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Original Scientific Paper

ARE COVID-19 PNEUMONIA FINDINGS DIFFERENT BETWEEN COMORBID AND NON-COMORBID PATIENTS? THE HIGH RESOLUTION COMPUTED TOMOGRAPHY FEATURES OF THE 108 FOLLOW-UP PATIENTS

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SUMMARY – The aim was to compare the computed tomography (CT) semi-quantitative severity scoring (CT-SS) system assessments of COVID-19 pneumonia on initial and follow-up examinations according to the presence of comorbidities. Of the 278 real-time reverse transcription-polymerase chain reaction positive patients, 108 with a follow-up CT scan were evaluated. Then, all CT images were independently reviewed for CT-SS analysis by two reviewers. Reviewers were unaware of the patient laboratory and clinical findings. A quarter of patients had negative findings on their initial CTs. Sixty-one (56.4%) patients showed progression. Disease progression was more frequently observed in patients with type 2 diabetes mellitus (DM) and malignancies (p=0.044 and p=0.019, respectively). Follow-up CTs of patients with comorbidities, especially those with cardiovascular disease (56.4%) and type 2 DM (70.0%), demonstrated an increased frequency of diffuse involvement. The white lung sign was more frequently observed in patients with malignancies (60.0%). In this study, COVID-19 patients with comorbidity showed a higher rate of disease progression than those without comorbidity. Patients with comorbidities more frequently had severe CT findings with high CT-SS. These findings may serve as a guide in the COVID-19 pneumonia follow-up and treatment.

Key words: *COVID-19 pneumonia; Semi-quantitative CT severity scoring system; Disease progression; Comorbidity; Radiological findings*

Introduction

After leaving the SARS-CoV-2 pandemic almost one year behind, which emerged at the end of 2019 in Wuhan and exponentially spread all over the world, the scientific community around the world is still investigating the effects of the virus on the human body[1]. As of December 6, 2020, a total of 66,608,379 cases and 1,529,969 deaths were reported from 191 countries, with the highest number of cases being reported in the United States, India, and Brazil. The case fatality rate of COVID-19 is estimated to be 2.2% worldwide[2,3]. Several factors that led to the progression of COVID-19 pneumonia were identified, including age, gender, comorbidity, maximum body temperature at admission, respiratory failure, and laboratory values. Also, the mortality rate increases

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as hospitals become overcrowded and have fewer resources or as the infection spreads among older populations with more comorbidities[4]. Guan *et al*. report an increased frequency of comorbidities in patients with the severe form of COVID-19 compared to the non-severe disease (38.7% *vs*. 21.0%)[5]. A study determined that the presence of a chronic illness increased the risk of mortality and morbidity for COVID-19 patients[6]. In another study, the authors revealed that disease severity in patients with chronic obstructive pulmonary disease (COPD) and coronary artery disease (CAD) comorbidities was higher in the severe and critical groups[7]. Patients with comorbidities, especially those with type 2 diabetes mellitus (DM) have a higher risk of developing adverse events resulting in the requirement of intensive care and intubation, or death[8]. In many cases, computed tomography (CT) is an important diagnostic modality, especially in cases with an initial false-negative real-time reverse transcription-polymerase chain reaction (RT-PCR) test in the early stage of the disease[9,10]. Serial chest CT imaging performed at different time intervals is also helpful in determining the progression of the disease. Furthermore, radiological quantification of pulmonary problems and their severity and progression is of high importance in determining effective care and respiratory aid for infected patients. In this study, we aimed to describe and determine the extent to which the findings of repeated CT examinations relate to COVID-19 progression and comorbidities, and their efficacy in detecting disease stages and estimating prognosis.

Patients and Methods

Participants

Between March 11 and April 25, 2020, adult patients who had positive RT-PCR test and initial CT scan within 2 days of the RT-PCR test, and follow-up CT scan, were included in the study. There were 278 patients with positive RT-PCR test and CT scan obtained at the time of diagnosis (within 2 days of PCR test). Among these 278 patients, 108 of them had follow-up CT scan at different time intervals due to various reasons (such as disease progression, clinical suspicion of secondary infection, or other complications). There were 56 men and 52 women, 55.6% of whom were below the age of 50 years. Eight (7.8%) patients were healthcare workers. Fifty-four patients had at least one comorbid disease, and 48 patients had a severe clinical course of COVID-19 (Fig. 1).

This retrospective study was approved by our Institutional Review Board (HNEAH- KAEK-2020/KK/61), and the requirement for written informed consent was waived.

Image interpretation

Computed tomography was performed using one of the CT scanners available at our hospital (General Electric Healthcare Optima CT 520, USA) allocated for patients with suspected COVID-19 pneumonia during the pandemic. The same device was used in all patients for initial and follow-up images, and the images were acquired using the following parameters: 100 kV, 120 mA, detector coverage 40.0 mm, helical thickness 5.0 mm, pitch, and speed (mm/rot) 1.531:1 and 61.25, respectively, and rotation time 0.5 s. In all patients, CT examinations were performed in the supine position during the end inspiration phase with breath-hold. The images were reconstructed using the lung window (width, 1000-1400 HU; level, 750 HU) and the mediastinal window (width, 350 HU; level, 35-40 HU). All the follow-up images were obtained using the same scanner as for the initial images. The time between the initial and follow-up CT studies was 8-38 days (median 10 days, mean ± standard deviation (SD) 12.93±8.14 days). The CT scans obtained at clinical presentation and follow-up during treatment were retrospectively reviewed by two radiologists (A.O.B. and B.Y.) who were blinded to the patient clinical progress. These two radiologists had 17 and 4 years of experience in thoracic radiology, respectively. After individual assessments, any disagreement was resolved through discussion and consensus. During the image review, the findings related to lung parenchyma were evaluated first. The distribution of lesions was categorized as central, peripheral, or both on each CT scan in the involved segments. The lesions were also categorized as unifocal or multifocal. The main pattern of involvement was first characterized as the predominant presence of ground-glass opacity (GGO) (increased density without obscured vessels) or consolidation (obscured vessels and presence of air bronchograms). Additional findings

were also recorded, such as the crazy-paving pattern (thickening of both interlobular septa and intralobular lines superimposed accompanied by GGO), curvilinear bands, tree-in-bud appearance, air bronchogram sign, air-bubble sign (a small aerated focus in the lung), reversed halo sign (a focal rounded area of GGO surrounded by a more or less complete ring of consolidation), pleural effusion, and bronchiectasis[11,12]. Other rare findings related to COVID-19 were also examined, especially the occurrence of cavitation, lymphadenopathy, and pleural effusion. At the end of evaluation, after all lesions had been characterized, the semi-quantitative CT severity scoring system (CT-SS) proposed by Yang *et al*.[13] was used to quantitatively measure the degree of pulmonary involvement. According to anatomical structure, the 18 segments of both lungs were divided into 20 regions, in which the posterior apical segment of the left upper lobe was subdivided into apical and posterior subsegments, while the anteromedial basal segment of the left lower lobe was subdivided into anterior and basal subsegments. Disease involvement in each segment was classified as none (0%), mild (1%-50% of segment volume), or severe (51%-100% of segment volume). An overall lung CT-SS was reached by summing all the segmental scores (possible score range for one lung 0-20; maximum score for both lungs 40). The same scoring was also applied to the follow-up images of each patient, and 50% or more progression of lung involvement was categorized as radiological progression.

Statistical analysis

Data were analyzed using the R statistics package program (ver. 3.5.3). Descriptive statistics were reported as number, percentage, mean and standard deviation, and median and interquartile range values for data that were not normally distributed. Pearson's χ^2-test and Fisher exact test were used to determine statistical significance of categorical data, and a p-value of 0.05 was accepted as the cut-off for significance. The normality of distribution for continuous variables was evaluated using the Shapiro-Wilk test and visual assessment of normalized Q-Q plots. For normally distributed data, the independent t-test was used to compare continuous variables between the groups, and in case of non-normal distribution, the Mann-Whitney U analysis was performed. The follow-up CT data were analyzed using a one-way factorial analysis of variance.

Results

Clinical findings and laboratory results

The initial CT exams of 27 (25%) patients were negative for any finding related to COVID-19. When we evaluated the indications for performing a CT scan, 105 patients had symptoms and clinical suspicion of COVID-19, whereas only 3 patients were asymptomatic and underwent CT due to a history of contact with a COVID-19 positive patient. Most patients had normal white blood cell count, with mildly elevated levels of alanine transaminase and aspartate transaminase (Table 1). Radiological progression was observed in 61 (56.4%) patients based on follow-up CT imaging findings. Of the follow-up patients, 54 had one or more comorbid diseases distributed as follows: malignancy in 5 (4.6%), type 2 DM in 20 (18.5%), congestive heart failure (CHF) in 8 (7.4%), systemic hypertension (HT) in 32 (29.6%), CAD in 7 (6.5%), chronic renal failure (CRF) in 4 (3.7%), and COPD in 17 (15.7%) patients. Cardiovascular disease (CVD) was defined as the presence of more than one of the comorbidities of CHF, HT, and CAD.

CT imaging findings in all patients

Table 2 illustrates the initial and follow-up CT findings in all patients. GGO was the dominant pattern seen on initial CT (Fig. 2). In the evaluation of follow-up CT examinations, the mean CT-SS increased from 7.3±8.1 to 13.14±11.38 (p=0.001). Also, consolidation (p=0.019), septal thickening (p=0.006), crazy-paving pattern (p=0.029), linear opacities combined (p=0.011), air-bronchogram sign (p=0.019) (Fig. 3), air-bubble sign (p=0.011) (Fig. 4), subpleural band formation (p=0.001), and white lung sign (p=0.001) lesions were significantly more frequent compared to the findings obtained on initial CTs. Pericardial effusion was not detected in any of our cases.

Demographic and clinical findings according to CT progression

When the patients who showed CT progression (n=61, 56.4%) were compared with non-progression cases, there were no significant differences between these two groups in terms of age (cut-

off, 50 years) (p=0.224) and gender (p=0.527) distribution. Progression was observed more frequently in patients with malignancies and type 2 DM (p=0.044 and p=0.019, respectively). When laboratory results were evaluated according to the progression status, only elevated level of the mean C-reactive protein (CRP) was significantly associated with CT progression status (5.08±5.36 mg/L, p=0.008).

Follow-up CT findings according to progression

According to the initial CT findings of the patients who showed progression, the presence of peripheral distribution (n=27, 75.0%) and multifocal involvement (n=25, 69.4%) were associated with disease progression (p=0.001). In the follow-up CTs of the patients who showed progression, both central and peripheral distribution was significantly more frequently observed as compared with only peripheral or only central distribution (p=0.001). In addition, the patients who showed CT progression also demonstrated an increased frequency of multifocal involvement (n=6, p=0.001), GGO (n=54, p=0.045), consolidation (n=28, p=0.001), septal thickening (n=31, p=0.032), crazy-paving pattern (n=21, p=0.027) (Fig. 5), linear opacities (n=33, p=0.007), white lung sign (n=17, p=0.002) and pleural effusion (n=11, p=0.011) in their follow up CTs (Fig. 6).

CT findings that significantly differed according to the comorbidity status

There were significant differences in the mean CT-SS values between the non-comorbid (n=54, 50%) and comorbid patient groups (mean ± SD 11.3±8.4 *vs*. 17.6±10.2, p=0.046). Among the cases with type 2 DM, air bronchogram (p=0.003), lymphadenopathy (p=0.010), linear opacities combined (p=0.043), pleural effusion (p=0.009), and tree-in-bud sign (p=0.020) were more frequently observed (Table 3, Fig. 7). Only the patients with COPD did not have any significantly different frequency of findings in their follow-up CT compared to patients with other comorbidities (p>0.05).

The Health Science Board defines patients with severe COVID-19 as those with a lymphocyte count <800.0×10^9/L, CRP >40 mg/L, and age over 50[14]. In the current study, the patients with severe disease were compared in terms of their initial and follow-up CT scores, type 2 DM (p=0.001), CVD (p=0.041), COPD (p=0.571), CRF (p=0.132), and malignancies (p=0.058). The patients with type 2 DM, CRF, and malignancy had lower CT-SS at initial presentation but demonstrated significantly higher scores in their follow-up CT examination than all other comorbid patients (Fig. 8).

Discussion

The clinical course of COVID-19 pneumonia involves the initiation, progression, and resolution phases[15-17], which heavily depend on several factors such as age, genetic characteristics and sex[18-20], and presence of comorbidities. In this study, we evaluated cases in which radiological progression was observed, and explored the relationship of disease progression with CT and clinical findings. During the initial stages of the pandemic, our hospital was largely dedicated to caring for COVID-19 patients, and in many patients, repeated CT imaging was performed as part of routine care due to various clinical reasons. This provided us with an opportunity to investigate changes in lung CT findings over time, i.e., at the time of initial presentation and during follow-up. The study sample comprised patients with at least one positive RT-PCR test for SARS-CoV-2. Twenty-seven (25%) patients who underwent CT examination as part of their initial evaluation had no finding of COVID-19 on CT. Chung *et al*. first described a similar situation in their study including 21 patients, where 3 (14%) patients initially presented with normal CT findings[21]. In terms of an asymptomatic incubation period, the Centers for Disease Control and Prevention state that the onset of symptoms may occur at any time from two days to two weeks after exposure, and this particular aspect of COVID-19 is similar to the Middle East respiratory syndrome (MERS)[22]. Our study showed a relatively high rate of normal initial CT findings compared to the literature, which is possibly due to our hospital being a tertiary healthcare center and access to CT scanners being easier in our country, especially in urban areas that were most affected by the first wave of the pandemic. CT is critical for the initial evaluation and investigation of non-response to treatment. When the distribution of lesions in this study was evaluated, the initial CT scans frequently showed peripheral distribution of involvement, whereas in case of disease progression, both central and peripheral involvement became

much more common. These findings are similar to the initial findings reported for SARS and MERS[23,24]. Multifocal involvement of lungs was observed more frequently on follow-up CT compared to initial presentation, which is consistent with the literature reporting that radiological progression is expected during the progression phase of disease (day 5-13 of infection)[25]. In the literature, the prevalence of GGO varies from 46% to 100%, and this pattern is usually seen in the early phases of the disease and/or mild pneumonia cases[10,26,27]. In our study with a mean difference of 8 days between the initial and follow-up scans, GGO was observed as the predominant pattern which increased in frequency throughout the disease, as some of the patients with normal initial CT scans developed GGO during the follow-up. In the progression phase, GGO coexists with consolidation, septal thickening, crazy-paving pattern, or cord shadows[28-30]. In a case series reported by Li *et al*., these unique findings in severe/critical patients were more frequent compared to non-severe patients[31]. In this study, the patients who showed radiological progression had increased GGO involvement, septal thickening, and crazy-paving pattern. Also, the incidence of crazy paving pattern was higher among DM and CHF patients compared to other comorbidities. Furthermore, the presence of consolidation was observed more frequently in the follow-up CT of progression cases. Organizing pneumonia is a common response to lung injury due to various etiologies, and is characterized by transformation of GGO into linear opacities[32]. Wu *et al*. demonstrated that internal interlobular septa thickened like a net on subpleural spaces which they named 'the spider web sign'[26]. They state that this was a specific finding for COVID-19 pneumonia, but its pathophysiology remained unclear. Considering that septal thickening was observed at an increased frequency in patients with progression, and in the follow-up CT scans of CHF, it is also possible that this finding is related to the pathophysiological mechanism that occurs due to impaired lymphatic drainage of the lung parenchyma, which is responsible for the formation of Kerley lines in the x-rays of these patient groups. The reversed halo sign is rare, and it was initially reported to be specific for cryptogenic organizing pneumonia. Our study failed to demonstrate a significant relationship of this sign with disease progression or presence of comorbidities. The air-bubble sign is postulated to be the pathological dilatation of physiological spaces, and considered to indicate a worse prognosis in COVID-19 patients[24]. In our study, the frequency of the air-bubble sign was increased in the follow-up CT, but no association was found between this sign, radiological progression and presence of comorbidities. Lung cavitation was not observed in any of our patients. Another finding indicating poor prognosis is the white lung sign, which is considered to be a radiological representation of the clinical picture of acute respiratory distress syndrome, which represents elevated CT-SS. Yang *et al*. found that a CT-SS score lower than 19.5 in their cohort could rule out severe or critical forms of pneumonia with a high negative predictive value of 96.3%[13]. In the current study, the patients with severe disease were compared in terms of their follow-up CT-SS, and type 2 DM patients and CVD patients had significantly higher scores in their follow-up CT examination as compared with other comorbidities. Antonio *et al*. evaluated 24 SARS patients after their discharge from the hospital and report that 62% of these patients (n=15) had evidence of fibrosis which was defined as the presence of parenchymal bands, traction bronchiectasis, linear opacities, or irregular interfaces[33]. In this study, linear opacities and bronchiectasis were observed to increase in the follow-up CT of the patients with comorbidities, except for those with malignancies (Fig. 9). In the light of these findings, it can be suggested that patients who survived severe COVID-19 pneumonia need to be followed-up for parenchyma pathologies such as pulmonary fibrosis. In the literature, lymphadenopathy is suggested to be one of the significant risk factors of severe/critical COVID-19 pneumonia[34]. However, the patients with type 2 DM are known to be more susceptible to bacterial superinfection. In the study, the concomitant presence of lymphadenopathy, tree-in-bud appearance, and pleural effusion was observed more frequently in type 2 DM patients than in the others.

One of the limitations of our study was that data were retrospectively obtained from a single institution. For this reason, the study may have resulted in a great number of variables acting as confounders. Another limitation was that the routine medication use in comorbidity patients was not considered.

Conclusion

This study revealed that the patients with type 2 DM and CVD had an increased frequency of some radiological findings that are reported to signify a worse prognosis for COVID-19 patients. These findings can potentially elucidate the mechanism behind the trend of decreased survival in these patient groups. Long-term studies conducted with these patient groups could better enlighten the prognosis and implications of treatment for these patients.

Acknowledgment

We would like to thank our colleagues at the Department of Infectious Diseases and Clinical Microbiology for making this study possible and for their valuable input. We also want to thank all of our clinical colleagues. Finally, we would like to thank all the patients and also our family members.

Table 1. Clinical symptoms and laboratory test results at initial presentation

Initial symptom in patients (N=105)	**n (%)**
Fever	54 (50.0)
Fatigue	30 (27.8)
Diarrhea	6 (5.6)
Nausea-vomiting	18 (16.7)
Anosmia	6 (5.6)
Myalgia	11 (10.2)
Shortness of breath	32 (29.6)
Cough	65 (60.2)
Chest pain	11 (10.2)
Laboratory results	**Mean ± SD (range values)**
WBC (10^9/L) (n=85)	6.91±3.7 (4-10)
Lymphocyte (10^9/L) (n=85)	1.50±0.72 (0.7-4)
BUN (mg/dL) (n=82)	17.90±14.47 (<26)
CRP (mg/L) (n=87)	3.45±5.08 (3.31-6.84)
D-dimer (ng/mL) (n=46)	838.66±1,167.54 (487.70-1,645.25)
CK (U/L) (n=72)	136.67±273.05 (<200)
Creatinine (mg/dL) (n=84)	1.15±1.24 (0.70-1.25)
LDH (U/L) (n=44)	270.66±161.90 (245.71-315.42)
ALT (U/L) (n=83)	42.70±75.82 (<42)
AST (U/L) (n=83)	38.13±4.34 (<37)

N = total number of study cases; n = number of cases; SD = standard deviation; WBC = white blood cell count; BUN = blood urea nitrogen; CRP = C-reactive protein; CK = creatine kinase; LDH = lactate dehydrogenase; ALT = alanine transaminase; AST = aspartate transaminase

Table 2. Initial and follow-up CT findings in all patients

	Initial CT	**Follow-up CT**	**p value**
Mean CT score (mean)	7.3±8.1 (min 0, max 34)	13.14±11.38 (min 0, max 38)	0.001 0.001
Distribution	n (%)	n (%)	0.269
Central	2 (2.5)	9 (8.5)	
Peripheral	42 (51.9)	53 (50.0)	
Central and peripheral	37 (45.7)	44 (41.5)	
GGO	78 (72.2)	88 (81.5)	0.143
Consolidation	18 (16.7)	35 (32.4)	0.019
Septal thickening	25 (23.1)	45 (41.7)	0.006
Crazy paving pattern	14 (13.0)	28 (25.9)	0.029
Linear opacities	28 (25.9)	46 (42.6)	0.008
Tree-in-bud appearance	4 (3.7)	4 (3.7)	1
Air bronchogram	8 (7.4)	21 (19.4)	0.019
Pleural effusion	6 (5.6)	12 (11.1)	0.238
Air-bubble sign	6 (5.6)	19 (17.6)	0.011
Bronchiectasis	4 (3.7)	9 (8.3)	0.267
White lung sign	4 (3.7)	19 (17.6)	0.001
Halo sign	6 (5.6)	6 (5.6)	1
Reversed halo sign	7 (6.5)	11 (10.2)	0.454
Subpleural band formation	1 (0.9)	28 (25.9)	0.001

n = number of cases; CT = computed tomography; GGO = ground-glass opacity

Table 3. CT findings that significantly differed according to comorbidities on follow-up CT examinations

CT finding	**All comorbidities (n=54)**	**No comorbidities (n=54)**	**p value**
Consolidation	23 (42.6%)	12 (22.2%)	0.039
Linear opacities combined	29 (53.7%)	17 (31.5%)	0.032
Pleural effusion	11 (20.4%)	1 (1.9%)	0.004
Right middle lobe involvement	38 (70.4%)	25 (46.3%)	0.019
Septal thickening	29 (53.7%)	16 (29.6%)	0.019
White lung sign	15 (27.8%)	4 (7.4%)	0.010
	CVD (n=39)	**No CVD (n=69)**	
Linear opacities combined	24 (61.5%)	22 (31.9%)	0.004
Pleural effusion	10 (25.6%)	2 (2.9%)	0.001
Septal thickening	25 (64.1%)	20 (29.0%)	0.001
White lung sign	12 (30.8%)	7 (10.1%)	0.009
	Malignancy (n=5)	**No malignancy (n=103)**	
Pleural effusion	3 (60.0%)	9 (8.7%)	0.009
White lung sign	3 (60.0%)	16 (15.5%)	0.037
	Type 2 DM (n=20)	**No type 2 DM (n=88)**	
Air bronchogram sign	9 (45.0%)	12 (13.6%)	0.003
Linear opacities	13 (65.0%)	33 (37.5%)	0.043
Pleural effusion	6 (30.0%)	6 (6.8%)	0.009
Tree-in-bud appearance	3 (15.0%)	1 (1.1%)	0.020

CT = computed tomography; n = number of cases (%); Type 2 DM = type 2 diabetes mellitus; CVD = cardiovascular diseases

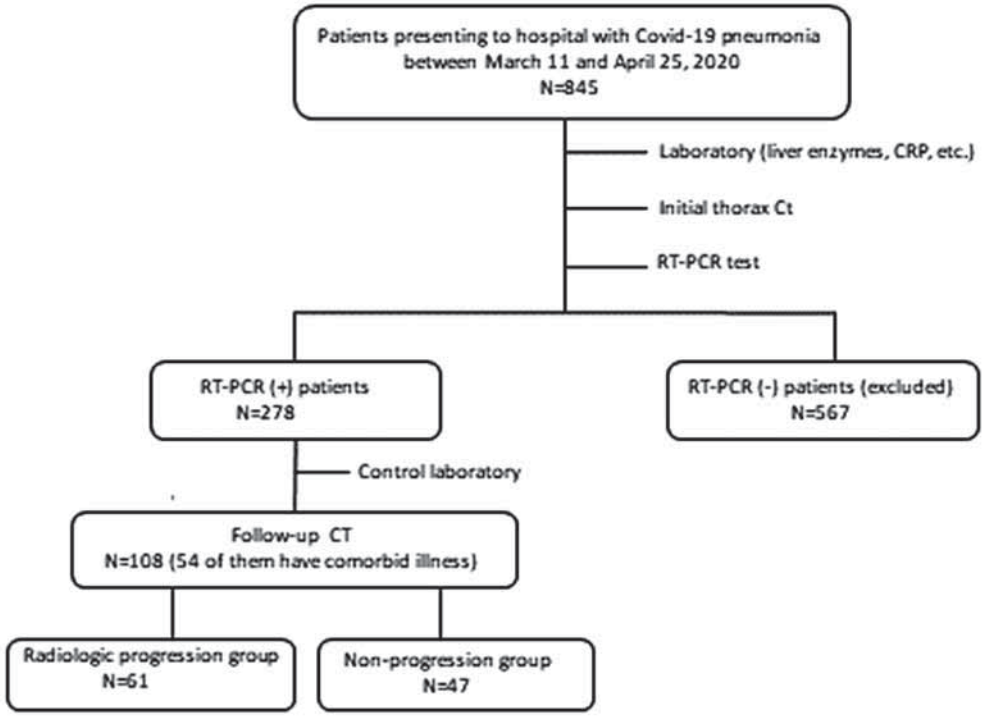

Fig. 1. Flow diagram of database search results.

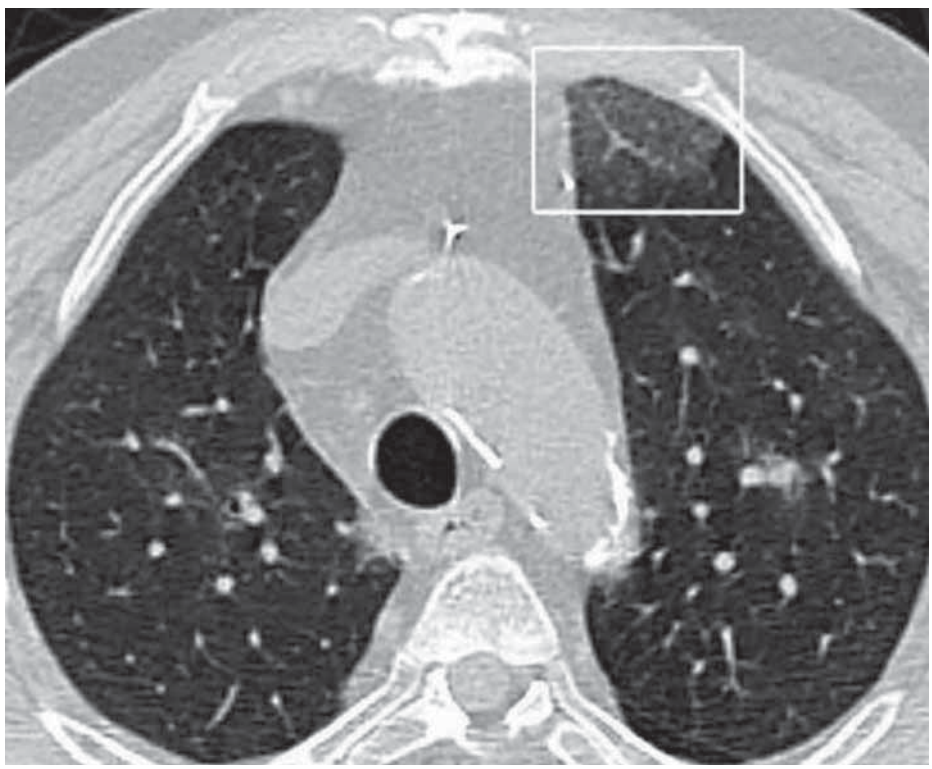

Fig. 2. A 67 year-old male patient who had undergone coronary bypass surgery 3 years before presenting with fever and dyspnea. Initial CT showed ground-glass opacity in the left upper lobe anterior segment (square).

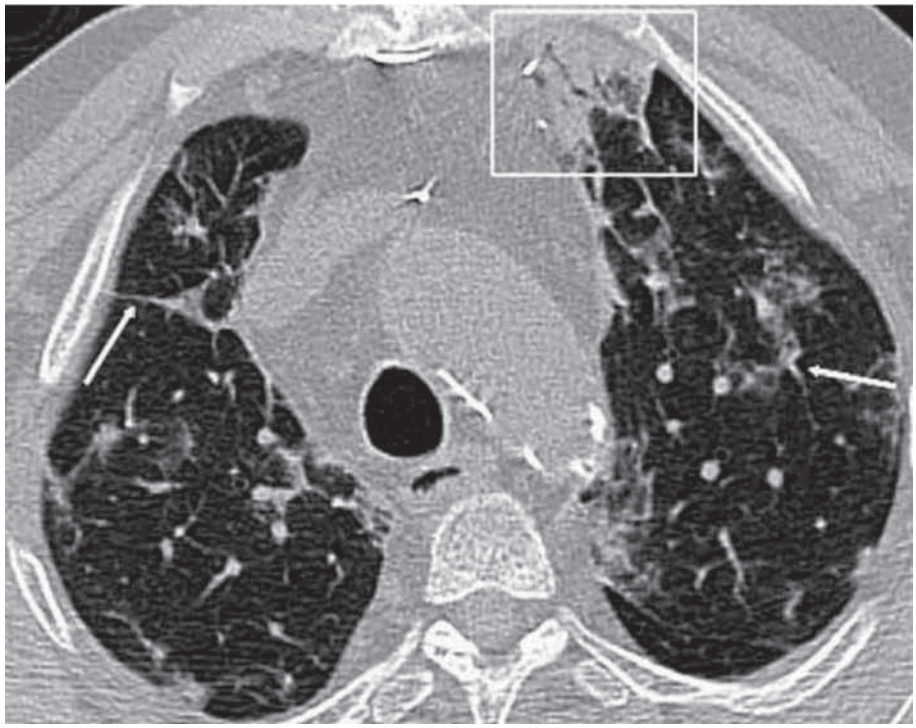

Fig. 3. The follow-up examination performed 8 days later in the same patient described in Figure 2 showed consolidation (square), air bronchogram sign, and linear opacities. CT severity score for initial and follow-up examinations was 12 and 19, respectively.

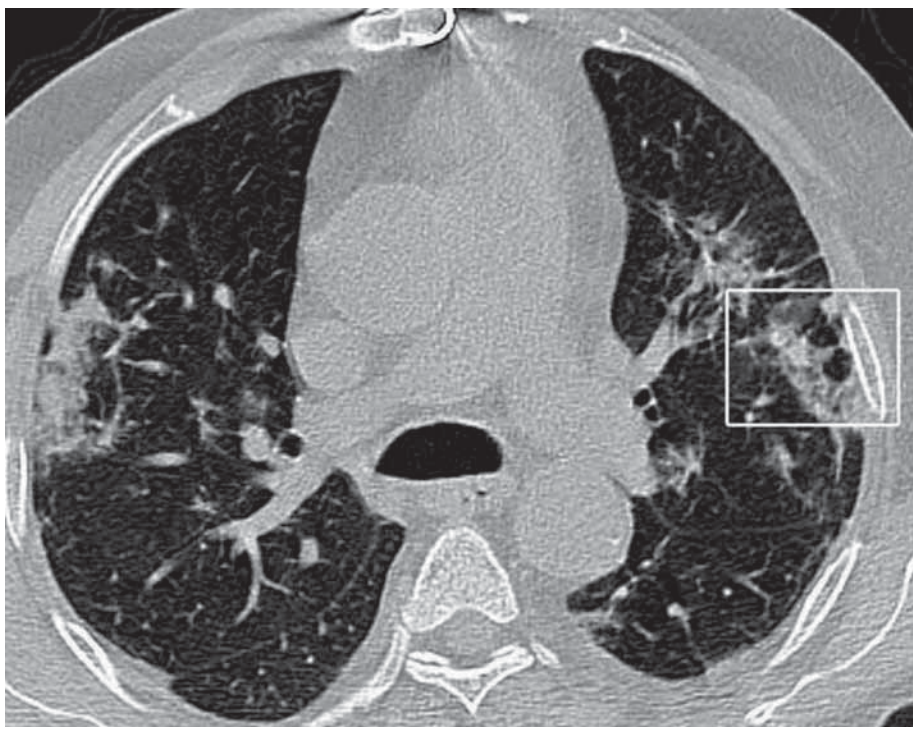

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Fig. 4. On follow-up examination of the same patient described in Figure 2, an air bubble sign (little square) in the left upper lobe posterior segment was noted.

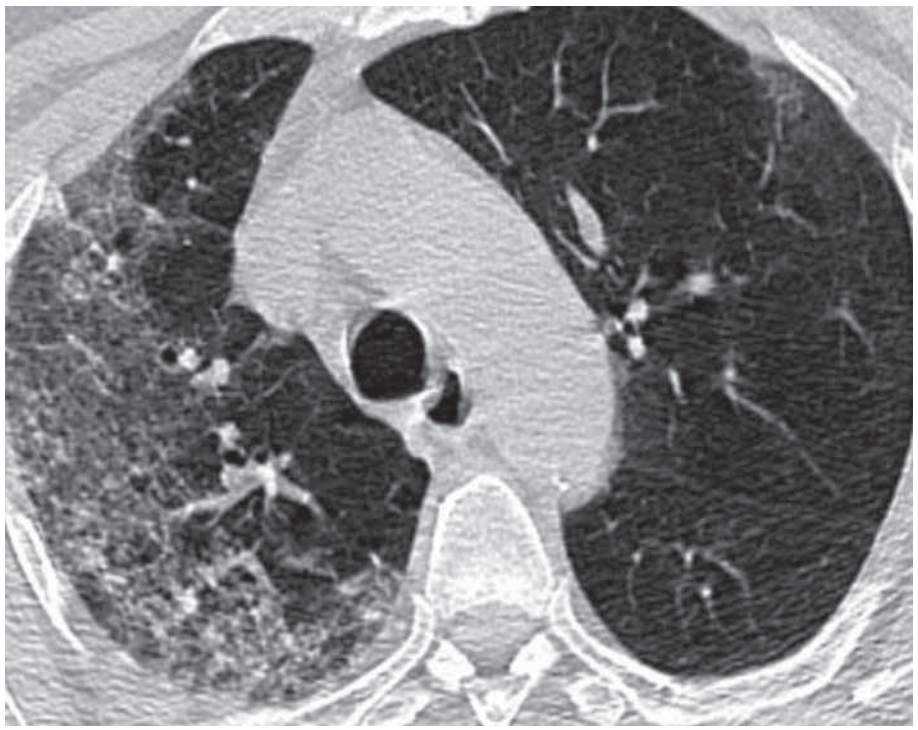

Fig. 5. A 74-year-old male patient with dyspnea and known CVD presented on the second day of symptom onset. The patient was hospitalized. In his follow-up, CT-SS was 22, and the upper and middle right lung lobes showed diffuse crazy paving pattern and linear opacities.

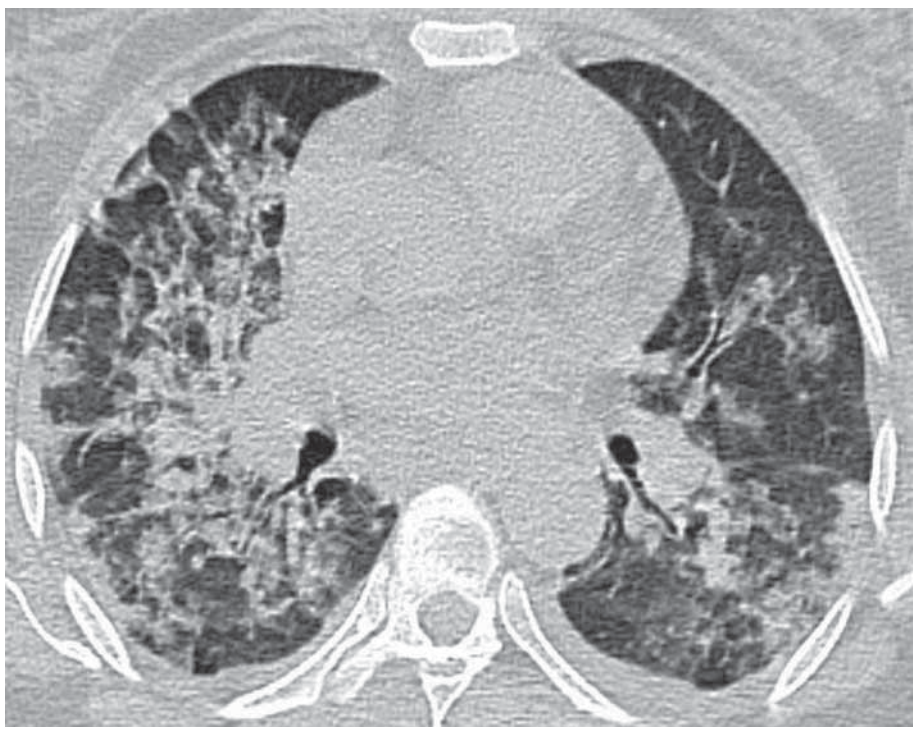

Fig. 6. A 53-year-old patient with known type 2 diabetes mellitus presented with ongoing chest pain and cough. Follow-up CT performed 8 days after admission showed pleural effusion and white lung sign; CT-SS was 28.

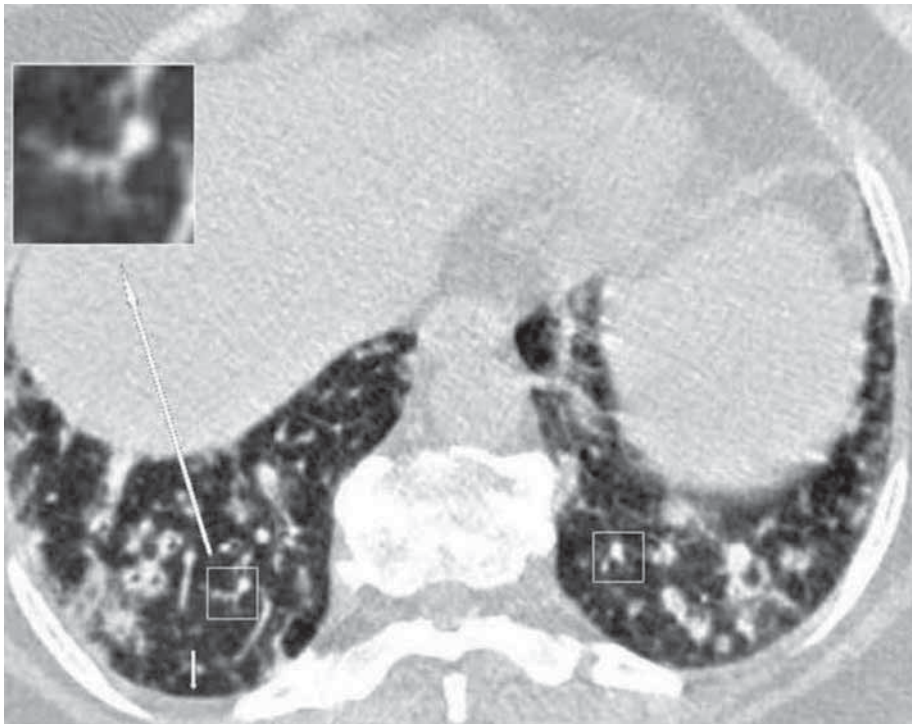

Fig. 7. A 56-year-old female patient with known type 2 diabetes mellitus presented on day 4 of symptom onset with nausea, fatigue and dyspnea. The patient was admitted for inpatient care when she exhibited clinical progression. In her follow-up, CT-SS was 28, and lower lung lobes showed tree-in-bud appearance (squares) and mild pleural effusion (little arrow), which prompted consideration of superinfection with another pathogen.

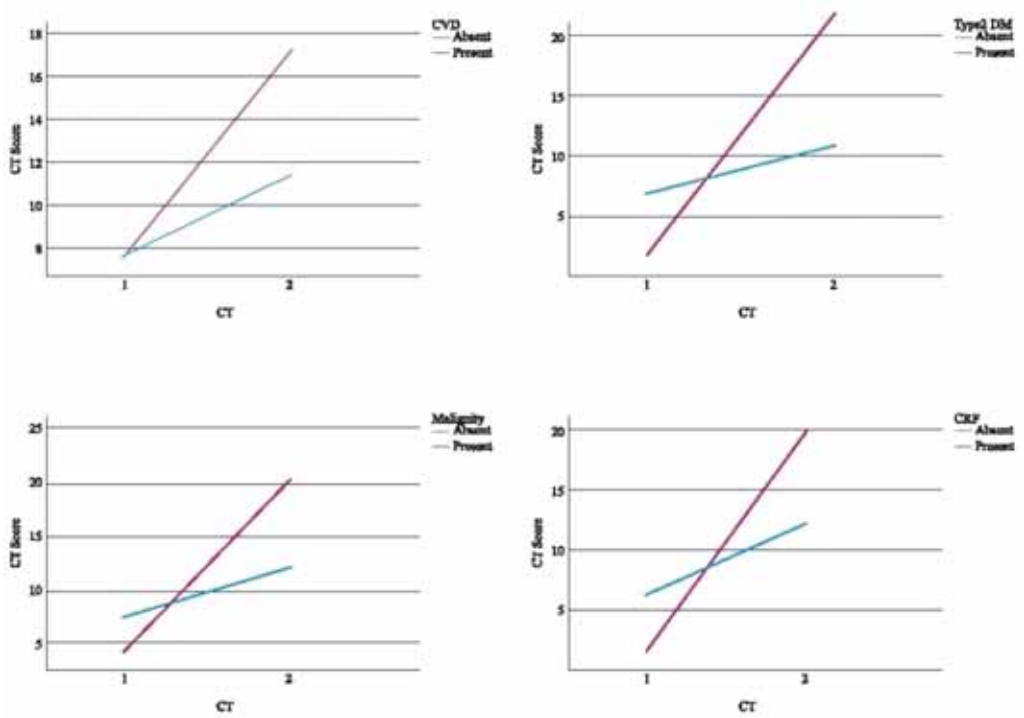

Fig. 8. Graphs of CT scores according to the severe group comorbidity status.

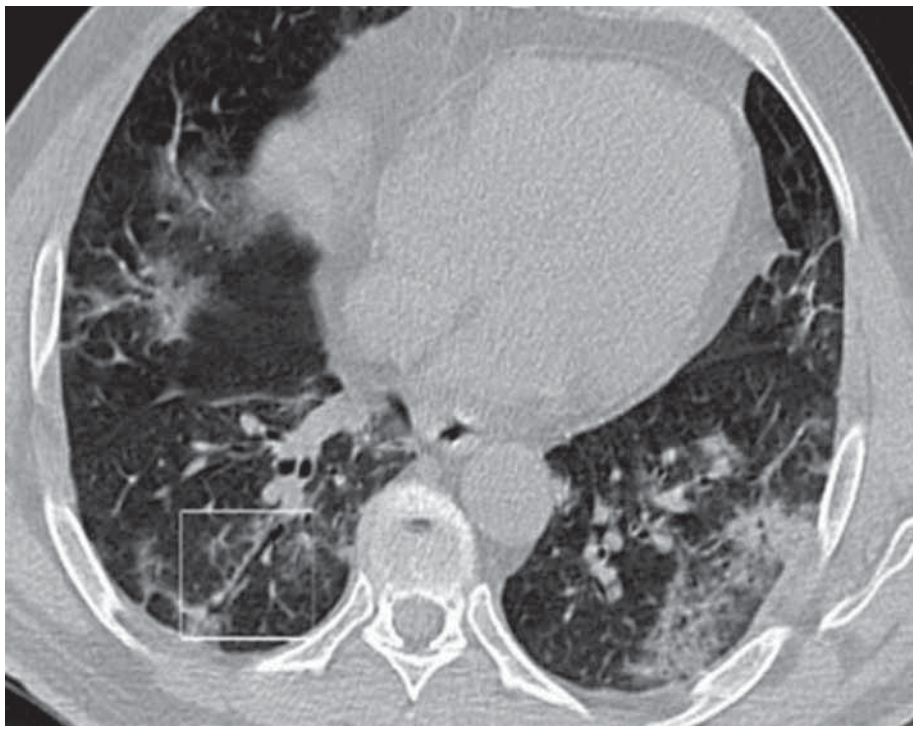

Fig. 9. A 54-year-old female patient with malignancy sought medical care for anosmia and fatigue lasting for 2 days. The patient progressed rapidly and follow-up CT after 7 days showed disseminated septal thickenings (spider web sign) and traction bronchiectasis, with a CT- SS of 24.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, *et al*. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727-33. https://doi.org/10.1056/NEJMoa2001017.
2. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). https://systems.jhu.edu/research/public-health/ncov/ (accessed December 6, 2020).
3. Dorn E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis. 2020;20:533-4. https://doi.org/10.1016/S1473-3099(20)30120-1.
4. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8:475-81. https://doi.org/10.1016/S2213-2600(20)30079-5.
5. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, *et al*. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-20. https://doi.org/10.1056/NEJMoa2002032.
6. Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, *et al*. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J. 2020;133:1025-31. https://doi.org/10.1097/CM9.0000000000000744.
7. Atik, D, Burak Kaya, H. Evaluation of the relationship of MPV, RDW and PVI parameters with disease severity in COVID-19 patients. Acta Clin Croat. 2021;60:103-13. https://doi: 10.20471/acc.2021.60.01.15.
8. Nandy K, Salunke A, Pathak SK, Pandey A, Doctor C, Puj K, *et al*. Coronavirus disease (COVID-19): a systematic review and meta-analysis to evaluate the impact of various comorbidities on serious events. Diabetes Metab Synd. 2020;14:1017-25. https://doi.org/10.1016/j.dsx.2020.06.064.
9. Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, *et al*. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology. 2020;295:22-3. https://doi.org/10.1148/radiol.2020200330.
10. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J, *et al*. Chest CT for typical coronavirus disease 2019 (COVID-19) pneumonia: relationship to negative RT-PCR testing, Radiology. 2020;296:41-5. https://doi.org/10.1148/radiol.2020200343.
11. Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raoof S, *et al*. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. Chest. 2020;158:106-16. https://doi.org/10.1016/j.chest.2020.04.003.
12. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy, J, *et al*. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008;246:697-722. https://doi.org/10.1148/radiol.2462070712.
13. 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. Radiology Cardiothoracic Imaging 2:e 2000 47. https://doi.org/10.1148/ryct.2020200047
14. COVID-19 Pandemic Management and Work Guide, Turkish Ministry of Health. 2020, October 1. https://covid19.saglik.gov.tr.
15. Shi H, Han X, Zheng C. Evolution of CT manifestations in a patient recovered from 2019 novel coronavirus (2019-NCoV) pneumonia in Wuhan, China. Radiology. 2020;295:20. https://doi.org/10.1148/radiol.2020200269.
16. 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;30:3306-9. https://doi.org/10.1007/s00330-020-06731-x.
17. Duan Y, Qin J. Pre- and post-treatment chest CT findings: 2019 novel coronavirus (2019-NCoV) pneumonia. Radiology. 2020;295:21. https://doi.org/10.1148/radiol.2020200323.
18. Conti P, Younes A. Coronavirus cov-19/SARS-cov-2 affects women less than men: clinical response to viral infection. J Biol Regul Homeost Agents. 2020;34:339-43. https://doi.org/10.23812/Editorial-Conti-3.
19. Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. Clin Rev Allergy Immunol. 2019;56:308-21. https://doi.org/10.1007/s12016-017-8648-x.
20. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. J Immunol. 2017;198:4046-53. https://doi.org/10.4049/jimmunol.1601896.
21. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, *et al*. CT imaging features of 2019 novel coronavirus (2019-NCoV). Radiology. 2020;295:202-7. https://doi.org/10.1148/ radiol.2020 200230.
22. Symptoms of Coronavirus, Centers of Disease Control. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html(accessed October 3, 2020).
23. Ooi GC, Khong PL, Müller NL, Yiu WC, Zhou LJ, Ho JCM, *et al*. Severe acute respiratory syndrome: temporal lung changes at thin-section CT in 30 patients. Radiology. 2004;230:836-44. https://doi.org/10.1148/radiol.2303030853.
24. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol. 2020;30:4381-9. https://doi.org/10.1007/s00330-020-06801-0.
25. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, *et al*. Time course of lung changes at chest CT during recovery from coronavirus disease 2019 (COVID-19). Radiology. 2020;295:715-21. https://doi.org/10.1148/radiol.2020200370.
26. Bernheim, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, *et al*. Chest CT findings in coronavirus disease 2019 (COVID-19): relationship to duration of infection. Radiology. 2020;295:685-91. https://doi.org/10.1148/radiol.2020200463.

27. Wu J, Wu X, Zeng W, Guo D, Fang Z, Chen L, *et al*. Chest CT findings in patients with coronavirus disease 2019 and its relationship with clinical features. Investig Radiol. 2020;55:257-61. https://doi.org/10.1097/RLI.0000000000000670.
28. Wang K, Kang S, Tian R, 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: 341-7. https://doi.org/10.1016/j.crad.2020.03.004.
29. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol. 2020;215:87-93. https://doi.org/10.2214/AJR.20.23034.
30. Gündüz Y, Öztürk MH¸ Tomak Y. The usual course of thorax CT findings of COVID-19 infection and when to perform control thorax CT scan. Turk J Med Sci. 2020;50:684-6. https://doi:10.3906/sag-2004-293.
31. Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, *et al*. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol. 2020;30: 4407-16. https://doi.org/10.1007/s00330-020-06817-6.
32. Kligerman SJ, Franks TJ, Galvin JR. From the radiologic pathology archives: organization and fibrosis as a response to lung injury in diffuse alveolar damage, organizing pneumonia, and acute fibrinous and organizing pneumonia. Radiographics. 2013;33:1951-75. https://doi.org/10.1148/rg.337130057.
33. Antonio GE, Wong KT, Hui DSC, Wu A, Lee N, Yuen EHY, *et al*. Thin-section CT in patients with severe acute respiratory syndrome following hospital discharge: preliminary experience. Radiology. 2003;228:810 -5. https://doi.org/10.1148/radiol.2283030726.
34. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Investig Radiol. 2020;55:327-31. https://doi.org/10.1097/RLI.0000000000000672.

Sažetak

RAZLIKUJU LI SE NALAZI UPALE PLUĆA IZMEĐU BOLESNIKA S INFEKCIJOM COVID-19 SA SUPOSTOJEĆIM BOLESTIMA I ONIH BEZ NJIH? OBILJEŽJA KOMPJUTORIZIRANE TOMOGRAFIJE VISOKE REZOLUCIJE U 108 PRAĆENIH BOLESNIKA

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Cilj je bio usporediti procjenu ozbiljnosti upale pluća u COVID-19 dobivenu pomoću sustava semikvantitativnog ocjenjivanja kompjutorizirane tomografije (CT-SS) u početnom i naknadnom skeniranju u odnosu na prisutnost supostojećih bolesti. Od 278 bolesnika s pozitivnim nalazom reverzne transkripcijske lančane reakcije polimeraze u stvarnom vremenu procjenjivalo se njih 108 s naknadnim pregledom CT. Zatim su analizu CT-SS svih snimaka CT pregledala dva neovisna stručnjaka. Ovi stručnjaci nisu bili upoznati s laboratorijskim i kliničkim nalazima bolesnika. Četvrtina bolesnika imala je negativne nalaze na početnom CT snimanju. Napredovanje bolesti pokazao je 61 (56,4%) bolesnik. Napredovanje bolesti češće je zabilježeno u bolesnika s tipom 2 dijabetes melitusa (DM) i u onih sa zloćudnim bolestima (p=0,044 odnosno p=0,019). Naknadni CT u bolesnika sa supostojećim bolesima, osobito u onih s kardiovaskularnim bolestima (56,4%) i tipom 2 DM (70,0%), pokazao je povećanu učestalost difuznog zahvaćanja bolešću. Znak bijelih pluća češće je zabilježen u bolesnika sa zloćudnim bolestima (60,0%). U ovom istraživanju su bolesnici s COVID-19 i supostojećim bolestima imali višu stopu napredovanja bolesti od onih bez supostojećih bolesti. Bolesnici sa supostojećim bolestima češće su imali teže nalaze CT uz visoke CT-SS. Ovi nalazi mogli bi služiti kao vodič u praćenju i liječenju bolesnika s upalom pluća uzrokovanom infekcijom COVID-19.

Ključne riječi: *Upala pluća u COVID-19; Semikvantitativni CT sustav bodovanja težine bolesti; Napredovanje bolesti; Supostojeće bolesti; Radiološki nalazi*