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Prognostic value of clinical and radiological findings in COVID-19 pneumonia

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Abstract:

BACKGROUND AND AIM: We aimed to examine the demographic, clinical, and imaging characteristics of patients with COVID-19 pneumonia and also to identify the factors affecting mortality.

MATERIALS AND METHODS: This study was designed as a retrospective single-center observational study. A total of 126 patients with COVID-19 pneumonia who were polymerase chain reaction confirmed and underwent thorax computer tomography (CT) were analyzed. The patients' demographic and clinical data were obtained from the electronic medical record. Thorax CT findings were re-evaluated retrospectively by thoracic radiologists according to the severe acute respiratory syndrome coronavirus 2 pneumonia guidelines of the Radiological Society of North America. The extent of lesions was evaluated by CT lobe score, which was the sum of individual lobe scores (0–5 point) of the lungs.

RESULTS: The mean age of the patients was 60.4 ± 18.6 years and 54% (n = 68) were male. The most common symptoms included cough, fever, and shortness of breath. The average time interval between the onset of symptoms and thorax CT acquisition was 6.6 ± 8.3 days. The most common radiological findings included ground-glass opacity (98.4%), consolidation (72.2%), and vascular enlargement (69.8%), respectively. The deceased patients had more common consolidation, vascular enlargement, and high lobe scores in thorax CT as compared to survivors. According to logistic regression analysis age (P = 0.003), lobe score (P = 0.001), numbers of comorbidities (P = 0.017), symptoms duration (P = 0.034), and vascular enlargement (P = 0.045) were independent risk factors on 30-day mortality.

CONCLUSION: This study indicated that age, symptoms duration, the number of comorbidities, lobe score, and vascular enlargement in thorax CT are associated with the prognosis of COVID-19 pneumonia.

Keywords:

Coronavirus disease 19, pneumonia, radiology finding, severe acute respiratory syndrome coronavirus 2, vascular enlargement

Introduction

In December 2019, a multitude of pneumonia cases with clinical manifestations substantially reminiscent of viral pneumonia was reported to be associated with the Huanan Seafood Wholesale Market in Wuhan, Hubei, China.[1-3] In early January 2020, the mysterious causative agent of pneumonia

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was found to be a novel coronavirus by several independent laboratories in China.[4] Later, the World Health Organization (WHO) called this new coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease was named COVID-19, which was officially announced to be a pandemic after SARS in 2002 and MERS in 2012.[5,6]

The new coronavirus (2019-nCoV) is the seventh member of the family of coronaviruses infecting humanity.[4,7,8] Studies reported that it could spread from person to person, mainly through respiratory droplets and contact, with an incubation period of 3–7 days and up to 14 days.[9] Unlike SARS and MERS, asymptomatic patients are also infectious.[5] According to the COVID-19 report of the WHO, the disease has a wide range of clinical signs, from completely asymptomatic to severe pneumonia and death.[6] Therefore, early diagnosis and isolation are crucial to controlling the spread of the pandemic.[3] Fever, fatigue, and nonproductive cough are the primary symptoms.[9] The most common symptom is fever. However, not all patients present with fever.[10] Severe patients often develop dyspnea a week later and are more likely to progress to acute respiratory distress syndrome (ARDS), septic shock, difficult-to-correct metabolic acidosis, and coagulation dysfunction.[9] Male sex and beyond 65 years were reported to be significant risk factors for ARDS, with comorbidities being a high risk of death.[10]

Thorax computer tomography (CT) plays an important role in the diagnosis and screening of COVID-19 pneumonia,[5] and it is critical in evaluating the severity and progression of the infection.[11] This study aimed to investigate the demographic, clinical, and radiographic features of patients with COVID-19 pneumonia and to determine the factors affecting mortality.

Materials and Methods

Setting and data collection

This single-center, retrospective study was conducted at Istanbul Medeniyet University Göztepe Training and Research Hospital, designated as a dedicated COVID-19 hospital to treat patients with SARS-CoV-2 pneumonia. The study was approved by the Institutional Ethics Committee (2020/0363). The study was carried out in accordance with the principles of the Helsinki Declaration.

Patients and definitions

The study included patients who received a diagnosis of polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection and underwent thorax CT. The patients were hospitalized and/or outpatient who received medical therapy between April 5, 2020, and May 5, 2020. Data included age, sex, symptoms, the time between the onset of symptoms and hospitalization, comorbidities, length of hospital stay, CT findings, and 30-day mortality. Clinical symptoms, the onset of symptoms, and comorbidities were obtained from patients' hospital electronic medical record system. Thirty-day mortality was defined as death within 30 days of a diagnosis of COVID-19. CT scans were interpreted by two thoracic radiologists according to the SARS-CoV-2 pneumonia guidelines of the Radiological Society of North America. CT findings were classified according to lesion patterns (ground-glass opacities, irregular consolidation, solid nodule, linear opacities, vascular enlargement, and pleurisy), the involved lung and lobes, and the distribution characteristics of the lesions [Figure 1]. The extent of lesions was evaluated by CT lobe score, which was calculated as the sum of individual lobe scores of the lungs. Lobe involvement was rated on a 0–5 point scale, with higher scores indicating a higher percentage of involvement (0 = No involvement, 1= <5% involvement, 2 = 5%–<25% involvement, 3 = 25%–50% involvement, 4 = 50%–<75% involvement, and 5= ≥75% involvement).[12]

Thorax CT studies were performed by a 16-slice CT scanner (GE Optima CT520) with the following acquisition parameters: Tube voltage 100 kV, tube current 70–120 mAs, slice thickness 1.25 mm, automatic dose modulation, CT volume-dose index 5.60 mGy, dose length product 179.32–210.48 mGy, and effective dose 2.5–2.9 mSv.

Statistical analysis

The statistical analysis of the data obtained was made with the program of Statistical Package for the Social

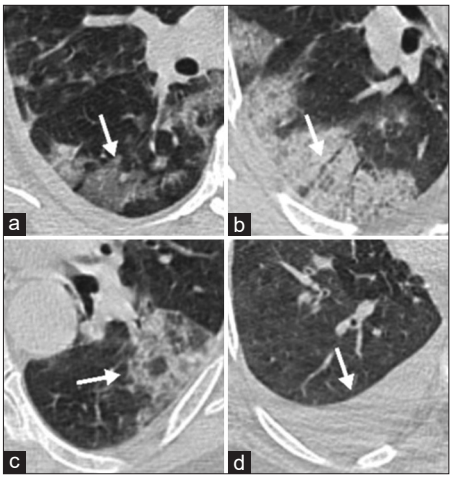

Figure 1: Computed tomography findings due to COVID-19 pneumonia. (a) Ground-glass opacity (an area of increased attenuation that does not obscure the bronchial structures or vessels); (b) air bronchogram surrounding by consolidation and ground-glass opacities; (c) reverse halo sign (a ground-glass opacity surrounded by a denser ring of consolidation); (d) pleural effusion

Sciences Version 26.0, IBM Corp., Armonk, NY, USA. Categorical variables were expressed as frequencies and percentages, and continuous variables as means, median, and interquartile range. Categorical variables were compared using the Chi-squared test and the Fisher's exact test when data were small. Continuous variables were compared using the Student's *t*-test or Mann–Whitney U-test for two group comparisons, and one-way ANOVA or Kruskal–Wallis test for multigroup comparisons. Correlations between the variables were sought using the Pearson–Spearman correlation efficiently. Binominal logistic regression analysis was also used to assess the strength of relationships between variables. 95% confidence intervals for each variable were given for all comparisons.

Results

A total of 167 patients with a positive reverse transcription-PCR (RT-PCR) test and who had undergone thorax CT at presentation were identified. Forty-one patients were excluded from the study because two patients were younger than 18 years old, and 39 patients did not have pneumonia. Thus, 126 patients with a mean age of 60.4 ± 18.6 years were included, of whom 54% (n = 68) were male. One hundred and two patients were hospitalized. Nearly 52% of symptomatic patients, the time between symptom onset and hospitalization was <5 days. Cough (51.0%), fever (41.2%), and shortness of breath (39.2%) were the most common symptoms. More than half of the patients (53.9%) had more than one comorbidity; most commonly hypertension (49.0%) and diabetes mellitus (25.5%). The demographic and clinical features of patients are given in Table 1.

The mean interval from the onset of symptoms to CT scanning was 6.6 ± 8.3 days. 111 (88.1%) patients had bilateral lung involvement (right lung involvement 93.7%; left lung involvement 94.4%) and 96 (76.2%) patients had peripheral–central lesions on radiologic evaluation. Multifocal distribution was found in 114 (90.5%) patients. The lower lobes were more commonly involved [Table 1].

The most frequent lesions on thorax CT were ground-glass opacities in 98.4% (n = 124), consolidation in 72.2% (n = 91), and vascular enlargement in 69.8% (n = 88) [Table 2]. Pleural effusion, pericardial effusion, thoracic lymphadenopathy, atelectasis, and pulmonary emphysema were rare radiologic findings [Table 3]. Two patients had pneumothorax of whom, and one had bilateral involvement and died. In addition, two patients' lesions were compatible with malignancy on thorax CT. Patients ≥65 years of age had a higher incidence of pleural effusions (P = 0.035) and pleural thickening (P = 0.005). Patients in whom

Table 1: Demographic and clinical characteristics of the study group

Variable	*n* (%)
Gender (female/male)	
Female	58 (46)
Male	68 (54)
Age categorized (years)	
<65	74 (58.7)
>65	52 (41.3)
Hospitalization status	
Outpatient	24 (19)
Inpatient and discharged	85 (67.5)
Inpatient and dead	17 (13.5)
Presence of symptoms	
No	5 (4.9)
Yes	97 (95.1)
Onset time of symptoms (days)	
<5	53 (52)
>5	49 (48)
Symptoms	
Cough	52 (51.0)
Fever	42 (41.2)
Shortness of breath	40 (39.2)
Fatigue	26 (25.5)
Body pain	22 (21.6)
Nausea-vomiting	10 (9.8)
Diarrhea	10 (9.8)
Headache	7 (6.9)
Sore throat	5 (4.9)
Loss of apatite	7 (6.9)
Chills	3 (2.9)
Loss of taste and sensation	4 (3.9)
Sputum	2 (2.0)
Other	12 (11.7)
Presence of comorbidities	
Yes	28 (27.5)
No	74 (72.5)
Comorbidities	
<2	47 (46.1)
>2	55 (53.9)
Comorbidities	
All cardiovascular diseases	59 (57.8)
Hypertension	50 (49.0)
Ischemic heart disease	17 (16.7)
All endocrine and metabolic diseases	32 (31.4)
Diabetes mellitus	26 (25.5
Other endocrine and metabolic diseases	8 (7.8)
All respiratory system diseases	14 (13.7)
Chronic obstructive pulmonary disease asthma	12 (11.8)
Other respiratory diseases	3 (2.9)
Neurologic diseases	18 (17.6)
Organ malignancy	6 (5.9)
Chronic renal failure	7 (6.9)
Connective tissue diseases	3 (2.9)
Other diseases	11 (10.8)
Unilateral-bilateral	
Unilateral lung involvement	15 (11.9)

Contd...

Table 1: Contd...

Variable	*n* (%)
Bilateral lung involvement	111 (88.1)
Distribution of lesions	
Peripheral	30 (23.8)
Peripheral-central	96 (76.2)
Central	0
The number of lesions	
Focal	12 (9.5)
Multifocal	114 (90.5)
Involvement of the right lung (yes)	118 (93.7)
The right upper lobe (yes)	89 (70.6)
The right middle lobe (yes)	90 (71.4)
The right lower lobe (yes)	114 (90.5)
Involvement of the left lung (yes)	119 (94.4)
The left upper lobe (yes)	102 (81.0)
The left lower lobe (yes)	113 (89.7)

the interval from the onset of symptoms to CT scanning was 5 days or longer were more likely to have subpleural lines (P = 0.014) and a lobe score of >10 (P = 0.026) as compared with those with a shorter interval. Patients who ended up with mortality more frequently had consolidation (P = 0.039), vascular enlargement in the lesion (P = 0.019), pleural thickening (P = 0.047), and a lobe score > 10 (P = 0.025) [Table 2].

The 30-day mortality rate of all patients was 13.5% (17/126). Those who died had a higher median age (73.8 ± 12.1 vs. 58.4 ± 18.5 years, P = 0.001), more comorbidities (2.8 ± 1.4 vs. 1.6 ± 1.5, P = 0.003), a higher lobe score (12.5 ± 6.6 vs. 7.4 ± 4.6, P = 0.003), and a longer hospital stay (14.8 ± 13.6 vs. 4.7 ± 5.23 days, P = 0.000). There was no difference between patients who died and survived in terms of the duration of symptoms until underwent thorax CT (3.9 ± 4.6 days vs. 7.2 ± 8.8 days, P = 0.115). In logistic regression analysis, age (P = 0.003), lobe score (P = 0.001), the number of comorbidities ≥2 (P = 0.017), the duration of symptoms <5 days (P = 0.034), and vascular enlargement on thorax CT (P = 0.045) were independent factors affecting 30-day mortality in patients with COVID-19 pneumonia [Table 4].

Discussion

This study indicated that age, the number of comorbidities, the duration of symptoms <5 days, and lobe score and vascular enlargement on thorax CT were independent risk factors on 30-day mortality in patients with COVID-19 pneumonia.

In previous studies showed that the elderly and male sex were more vulnerable to SARS-CoV-2 infection.[3,10,12] Symptoms of COVID-19 infection such as fever, dry cough, and fatigue are not specific in the prodromal phase.[4,13,14] The most common symptoms at baseline in patients with COVID-19 pneumonia were fever 43.8%–98.6%, cough 59.4%–82%, fatigue 44%–69.6%, shortness of breath 31.2%–55%, and myalgia 34.8%–44%.[3,13-17] In our study, the mean age and sex distribution of patients with RT-PCR-confirmed and radiologically manifest COVID-19 pneumonia were similar to those previously reported.[3,10,12] Furthermore, the most common symptoms were respectively cough (51.0%), fever (41.2%), and shortness of breath (39.2%). Nausea-vomiting and diarrhea were present in 10% of the patients. The incidence of fever as the initial presentation was relatively low, which could also be due to different physicians taking the histories of patients, the possibility of missing the evaluation of fever on examination. Besides, as several studies indicated,[10,14,15] fever may have developed after hospitalization in patients who have no fever at the beginning. In more than half of the patients, the interval from the onset of symptoms and thorax CT scan was <5 days. The patients in whom the interval from hospital presentation to the onset of symptoms was <5 days and who had higher involvement was on chest CT had higher mortality rates. Patients in whom the interval from onset of symptoms to hospital presentation was longer had a better disease course, shorter hospital stay, and a lower mortality rate.

Cardiovascular and endocrine comorbidities are commonly encountered among patients with COVID-19. Respiratory diseases, especially chronic obstructive pulmonary disease (COPD), are rarely reported.[15] Several studies reported rate of hypertension (15%–31.2%), diabetes (6%–20%), cardiovascular disease (3%–14.5%), malignancies (7.2%), and COPD (1%).[3,7,12] The presence of comorbidities was associated with poorer clinical outcomes.[18] In our study, the presence of comorbidities was significantly correlated with mortality. In addition, in line with the literature,[18] the higher number of comorbidities resulted in poorer prognoses. In COVID-19 pneumonia, thorax CT was reported to have a high sensitivity (97%) but a lower specificity (56%–68%).[19,20] Image findings of COVID-19 pneumonia are not specific.[11] The imaging features of the novel coronavirus pneumonia are very similar to those of MERS, SARS,[11] and other viral pneumonia but also have their imaging features.[9] Abnormal findings on thorax CT at baseline were reported rates between 77% and 86.2% of patients.[7,15,16] Besides, studies were reported bilateral lung involvement at rates from 59% to 98%.[5,7,17] We detected lesions on chest images in 126 (76.4%) of 165 patients who had undergone baseline CT scans. Of the patients who had lung involvement, 88.1% had bilateral lung involvement. Besides, we observed that lung involvement was equally frequent in both lungs, with more frequent involvement in the lower lobes. Of patients, 90.5% had multifocal, 23.8% had peripheral,

Table 2: Distribution of radiographic findings in patients with coronavirus disease-19 pneumonia

Variable	*n*	Ground-glass opacity, *n* (%)	Consolidation, *n* (%)	Paving stone, *n* (%)	Vascular enlargement, *n* (%)	Subpleural stripes, *n* (%)	Lobe score >10, *n* (%)
Gender							
Female	58	58 (100.00)	41 (70.70)	17 (29.30)	38 (65.50)	13 (22.40)	15 (25.90)
Male	68	66 (97.10)	50 (73.50)	26 (38.20)	50 (73.50)	20 (29.40)	14 (20.60)
P		0.498	0.723	0.292	0.329	0.373	0.483
Age (years)							
<65	74	73 (98.60)	51 (68.90)	23 (31.10)	48 (64.90)	18 (24.30)	14 (18.90)
>65	52	51 (98.10)	40 (76.90)	20 (38.50)	40 (76.90)	15 (28.80)	15 (28.80)
P		1.000	0.323	0.390	0.147	0.570	0.192
Onset of symptoms before CT (days)							
<5	53	52 (98.10)	38 (71.70)	17 (32.10)	38 (71.70)	9 (17.00)	10 (18.90)
>5	49	48 (98.00)	39 (79.60)	22 (44.90)	39 (79.60)	19 (38.80)	19 (38.80)
P		1.000	0.354	0.183	0.354	0.014	0.026
Comorbidity							
<2	47	46 (97.90)	36 (76.60)	21 (44.70)	37 (78.70)	13 (27.70)	15 (31.90)
>2	55	54 (98.20)	41 (74.50)	18 (32.70)	40 (72.70)	15 (27.30)	14 (25.50)
P		1.000	0.810	0.216	0.483	0.965	0.471
Mortality							
Discharged	109	107 (98.20)	75 (68.80)	35 (32.10)	72 (66.10)	28 (25.70)	21 (19.30)
Dead	17	17 (100.00)	16 (94.10)	8 (47.10)	16 (94.10)	5 (29.40)	8 (47.10)
P		1.000	0.039	0.227	0.019	0.770	0.025

P is significant at the *P*<0.005 (Chi-Square tests). CT: Computer tomography

Table 3: Distribution of extrapulmonary findings in patients with coronavirus disease-19 pneumonia

Variable	*n*	Lymph node, *n* (%)	Pleural effusion, *n* (%)	Pleural thickening, *n* (%)
Gender				
Female	58	9 (15.50)	11 (19.00)	14 (24.10)
Male	68	8 (11.80)	6 (8.80)	12 (17.60)
P		0.539	0.097	0.370
Age (years)				
<65	74	9 (12.20)	6 (8.10)	9 (12.20)
>65	52	8 (15.40)	11 (21.20)	17 (32.70)
P		0.602	0.035	0.005
Onset of symptoms before CT (days)				
<5	53	7 (13.20)	8 (15.10)	11 (20.80)
>5	49	9 (18.40)	8 (16.30)	15 (30.60)
P		0.474	0.864	0.254
Comorbidity				
<2	47	7 (14.90)	6 (12.80)	10 (21.30)
>2	55	9 (16.40)	10 (18.20)	16 (29.10)
P		0.839	0.453	0.367
Mortality				
Discharged	109	14 (12.80)	13 (11.90)	19 (17.40)
Dead	17	3 (17.60)	4 (23.50)	7 (41.20)
P		0.701	0.245	0.047

P is significant at the *P*<0,005 (Chi-Square tests). CT: Computer tomography

76.2% had peripheral-central involvement, and none had pure central involvement.

The predominant CT findings mainly were ground-glass opacity and consolidation with a peripheral, bilateral, and widespread distribution similar to those previously reported.[8,19-25] The development of consolidations was associated with the progression of the disease and was a warning sign for a serious course that was similar to those previously reported.[5,20] Other unusual imaging findings included mediastinal and hilar lymph nodes, pleural effusion, pleural thickening, pneumothorax, pericardial effusion, cavitation, and pulmonary emphysema.[5,6,7,25] The presence of pleural effusion and pneumothorax was considered to be an important indicator of poor prognosis.[5] Unlike other studies, we found no association between pleural effusion and prognosis.

Table 4: Logistic regression analysis for 30 days mortality among patients with coronavirus disease-19 pneumonia

	B	SE	Wald	df	*P*	Exp(B)	95% CI for EXP(B) (lower-upper)
Gender	−0.048	0.523	0.008	1	0.927	0.953	0.342-2.655
Age (years)	0.051	0.017	9.073	1	0.003	1.052	1.018-1.087
Duration of symptoms (<5 days)	1.296	0.612	4.492	1	0.034	3.656	1.102-12.125
The number of comorbidities	0.471	0.172	7.509	1	0.006	1.601	1.143-2.242
Lobe score (0-25)	0.169	0.049	11.693	1	0.001	1.184	1.075-1.075
Vascular enlargement	2.107	1.050	4.023	1	0.045	8.222	1.049-64.435
Consolidation	−1.981	1.051	3.552	1	0.059	0.138	0.018-1.082
Comorbidities (≥2)	−1.611	0.672	5.744	1	0.017	0.200	0.053-0.746

P is significant at the *P*<0.05. CI: Confidence interval, SE: Standard error

One striking result of our study was that two-thirds of patients had vascular enlargement [Figure 2]. However, we found that consolidation and vascular enlargement were associated with a poor prognosis. Among the radiological findings of COVID-19 pneumonia, there are only a few studies reporting the incidence of vascular enlargement and its effect on prognosis. Recent studies show that vascular abnormalities can also be observed on chest CT. In addition, some authors attached diagnostic and prognostic significance to these findings.[6] Our study is important in that it shows that vascular enlargement has an effect on the course of the disease and should be taken into consideration on prognostic evaluation.

Guan *et al*. reported a mortality rate of 1.4%, while Huang *et al*. reported a mortality rate of 14%.[3,15] In our study, since asymptomatic or mild patients were treated at home, these patients did not undergo thorax CT; therefore, no history of the disease existed. We can explain the high mortality rates (13.5%) based on the fact that the majority of patients were inpatients whose COVID-19 pneumonias were more severe.

This study has some important limitations. First, our study is a single-center retrospective study. Second, the data were produced based on clinical histories. The fact that the histories were taken by different physicians and also a failure of patients to remember the exact dates of the onset of the symptoms might have inevitably affected our evaluations. Third, only baseline chest CTs were evaluated. Radiological diagnostic evaluations were not performed with control CTs achieved at intervals during the disease.

Conclusion

It is important to take account of lesions noted on radiological images and the extent of lesions of the COVID-19 along with age, duration of symptoms, and the number of comorbidities to predict prognosis. More comprehensive and systematic studies are needed to fully clarify the diagnostic and prognostic effects of radiological findings with serial chest CTs during the course of the disease, especially considering the importance of lobes score and the vascular enlargement lesion.

Figure 2: A 36-year-old man with coronavirus pneumonia (COVID-19). Axial computed tomography image shows ground-glass opacity, air bronchogram, and significant vascular enlargement (white arrow)

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Conflicts of interest

There are no conflicts of interest.

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