-value was very close to 0,05 (p=0,052). A statistically significant difference was found between ELV of CT1 and CT2 with a 95% confidence interval (p=0,017). After applying the Wilcoxon rank test to the percentage of CT1 and CT2, negative rank (mean rank; 9,83, the sum of ranks; 59) was found in 6 patients, and positive rank (mean rank; 13,39, the sum of ranks; 241) was found in 19 patients. There was a strong indication that the medians were significantly different, equal to a two-tailed p-value of 0,009.

Table 1. *The total lung volume and emphysematous lung volume of first and second computed tomography in males and females.*

	Male	Female
TLV CT1	4410 ± 1334	3476 ± 802
TLV CT2	4632 ± 1133	3800 ± 799
ELV CT1	863 ± 577	570 ± 291
ELV CT2	1064 ± 555	810 ±3 89

*Results were presented as mean ± SD * cm3*
Abbreviations; CT1, computed tomography at the time of diagnosis; CT2, computed tomography after treatment; ELV, emphysematous lung volume; TLV, total lung volume

4. DISCUSSION

In our study population, only 8 of 25 patients were hospitalised, and no one was needed intensive care unit. All patients had no severe pneumonia and complicated disease according to the COVID-19 treatment guideline of the Turkey health ministry. In our study, the most crucial finding was that ELV and PEA are statistically higher in follow-up CT with a threshold value of – 950 HU. The study designed by Bradley et al. reported that the main findings in COVID-19 pneumonia were alveolar damage and focal micro-thrombi (14). Moreover, autopsy studies have shown that alveolar damage is more widespread with disease progression, and fibrotic changes are revealed in the alveolar wall in two weeks (15). Therefore, we think that increased ELV and PEA in follow-up CT in our study were associated with diffuse alveolar damage caused by COVID-19 pneumonia consistently with the literature.

Lemmers et al. was reported that pneumothorax, pneumomediastinum and subcutaneous emphysema are the indicators of alveolar damage in severe disease and these complications are 7 times higher in COVID-19 patients, treated with mechanic ventilation than non-COVID-19 patients (16). Previous studies show that COVID-19 patients have similar mechanic ventilation parameters with non-COVID-19 patients, and pneumothorax is not associated with barotrauma. (17, 18). Pathophysiologic process in pneumomediastinum and subcutaneous emphysema was identified as Macklin effect, characterised by air dissection across bronchovascular sheaths and spreading interstitial emphysema into the mediastinum (19). These patients supported this theory by the absence of smoking history and no significant comorbidities predisposing air leak. Diffuse alveolar damage, cellular fibromyositis exudates, evident desquamation of pneumocytes, and hyaline membrane formation was shown in COVID-19 pneumonia similarly SARS (20). Wintermark et al. reported that increased pressure in the chest, such as cough episodes and Valsalva manoeuvre,

and severe diffuse alveolar damage leads to interstitial emphysema and causes alveolar rupture and air dissection along bronchovascular sheaths. Moreover, they specified that presence of pneumothorax and pneumomediastinum after progression of pulmonary lesions in thorax CT is associated with alveolar damage (21).

The value of qualitative visual evaluation of lung injury in thorax CT for predicting prognosis in COVID-19 was proved in previous studies (22). Although the recommendation of qualitative and visual evaluation score according to CT patterns in COVID-19 pneumonia, some limitations such as the absence of standardisation and lack of experience were reported (23). Some clinical studies also reported that CT densitometry reveals emphysematous areas qualitatively before spirometry test, there is a good correlation with pulmonary function tests, and there is a better correlation in determining emphysema with CT densitometry in inspiratory phase than visual evaluation (24, 25).

In the literature, qualitative CT studies focused on parenchymal lesions, such as GGO, consolidation, on CT between diagnosis and the 14th day of COVID-19 (26). To evaluate average lung volume, area of both consolidation and GGO quantitatively and objectively for measuring disease burden in follow-up examinations may provide information about disease progression and treatment response (23). In previous studies, evaluation of quantitative thorax CT was found successful in predicting clinical outcome in COVID-19. Furthermore, involved lung volume to total lung volume ratio showed high accuracy to predict oxygen support and need of mechanic ventilation. As a result, studies were revealed that quantitative CT was critical in COVID-19 triage (27). The other important finding in these studies was that quantitative evaluation of thorax CT at the time of diagnosis and the 4th day of COVID-19 might predict the risk of progression into severe disease better than clinical biomarkers (28). However, there is no study evaluating the literature on lung parenchyma changes after COVID-19 infection with quantitative CT.

Our study has several limitations. The first limitation of our study was designed as a retrospective study. Another limitation was the small study population, and no long term follow up of patients.

5. CONCLUSION

In conclusion, this is the first study showing that quantitative CT can reveal lung changes after COVID-19 infection. Additionally, the results of our study showed that mild COVID-19 pneumonia might cause emphysema, and this effect may reveal by CT quantitatively. Therefore, even though it is possible to infer that mild COVID-19 infection may cause emphysema after healing, the accuracy of the results obtained from our study should be supported by larger patient groups and with multi-centre studies.

REFERENCES

[1] Zhou S, Wang Y, Zhu T, Xia L. CT Features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. AJR Am J Roentgenol. 2020;214(6):1287-1294.

[2] Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, Liu X, Huang M, Liao Y, Li S. CT image visual, quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol. 2020;30(8):4407-4416.

[3] Application of hayat eve sığar, visit website: yazilimdestek@saglik.gov.tr. Ministry of health, Turkey. 2021.

[4] Tercanlı Alkış H., Yeşiltepe S., Kurtuldu E.. Examination of the knowledge levels, attitudes and anxiety sources regarding coronavirus disease-2019 infection in dentistry students in clinical practice. Meandros Med Dent J 2021;22(1):69-76

[5] Wang K, Kang S, Tian R, Zhang X, Zhang X, Wang Y. Imaging manifestations and diagnostic value of chest CT of coronavirus disease 2019 (COVID-19) in the Xiaogan area. Clin Radiol. 2020;75(5):341-347.

[6] Zhao X, Liu B, Yu Y, Wang X, Du Y, Gu J, Wu X. The characteristics and clinical value of chest CT images of novel coronavirus pneumonia. Clin Radiol. 2020;75(5):335-340.

[7] Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, Tao Q, Sun Z, Xia L. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: A report of 1014 cases. Radiology. 2020;296(2):32-40.

[8] Fan N, Fan W, Li Z, Shi M, Liang Y. Imaging characteristics of initial chest computed tomography and clinical manifestations of patients with COVID-19 pneumonia. Jpn J Radiol. 2020 ;38(6):533-538.

[9] Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation Between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. AJR Am J Roentgenol. 2020 ;214(5):1072-1077.

[10] Pan F, Ye T, Sun P, Gui S, Liang B, Li L, Zheng D, Wang J, Hesketh RL, Yang L, Zheng C. Time course of lung changes at chest CT during recovery from coronavirus disease 2019 (COVID-19). Radiology. 2020 ;295(3):715-721.

[11] Özer H, Kılınçer A, Uysal E, et al. Diagnostic performance of Radiological Society of North America structured reporting language for chest computed tomography findings in patients with COVID-19. Jpn J Radiol. 2021;39(9):877-888.

[12] Iwasawa T, Sato M, Yamaya T, Sato Y, Uchida Y, Kitamura H, Hagiwara E, Komatsu S, Utsunomiya D, Ogura T. Ultra-high-resolution computed tomography can demonstrate alveolar collapse in novel coronavirus (COVID-19) pneumonia. Jpn J Radiol. 2020;38(5):394-398.

[13] Hruban RH, Meziane MA, Zerhouni EA, Khouri NF, Fishman EK, Wheeler PS, Dumler JS, Hutchins GM. High resolution computed tomography of inflation-fixed lungs. Pathologic-radiologic correlation of centrilobular emphysema. Am Rev Respir Dis. 1987 ;136(4):935-940.

[14] Bradley BT, Maioli H, Johnston R, Chaudhry I, Fink SL, Xu H, Najafian B, Deutsch G, Lacy JM, Williams T, Yarid N, Marshall DA. Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series. Lancet. 2020; 396(10247):320-332.

[15] Kommoss FKF, Schwab C, Tavernar L, Schreck J, Wagner WL, Merle U, Jonigk D, Schirmacher P, Longerich T. The Pathology of Severe COVID-19-Related Lung Damage. Dtsch Arztebl Int. 2020;117(29-30):500-506.

[16] Lemmers DHL, Abu Hilal M, Bnà C, Prezioso C, Cavallo E, Nencini N, Crisci S, Fusina F, Natalini G. Pneumomediastinum and subcutaneous emphysema in COVID-19: barotrauma or lung frailty? ERJ Open Res. 2020;6(4):00385-2020.

[17] Anzueto A, Frutos-Vivar F, Esteban A, Alía I, Brochard L, Stewart T, Benito S, Tobin MJ, Elizalde J, Palizas F, David CM, Pimentel J, González M, Soto L, D'Empaire G, Pelosi P. Incidence, risk factors and outcome of barotrauma in mechanically ventilated patients. Intensive Care Med. 2004 ;30(4):612-9.

[18] Ioannidis G, Lazaridis G, Baka S, Mpoukovinas I, Karavasilis V, Lampaki S, Kioumis I, Pitsiou G, Papaiwannou A, Karavergou A, Katsikogiannis N, Sarika E, Tsakiridis K, Korantzis I, Zarogoulidis K, Zarogoulidis P. Barotrauma and pneumothorax. J Thorac Dis. 2015 ;7(Suppl 1):38-43.

[19] Murayama S, Gibo S. Spontaneous pneumomediastinum and Macklin effect: Overview and appearance on computed tomography. World J Radiol. 2014;6(11):850-854.

[20] Xu Z, Shi L, 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 ;8(4):420-422.

[21] Wintermark M, Schnyder P. The Macklin effect: a frequent etiology for pneumomediastinum in severe blunt chest trauma. Chest. 2001 ;120(2):543-547.

[22] Lei J, Li J, Li X, Qi X. CT Imaging of the 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology. 2020; 295(1):18-19

[23] Caruso D, Polici M, Zerunian M, Pucciarelli F, Polidori T, Guido G, Rucci C, Bracci B, Muscogiuri E, De Dominicis C, Laghi A. Quantitative Chest CT analysis in discriminating COVID-19 from non-COVID-19 patients. Radiol Med. 2021;126(2):243-249.

[24] Crossley D, Renton M, Khan M, Low EV, Turner AM. CT densitometry in emphysema: a systematic review of its clinical utility. Int J Chron Obstruct Pulmon Dis. 2018;13(1):547-563.

[25] Mascalchi M, Camiciottoli G, Diciotti S. Lung densitometry: why, how and when. J Thorac Dis. 2017 ;9(9):3319-3345.

[26] Yu N, Shen C, Yu Y, Dang M, Cai S, Guo Y. Lung involvement in patients with coronavirus disease-19 (COVID-19): a retrospective study based on quantitative CT findings. Chin J Acad Radiol. 2020 11(2):1-6.

[27] Lanza E, Muglia R, Bolengo I, Santonocito OG, Lisi C, Angelotti G, Morandini P, Savevski V, Politi LS, Balzarini L. Quantitative chest CT analysis in COVID-19 to predict the need for oxygenation support and intubation. Eur Radiol. 2020 ;30(12):6770-6778.

[28] Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, Ling Y, Jiang Y, Shi Y. Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology. 2020 ; 295(1):210-217.

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