

Differential diagnosis of COVID-19 from community acquired pneumonia by CT scan and follow-up

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Abstract

Objective

Coronavirus disease-19(COVID-19) is the most serious infectious disease outbreak in the world at present. Accurate diagnosis of this disease in clinic is very important. this study aims to improve the differential ability of COVID-19 and other community acquired pneumonia(CAP) by CT, and to evaluate the short-term prognosis of patients.

Methods

The clinical and imaging data of 165 COVID-19 and 118 CAP patients diagnosed in seven hospitals in Anhui Province, China from January 21, 2020 to February 28, 2020 were retrospectively analyzed.

Results

The sensitivity and specificity of age, white blood cell count, and ground glass shadow in the diagnosis of COVID-19 were 92.7% and 66.1%, respectively. Pulmonary consolidation, fiber cord, and bronchial wall thickening were used as indicators to exclude COVID-19. The sensitivity and specificity were 78.0% and 63.6%, respectively. The follow-up results showed that 67.8% (112/165) of the cases of COVID-19 had abnormal changes in lung residual levels, and the pulmonary sequelae of patients over 60 years of age became more severe with age.

Conclusion

CT combined with clinical conditions, density of lung lesions, morphological features and other associated signs, has a high accuracy for the early diagnosis of COVID-19 and the differential diagnosis of CAP. patients with COVID-19 infection over 60 years have poor prognosis.

1. Introduction

Coronavirus disease-19(COVID-19) is an acute respiratory infectious disease caused by new coronavirus infection [1]. As of April 17, 2020. a total of 2213587 cases were diagnosed worldwide. Common signs of coronavirus after infection are respiratory symptoms such as fever, cough, shortness of breath, dyspnea and so on [2-4]. In more serious cases, infection can lead to pneumonia, severe acute respiratory syndrome, renal failure, and even death. No specific treatment for diseases caused by the new coronavirus is currently available[5].

The gold standard for COVID-19 diagnosis is positive for new coronavirus nucleic acid test [6-7], but due to the hysteresis of the test results or "false negatives" in the report, some patients cannot be diagnosed and treated in time.COVID-19 has certain imaging characteristics in lungs .chest CT examination is an important method for clinical diagnosis of COVID-19. During the current outbreak of COVID-19, early detection of lesions is very important for early isolation and treatment, and to prevent the spread of

disease. Previous studies have mostly focused on the imaging manifestations and changes of COVID-19 [8-10]. The disease needs to be distinguished from many diseases in imaging, especially the community-acquired pneumonia (CAP). However, a large number of comparative studies on imaging in this area are still lacking.

Therefore, the purpose of this study is to compare the clinical features and CT imaging manifestations of COVID-19 with community-acquired pneumonia, to explore the value of CT in the diagnosis and differential diagnosis of COVID-19, and to evaluate the short-term prognosis of the two types of pneumonia.

2. Materials And Methods

2.1 Patient cohort

From January 21 to February 28, 2020, the clinical data of 165 patients with COVID-19 from 7 hospitals in Anhui Province, China were reviewed, including 76 males and 89 females, aged 5 to 91 years, with an average of 45.06 ± 17.58 years old. The diagnosis complies with the Guidelines for the Diagnosis and Treatment of New Coronavirus Pneumonia (Seventh Edition) formulated by the National Health Committee of the People's Republic of China [11]. a total of 118 cases of CAP were selected from patients admitted to the First Affiliated Hospital of the University of Science and Technology of China for pneumonia in the same period. The pathogens or pathogens were confirmed in all patients by the RT-PCR detection of sputum throat swab, and blood or other pathogenic tests. There were 48 males and 70 females, aged 1 to 76 years, with an average of 15.59 ± 21.37 years. CT images and clinical data were collected in all patients. The inclusion and exclusion process of patients is shown in Figure 1, and the results of CAP-RPP are shown in Figure 2.

2.2 CT examination

CT scan was performed in all patients with 64- slice multi-detector row CT scanners (CT System in seven hospitals are Toshiba Aquilion-64, Philips Brilliance-64, GE LightSpeed-64, Siemens Sensation-64, and Neusoft Viz-64).The acquisition parameters were as follows: tube voltage 100–130 kV, tube current 120–350 mA, pitch 0.6–1.375, FOV 350–400 mm, Image thickness 1.25 –2.5 mm.All images are displayed and stored in PACS system.

2.3CT image evaluation

CT images of patients in the COVID-19 and CAP groups were performed by 3 experienced radiologists (working in radiography for > 5 years). Use double-blind method to read independently. Carefully observe and record the location, shape, number, size, burr and extent of the lesion. If the diagnosis is inconsistent, the consensus reached by the 3 experts shall prevail.

2.4 Statistical analysis

The measurement data is expressed by $\bar{x} \pm s$, the comparison between groups is expressed by independent sample t test; the count data is expressed by percentage(%), and the comparison between groups is expressed by χ^2 test. Correlation analysis was used to examine the relationship between age and the size of the lung lesions, the number of involved lobes, and the CT findings of patients with COVID-19. SPSS 20.0 software package was used for the above statistical analysis.

3. Result

3.1 Study Population Characteristics

The baseline data and clinical manifestations of the two groups of with are shown in Table 1. The differences in age, white blood cell (WBC) and the presence or absence of underlying disease in the lungs of the two groups of patients were significant. $\chi^2 = 8.03, P < 0.001$; $t = 4.62, P = 0.003$; $\chi^2 = 21.72, P < 0.001$.

3.2 CT imaging

CT findings of chest in patients with COVID-19 and CAP group onset 3-7 days were showed in Table 2. The ground glass opacities (GGO) on chest CT images were found in 140 cases (84.8%) of in COVID-19 group. The typical lesions early in the COVID-19 group were shown as single or multiple small rounds. In this group, 53 cases (32.1%) were found, 87 cases (52.7%) of ground-glass-like density shadows with small spot, large piece or fusion (Figure 3). In the CAP group, there were 47 cases (39.8%) of ground glass shadow in the lungs, 71 cases (60.2%) showed consolidation, and the density difference between the two groups was significant ($\chi^2 = 48.75, P < 0.001$). In the COVID-19 group, 54 cases (32.8%) of "paving stone" sign were also observed, which was mainly characterized by interlobular septal thickening (Fig.4) were different from the subpleural reticular or honeycomb changes of 34 cases (28.8%) in the CAP group. Eight (4.8%) patients in the COVID-19 group showed "walking" lung lesions (Figures 5-6).

In addition to some fresh exudative inflammatory lesions mentioned above, chest CT in the CAP group is often accompanied by chronic obstructive manifestations such as emphysema, bullae, and "mosaic" signs or small airway obstructive changes. In the CAP group, 68 cases (57.6%) with fibrous cords or pulmonary texture aggregates were significantly higher than those in the COVID-19 group (5 cases, 3.1%) ($\chi^2 = 107.14, P < 0.001$); the bronchial wall thickening was also in the CAP group (37 cases, 31.4%) and 18 case (10.1%) was seen in the COVID-19 group, the difference between the two groups was significant ($\chi^2 = 18.4, P < 0.001$). In cap group, there were 12 cases (10.2%) with small cavities and 8 cases with pulmonary bullae, which were significantly higher than those in COVID-19 group.

3.3 The relationship between clinical characteristics and imaging manifestations

The total number of lung lobes involved in the COVID-19 and CAP groups was 384 and 257, respectively. The single lesion in the COVID-19 was significantly higher than that in the CAP group ($\chi^2 = 8.38, P = 0.03$), and the multi-leaf multi-foci of the CAP were significantly higher than the COVID-19 group ($\chi^2 = 6.68, P =$

0.01). The lesions in both groups were mainly in the middle and outer of lobes. There were 148 cases (89.7%) of COVID-19 group located in the outer or outer zone, and 62 cases (52.5%) of cap. There was a significant difference between the two groups ($\chi^2 = 49.6, P < 0.001$). Statistics showed that there was a positive correlation between the age of onset and the number of involved leaf segments ($r = 0.62, P < 0.001$).

Among the above clinical and imaging manifestations, the age factor, the total number of white blood cells, and the ground glass opacities of the lung lesions have higher sensitivity as indicators for the diagnosis of COVID-19, But the specificity is not high (Table 3). Intrapulmonary lesions show consolidation, with fibrous cords or texture accumulation in the lungs, and thickening of the bronchial wall are the characteristics of the CAP group, which become the anti-indications of COVID-19 and have a high sensitivity to the exclusion of COVID-19 (Table 4).

3.4 CT follow-up of COVID-19

A total of 135 cases in COVID-19 group were reexamined 3-7 days after the first CT examination, 32 cases (23.70%) showed enlargement of lesion size and increase of the number, which were classified as progressing, 25 cases (18.5%) were stable, and 78 cases (57.8%) were improvement.

All patients with COVID-19 underwent CT Re-examination one month after treatment, , and 15 cases (15.6%) showed no abnormalities in both lungs at the time of reexamination [Figures 7-8]; the rest 87 cases (52.7%) showed localized strip shadow, 43 cases (26.1%) of extensive fibrosis, 10 cases (6.1%) of limited flaky shadow, 6 (3.6%) cases of wide strip shadow [4 cases (2.4%) of diffuse grid shadow (Figure 9-10)]. The relationship between age and prognosis shows that in patients with COVID-19 <60 years of age, the late CT changes have no significant relationship with age; in patients over 60 years of age, the CT sequelae changes with increasing age.

4. Discussion

At present, retrospective studies on various aspects of COVID-19 are being further developed. Due to the strong infectivity of COVID-19, the source of the pathogen is unknown, no specific treatment method, and the mortality rate is high [12], so the early diagnosis of COVID-19 a challenge for us. Correct and timely diagnosis is of great significance for the prognosis and prevention of dissemination. Due to the delayed laboratory etiology results and limited sensitivity, there is still controversy for early clinical diagnosis [13]. Thoracic imaging plays an important role in early diagnosis. This study believes that in the case of an epidemic area, the key to early imaging diagnosis is to distinguish it from other CAP.

The data were similar to most clinical observations. [14-16] COVID-19 group age was mostly young adults, 46 cases (71.9%) were <60 years old, and only 7 cases (15.2%) in the CAP group, It does not comply with the general law of spread of infectious diseases, that is, children and the elderly are often susceptible groups, Young adults had the strongest resistance to infectious diseases and the incidence rate should be low. 72314 cases of Chinese Center for Disease Control and Prevention showed that the incidence rate of

China under 10 years old was less than 1%[17].The incidence rate of children is low, clinical manifestation is light, and infectious is slight. This may be related to cross immunity of antibodies produced by children's vaccination and coronavirus. The high incidence rate of young adults can't exclude the possibility of more virus contact and infection opportunities due to more social interactions. Of course, further studies on epidemiology and pathogenesis are needed. Fever was the prominent clinical manifestation in both groups, but the degree of temperature rise was more obvious in COVID-19 group than that in cap group. In the early stage of the disease (within 7 days), the total number of leukocytes in the observed cases of COVID-19 was normal or low ($< 4 \times 10^9 / L$), or showed a decreasing trend, similar to that reported in the literature [18], which may be caused by the decrease of lymphocytes in the first few days after the disease. The symptoms of muscle soreness and fatigue in COVID-19 group were significantly higher than those in cap group, while the symptoms of expectoration in the latter group were significantly higher than those in the former group, 62 cases (52.5%) and 39 cases (23.6%) in cap group and COVID-19 group, respectively, which may be related to the fact that cap is prone to produce more purulent secretion due to bacterial infection[19]. The results showed that the incidence of heart disease, hypertension, chronic lung disease and diabetes in cap group was significantly higher than that in COVID-19. The average age of patients with comorbidities in COVID-19 group and cap group was 68.8 years (range 39-93 years) and 63.25 years (range 49-76 years), respectively, suggesting that the majority of patients with comorbidities in the two groups were older than 60 years old.

The chest CT changes of COVID-19 usually showed ground glass opacities shadow of different size 3-4 days after clinical onset. The incidence of this group was 78.2% (129 cases). The size and shape of COVID-19 ground glass opacities shadow are various, among which the most typical is round or quasi round ground glass shadow, accounting for 32.1% (53 cases) in this group, most of which are the early changes of young people. The statistics of this group showed that the single lesion of COVID-19 was significantly higher than that of cap group, which may be related to the early stage of COVID-19. With the progress of the disease, the area of ground glass opacities shadow in some patients has expanded, and gradually developed into ground glass shadow with multiple patches, large fusion or large and small pieces coexisting, but the density change is relatively small, which is in contrast with the rapid consolidation in the progress of CAP pneumonia, while the area expansion is relatively not obvious. Of course, there are also some light patients with lung lesions area no longer expanded until absorption. The pathological basis of ground glass changes is mainly related to the local severe pulmonary edema, hyaline membrane formation and fluid exudation in the alveolus cavity in the early lesions, but little to the infiltration of polynuclear and monocyte. Another 32.7% (54 cases) of COVID-19 showed fine reticular shadow overlapped in ground glass shadow, which may be related to the alveolar edema in the lung lesion area of COVID-19 and the slight thickening of alveolar septum with infiltration of monocyte, lymph and plasma cells[20]. Because some CAP patients also showed ground glass opacities shadow (47 cases, 39.8%), which overlapped with the change of COVID-19 lung disease, the imaging manifestations must be combined with clinical and other lung changes.

In CAP group, the new exudative inflammatory lesions were often accompanied by obvious fibrous components or texture aggregation and cord adhesion in other parts of the lung. In this group, the

incidence was 57.6% (68 cases), and 31.4% (37 cases) with thickening of bronchitis or peribronchitis and blurring of the outer edge, suggesting that these patients had experienced the process of lung inflammation in the past, and left some chronic inflammation or later changes, This is quite different from the acute onset, rapid progress and multiple onset of lung inflammation of COVID-19. Therefore, this study suggests that the lung with fibrous cord and bronchial wall thickening can be used as a counter indication to exclude COVID-19. In addition, a certain proportion of emphysema, pulmonary bullae, reticular or honeycomb changes under the pleura and "mosaic" sign and/or small cavity shadow in the consolidation area were observed in cap group. In conclusion, the diversity of lung lesions and the coexistence of new and old lesions in cap group are helpful to distinguish from COVID-19.

In this group, 6 patients with COVID-19 underwent chest CT Reexamination about one week after the onset of the disease, the lesions showed "wandering" characteristics, which may indicate the heterogeneity of pathological changes in different lung areas, that is, the early changes and the changes in the organic phase of diffuse alveolar injury can appear in different segments at the same time, which is more common in young patients. Due to the small number of cases in this group, whether it has a good diagnostic specificity remains to be further confirmed.

The results of this study showed that there was a positive correlation between the age and the size of lesion and the total number of segments involved in the lesion in the COVID-19 group. The correlation coefficient between the age and the size of lesion was 0.522, $P < 0.001$, and the correlation coefficient between the age and the total number of segments involved was 0.531, $P < 0.001$. In this group, the range of lesions in the first visit of the elderly patients was significantly larger than that in the young patients, and the number of involved segments was also significantly higher than that in the latter. This may be due to the rapid development of the disease in the elderly infected patients. The first CT scan has involved multiple segments, which is also one of the reasons affecting the prognosis of the patients.

The follow-up of COVID-19 group in the later period showed that the patients aged more than 60 years old had a lot of changes left in the lung in the later period, and the most serious manifestation was extensive fibrous cord shadow in the lung. In this group, 32 patients (19.4%) were all over 60 years old, suggesting that the prognosis of the patients over 60 years old was poor. The follow-up of 2-3 months showed that the remaining changes in the lung could still be absorbed, but the absorption was slow.

5. Conclusion

At present, the most widely used clinical diagnosis of COVID-19 is the positive detection of new coronavirus nucleic acid, but the rapid spread and strong infectivity of COVID-19, the detection reagent can not meet the clinical application in time. imaging examination, especially CT examination plays an important role in the early diagnosis and screening of COVID-19, At present, most of the early diagnosis of COVID-19 is based on imaging. Therefore, for the diagnosis of COVID-19, the accuracy of differential diagnosis between COVID-19 and cap should be improved by closely combining the epidemiological history, the clinical situation of patients and the changes of lung image.

Declarations

Ethics approval and consent to participate

Acquisition of all clinical images was granted by subject verbal consent. The images in this paper are obtained from 7 research centers. These are repositories of anonymised images accessible locally for educational purposes and no identifiable information is stored or available. Ethical approval for their use in publication was therefore deemed unnecessary.

Consent for publication

Written informed consent for publication from the patient was obtained

Availability of data and materials

Extra data is available by emailing to Kai-Cai Liu (ahsllkc@163.com) on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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None

Authors' contributions

Kai-Cai Liu: Data curation, Writing - original draft. Ping Xu and Wei-Fu Lv : Conceptualization, Methodology, Writing - review & editing, Supervision. Lei Chen, Xiao-Hui Qiu, Jin-Long Yao, Jin-Feng Gu, Bo Hu and Wei-Wei: Data curation

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Tables

Table 1. baseline data and clinical manifestations between COVID-19 and CAP patients

	COVID-19	CAP	t/x ²	p
Gender			0.91	0.34
men	72	48		
women	83	70		
Age (year)				
Mean age	45.06±17.58	15.59±21.37	8.03	<0.01
<20	4	52		
20-40	57	8		
40-60	72	10		
>60	32	48		
Fever			0.52	0.47
Yes	146	101		
No	19	17		
Chest tightness			0.25	0.62
Yes	31	25		
No	134	93		
Muscle soreness			4.76	0.03
Yes	48	21		
No	117	97		
Fatigue			5.11	0.02
Yes	52	23		
No	113	95		
Cough			2.08	0.15
Yes	85	71		
No	80	47		
Expectoration			25.04	<0.01
Yes	39	62		
No	126	56		
Headache			1.94	0.16

Yes	10	3		
No	155	118		
Chills			2.76	0.10
Yes	21	8		
No	144	110		
Diarrhea			0.37	0.54
Yes	6	6		
No	159	112		
WBC $\times 10^9$	9.61 \pm 5.11	5.91 \pm 3.02	4.62	<0.01
≤ 9.5	153	67		
>9.5	12	51		
C-reactive protein (mg/L)	27.81 \pm 34.50	46.91 \pm 56.67	1.81	0.078
≤ 8	86	14		
>8	79	111		
Neutrophil proportion %	68.13 \pm 15.28	61.69 \pm 23.62	1.76	0.08
≤ 75	104	62		
>75	61	56		
ESR (MM/h)	32.45 \pm 24.32	57.44 \pm 29.81	1.99	0.08
≤ 15	52	26		
>15	113	92		
Calcitonin (mg/ml)	0.51 \pm 0.69	0.39 \pm 0.38	0.53	0.61
≤ 0.5	32	61		
>0.5	133	57		
Past Medical History				
Heart disease			2.37	0.12
Yes	4	7		
No	161	111		
Hypertension			2.67	0.10
Yes	17	20		

No	148	98		
COPD			21.72	<0.01
Yes	6	25		
No	159	93		
Diabetes			0.06	0.81
Yes	5	3		
No	160	115		

ESR=erythrocyte sedimentation rate, WBC=white blood cell, COPD=chronic obstructive pulmonary disease

Table 2. Comparison of various chest CT manifestations in COVID-19 and CAP patients

	COVID-19	CAP	χ^2	P
Pathological morphology and density				
Round ground glass shadow	53	2	40.68	<0.001
Small ground glass shadow	35	27	0.11	0.74
Large ground glass shadow	23	13	0.53	0.47
Large and small mixed ground glass shadow	18	5	4.1	0.04
Ground glass shadow and solid shadow	11	7	0.20	0.66
Small patch consolidation	12	31	19.27	<0.001
Large and small mixed patch consolidation	13	33	0.40	0.53
Other imaging signs				
Lesion wandering	22	3	9.05	0.002
Fibrous tissue	5	68	107.14	<0.001
air bronchogram	52	46	1.69	0.19
Bronchial wall thickening	18	37	18.37	<0.001
Paving stone sign	54	34	0.49	0.48
Pulmonary cavity	0	12	17.52	<0.001
lung bullae	0	8	11.51	<0.001
Total number of lobes involved				
Single leaf single shot	48	17	8.38	0.03
Single leaf multiple occurrence	12	9	0.01	0.91
Multilobed multiple lesions	105	92	6.68	0.01
Other chest diseases				
Enlargement of heart shadow	1	5	4.37	0.04
Lymphadenopathy	1	18	23.57	<0.001
Pleural effusion	3	26	30.57	<0.001
Pleural thickening	2	31	41.94	<0.001

Table 3. statistical prediction of some clinical and CT features for the diagnosis of COVID-19

Clinical and CT features	Accuracy (%)	sensitivity(%)	specificity(%)	positive predictive value(%)	negative predictive value(%)
20< age <60	68.9 [195/283]	59.4 [98/165]	82.2 [97/118]	82.4[98/119]	59.1[97/164]
WBC<9.5	68.2 [193/283]	91.5 [151/165]	69.5 [82/118]	80.7[151/187]	85.4[82/96]
GGO	62.5 [177/283]	63.6 [105/165]	61.0 [72/118]	69.5[105/151]	54.5[72/132]
comprehensive	81.6 [231/283]	92.7 [153/165]	66.1 [78/118]	79.3[153/193]	86.7[78/90]

WBC=white blood cell GGO=ground glass opacity

Table 4. statistical prediction of the diagnosis of CAP by some CT signs

CT features	Accuracy (%)	sensitivity(%)	specificity(%)	positive predictive value(%)	negative predictive value(%)
Consolidation	65.7 [186/283]	60.2 [71/118]	69.7 [115/165]	58.7[71/121]	71.0[115/162]
Fibrous tissue	80.1 [228/283]	57.6 [68/118]	97.0 [160/165]	93.2[68/73]	97.0[160/165]
Bronchial wall thickness	65.0 [184/283]	31.4 [37/118]	89.1 [147/165]	67.3[37/55]	64.5[147/228]
comprehensive	69.6 [197/283]	78.0 [92/118]	63.6 [105/165]	63.0[92/146]	80.2[105/131]

Figures

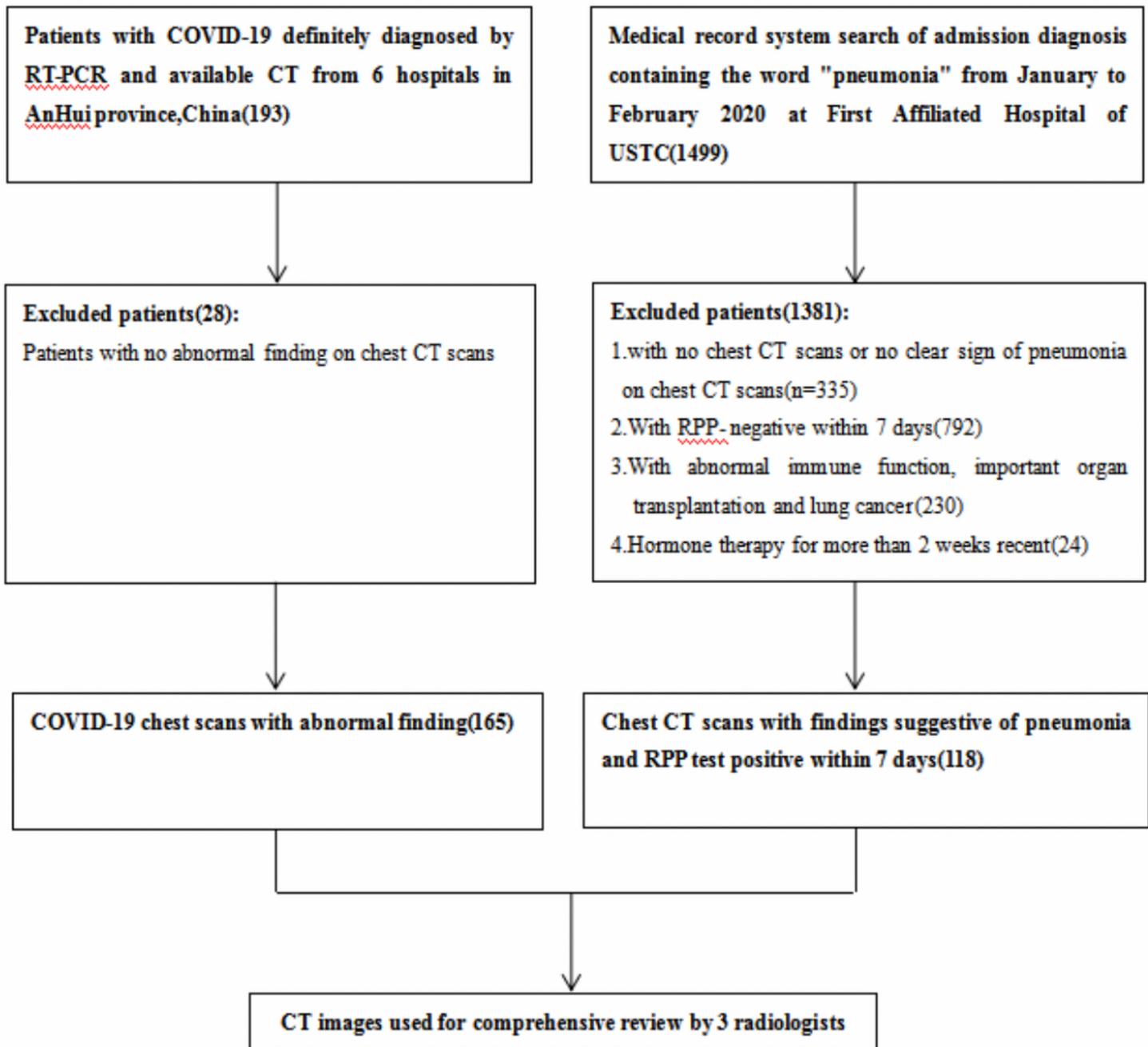


Figure 1

Flow diagram illustration.

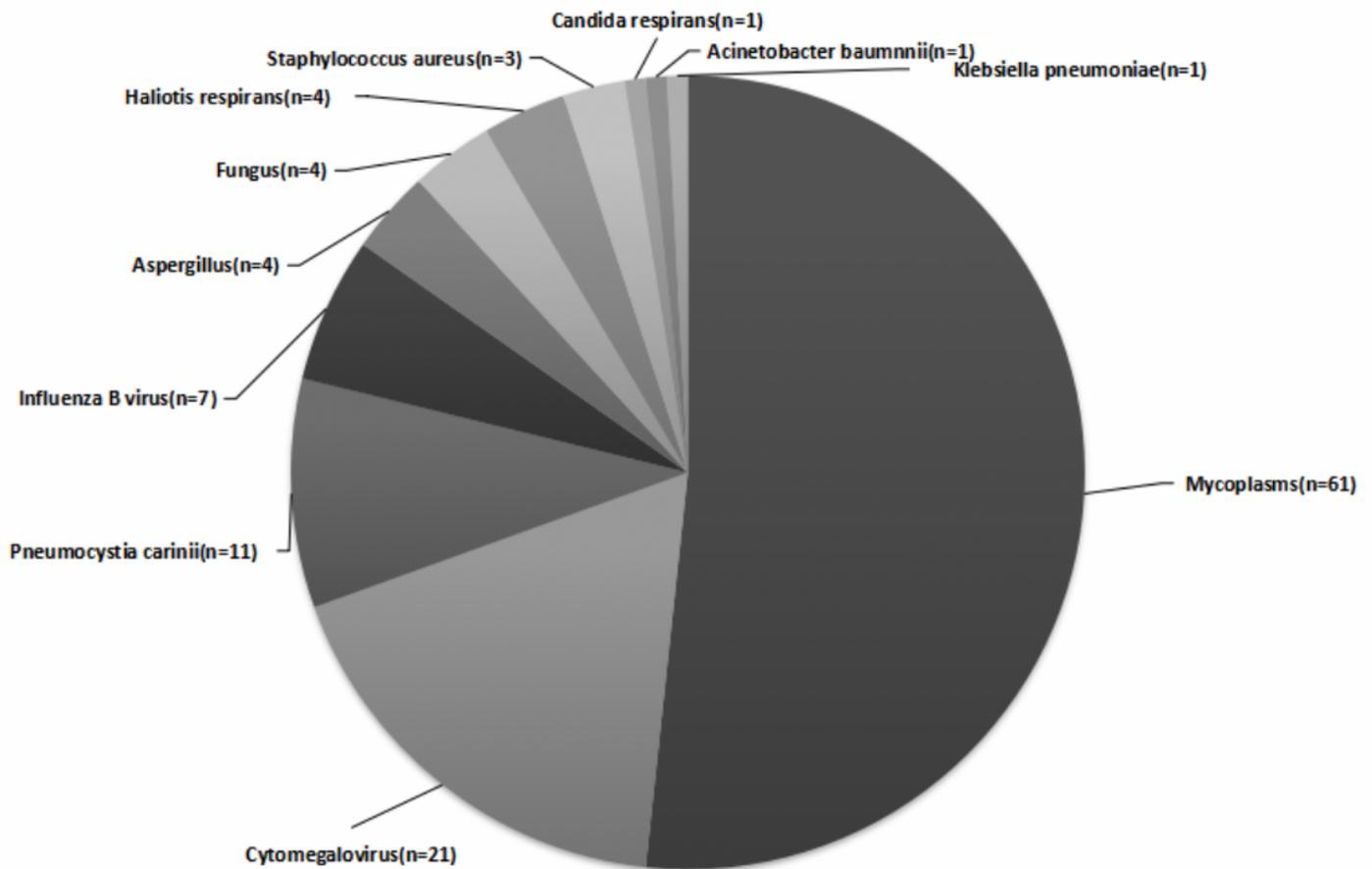


Figure 2

Distribution of pathogens in CAP group based on RPP experiment



Figure 3

CT features of coronavirus disease-2019 A. CT images of a 45 year old female patient showed multiple ground glass shadows of both lungs, partially fused B. CT images of a 42 year old male patient showed paving stone sign under the pleura of the right lung C-D. A 56-year-old female patient's CT was reviewed 7 days later, showing that the original consolidation of both lungs was diminished, and another ground glass-like density shadow appeared in the middle lobe of the right lung, and the lesions in the lungs showed "walking" E-F. A 32-year-old female patient reexamined after 10 days of treatment. CT showed that multiple lung lesions disappeared G-H. a 68-year-old female patient, was reexamined after 15 days of treatments. CT showed that the diffuse lesions of both lungs were absorbed into extensive fibrosis.

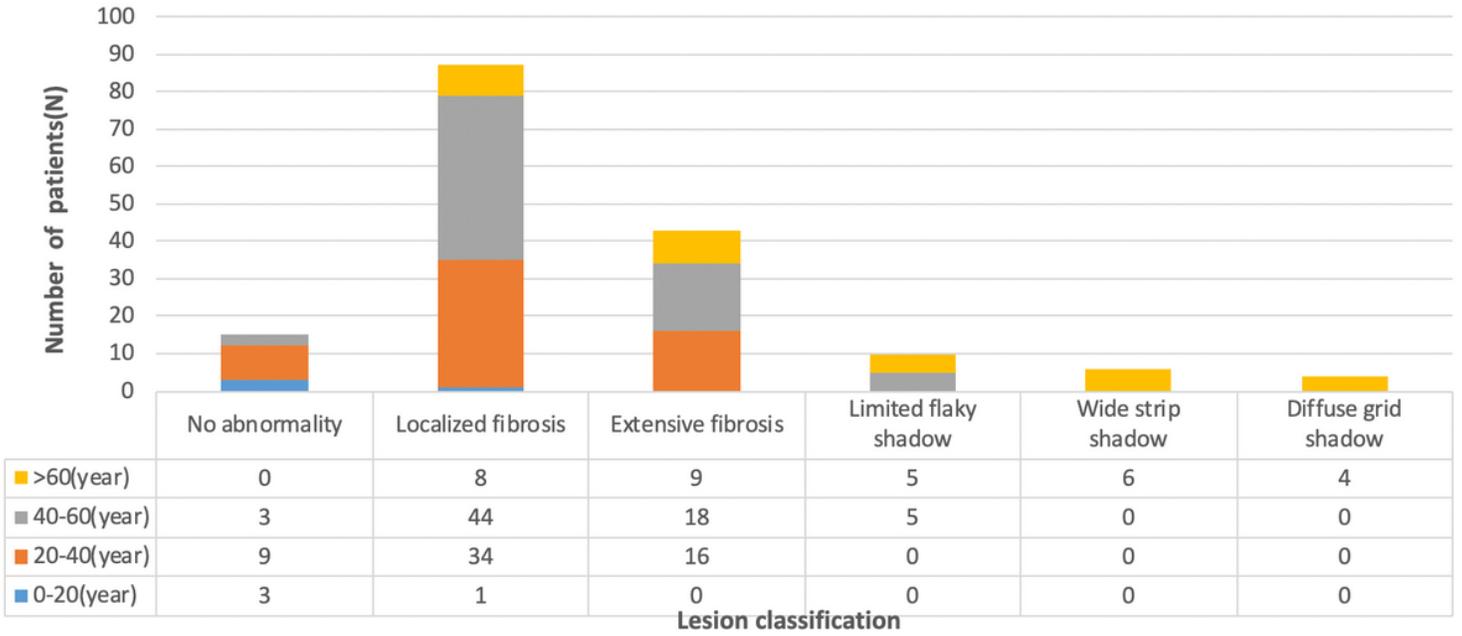


Figure 4

The relationship between the age and the prognosis of COVID-19 patients in this group.