Role of pulmonary circulation assessment in CT imaging in evaluating the severity and tendency of severe and critical COVID-19 pneumonia

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Research Article

Keywords: COVID-19, pneumonia, pulmonary circulation, Computed Tomography

Posted Date: May 29th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-32243/v1>

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Abstract

Objective: To investigate the value of changes of pulmonary circulation in CT imaging in evaluating the severity and tendency of 2019 novel coronavirus disease (COVID-19) pneumonia.

Methods: This retrospective study analyzed 99 severe and critical COVID-19 pneumonia patients including the 47 improved cases and 52 dead cases. Demographic data, laboratory findings, comorbidities, and CT imaging features including the diameters of pulmonary vein (PV), pulmonary artery (PA) and ascending aorta were collected and assessed.

Results: The PV diameters of the deceased patients were larger than recovered patients in the severe phase. Compared with the severe phase in the improvement group, the diameters of the pulmonary veins during the improved phase were smaller, and the total CT scores were significantly decreased ($p < 0.001$). Instead, there was no significant difference in the ratio of main PA to aorta diameter between the recovered group and the deceased group, nor did the self control of the recovered group and the deceased group ($p > 0.05$). Construction of a ROC curve yielded an optimal cut-off value of the PV diameters for prediction of survival ($p < 0.05$).

Conclusion: The changes of the PV diameters might indirectly reflect the activity of pulmonary inflammation and cardiac insufficiency. Pulmonary manifestations of severe and critical COVID-19 pneumonia might be related to myocardial injury and cardiac insufficiency, especially accompanied by dilated PVs. Evaluation of changes in pulmonary circulation by chest CT images may be considered as a useful tool for determining the severity, fatal outcome and tendency of COVID-19.

Key words: COVID-19, pneumonia, pulmonary circulation, Computed Tomography

Introduction

Key Points:

- The changes of the pulmonary vein diameters might indirectly reflect the activity of pulmonary inflammation and cardiac insufficiency.
- The dilation of pulmonary vein was a predictor of poor clinical outcomes and tendency of COVID-19.
- Pulmonary manifestations of severe and critical COVID-19 pneumonia might be related to myocardial injury and cardiac insufficiency.

Since December 2019, the ongoing coronavirus disease 2019 (COVID-19) has spread globally, and evolved into a pandemic [1]. In almost four months, coronavirus disease 2019 (COVID-19) has resulted in considerable morbidity and mortality all over the world. As of 7:10pm CEST, 14 May 2020, it has spread

to more than 200 countries or areas around the world, with a total of 4,258,666 confirmed cases and 294,190 deaths globally, including 84,464 confirmed cases within China[2].

Some studies have found that COVID-19 could cause a series of complications such as acute respiratory distress syndrome (ARDS), respiratory failure, acute heart injury, renal failure and multiple organ dysfunction syndrome [3,4]. For severe or critical patients, severe complications such as ARDS or cardiac injury could increase the risk of mortality in patients with COVID-19 [5]. However, to the best of our knowledge, pulmonary circulation in these patients has not yet been reported. Pulmonary circulation can be affected by myocardial involvement or pulmonary inflammation. In this study, we did a comprehensive evaluation clinical, laboratory, and radiological characteristics of 52 deceased patients and 47 recovered patients with COVID-19 infection so as to examine the potential association between pulmonary vascular changes and disease severity and the value of pulmonary circulation in evaluating the severity and tendency of COVID-19 pneumonia.

Materials And Methods

Patients

This retrospective, observational study was performed at the Tongji Hospital ,Tongji Medical College, Huazhong University of Science & Technology, Wuhan City, China, which is one of the designated hospitals by Chinese government to treat severely or critically patients with COVID-19 and was approved by the Ethics Commission (IRB ID: TJ-C0200108). The patient consent in this retrospective study was considered as exemption. The patients with COVID-19 enrolled in this study were diagnosed according to World Health Organization interim guidance [6]. All patients were confirmed to be positive for COVID-19 from nucleic acid testing using throat or nasopharyngeal swab specimens. The patients were diagnosed as severe cases according to the diagnosis and treatment program (6th trial version) published by the National Health Commission of the People's Republic of China [7], the diagnostic criteria for adult severe cases are any of the following: breathlessness with respiratory rate ≥ 30 breaths/min; $SpO_2 \leq 93\%$ on room air; $PaO_2/FiO_2 \leq 300$ mmHg. And the diagnostic criteria for critical cases are any of the following: respiratory failure and require mechanical ventilation; shock; other organ failure requires ICU monitoring treatment. Besides, some patients whose CT images had too much motion artifacts to be measured were excluded. The recruitment period was from January 14 to February 28, 2020. Finally, a totally of 99 severe and critical patients (mean age, 60.53 ± 15.00 years; 70% [69/99] male) were enrolled in this retrospective cohort study. According to the outcome of the disease, patients were divided into two groups: the improvement group (47 cases) and the deceased group (52 cases). For patients whose condition improved, the critical period and the improvement period were evaluated. The medical records of COVID-19 patients including demographic, clinical, laboratory, and outcome data were collected and extracted, and the disease classification & progression and clinical characteristics of these patients were assessed and collected by two doctors (KYL and HLZ).

CT Protocol

All patients underwent non-enhanced chest CT scanning using standard-dose chest CT protocols (GE Healthcare, Philips, or Toshiba Medical Systems) in the supine position during end-inspiration. High-resolution computed tomography (HRCT) could overcome heart beat artifacts, and cases with excessive artifacts were excluded. The main scanning parameters were as follow: tube voltage =80- 120 kVp, automatic tube current modulation(60-300 mA), pitch = 0.984:1, matrix = 512×512, slice thickness = 1.25mm, which were all selected according to the machine model.

CT Review

For the recovered group, two CT scans for each patient were collected, including the CT in the severe phase and in the recovered phase. In addition, the first available CT after symptoms onset and the last CTs before death were collected for the deceased group. The radiologic assessments included vascular measurements, chest CT imaging features and CT score, which were independently assessed and counted by two chest radiologists (HXG and QJH, with 20 and 10 years of work experience, respectively). Final decisions were reached by consensus. Diameters of pulmonary arteries and pulmonary veins were measured by CT images. The main pulmonary artery (PA) and ascending aorta were measured in the axial plane at the level of the pulmonary artery bifurcation. The ratio of the main pulmonary artery to the ascending aorta was calculated. Dividing the main PA by the aortic diameter measured at the same chest level and during the same phase of the cardiac cycle can adjust for some potential differences due to the association between the mean PA diameter and body surface area[8,9]. Using multiple-plane reconstruction, we could delineate clearly the junction of each pulmonary vein (PV) to left atrial (LA). The diameter of the PV was measured at the position 5mm distance to the junction of the LA and each PV in axial images [10,11]. Pulmonary vein-pulmonary artery and ascending aorta diameters were measured by two independent observers with no knowledge of the patients' clinical data.

All CT scans were evaluated for the following characteristics: (a) ground-glass opacities, (b) consolidation, (c) number of lobes affected by ground-glass or consolidative opacities, (d) degree of lobe involvement in addition to overall lung "total severity score", (e) nodules, (f) pleural effusion and pleural thickening, (g) pericardial effusion thoracic, (h) lymphadenopathy(defined as lymph node size of 10 mm in short-axis dimension) and (i) hilar involvement. The degree of lung involvement was visually assessed from 0 to 5 as: none (0%), minimal (1%-25%), mild (26%- 50%), moderate (51%-75%), or severe (76%-100%). No involvement corresponded to a lobe score of 0, minimal involvement to a lobe score of 1, mild involvement to a lobe score of 2, moderate involvement to a lobe score of 3, and severe involvement to a lobe score of 4. The total CT scores were reached by summing the five lobe scores (range, 0 none, 25 maximum) [12]. Ground-glass opacification was defined as increased lung attenuation with blurred bronchi and vascular margins, and consolidation was defined as blurred vascular margins and airway walls [13]. The criterion of hilar involvement is that the CT image shows enlarged hilar, unclear structure, and blurred blood vessel edges.

Statistical Analysis

All categorical variables were compared for the study outcome by using the Fisher exact test or χ^2 test, and continuous variables were compared using the t test or the Mann-Whitney U test, as appropriate. Wilcoxon signed-rank tests were used to analyze quantitative data for every patient's two CT scans. Kappa consistency test was used for self-comparison of qualitative data. To analyze the PV diameters as a predictor of survival, receiver operator characteristic (ROC) curves and the corresponding area under the curve (AUC) was used to determine the cut-off value of the PVs yielding the highest sensitivity and specificity. All statistical analyses were performed with SPSS, version 21.0 (IBM Corp) for Windows and $p < 0.05$ was considered statistically significant.

Results

Clinical and Laboratory Findings

Characteristics, Symptoms and complications of patients were showed in Table 1. A total 99 severe and critical COVID-19 patients (mean age, 60.53 ± 15.00 years; 70%[69/99] male) were enrolled in the research, including 47 recovered cases and 52 deceased cases. There was a significant difference in age between the recovered group and the deceased group (50.23 vs 68.02 years, $p < 0.001$). There was no significant difference in the male/female ratio between two groups ($p = 0.062$).

For all patients, the most common initial symptoms were fever(86.4%), cough (18.6%) and shortness of breath(18.6%), and no differences in initial symptoms between two groups (all $p > 0.05$). Hypertension (34 patients [35.1%]) was the most common underlying disease. 16 patients (16.3%) have the previous operation history. Other common comorbidities included glycuressis, chronic lung disease, heart disease and chronic renal disease. The proportion was 13.3% (13 patients), 13.3% (13 patients), 10.2% (10 patients) and 6.1% (6 patients), respectively.

There were significant differences in most laboratory investigations between the recovered group and the deceased group, including white blood cell counts (WBC), platelet counts, creatinine, urea, neutrophils, glomerular filtration rates, cystatin c, high-sensitivity troponin, lactic dehydrogenase (LDH), high-sensitivity C-reactive protein(hs-CRP), D-dimer (DD2) and N-terminal proB-type natriuretic peptide (NT-proBNP) (Table 2).

CT Review

The measurement results of PVs and PAs are listed in **Table 3 and Table 4**. The PV diameters of the deceased patients were larger than recovered patients in the severe phase, especially the right inferior pulmonary vein and the left superior pulmonary vein, the differences were significant (all $p < 0.05$). For patients in the recovered group, the PV diameters in the improved phase were significantly smaller than those in the severe phase (all $p < 0.001$). Only 12 deceased patients underwent two effective chest CT scans: the initial CT and the last CT before death. For those cases, compared with the initial CT, PVs were more dilated on the last CT (all $p < 0.05$). Construction of a ROC curve yielded an optimal cut-off value of the PV diameters for prediction of survival (all $p < 0.05$) (**Table 5**).

Instead, there was no significant difference in the ratio of main PA to aorta diameter between the recovered group and the deceased group, nor did the self control of the recovered group and the deceased group (all $p > 0.05$). 36 cases (69%) of 52 deceased patients and 20 cases (42.55%) of 47 recovered patients shown hilar involvement on chest CT images in the severe phase ($p = 0.009$).

The total CT scores in the recovered group were lower than that in the deceased group in the severe phase (medium 15 vs 19.5, $p = 0.001$). The CT scores of the right lobe and LU (the left upper lobe) in deceased patients were significantly higher than those of the recovered patients (all $p < 0.05$). Besides, in the recovered group, the CT scores of each lung lobe in the improved phase were significantly smaller compared with those in the severe phase (all $p < 0.001$) and the difference in total CT scores was also significant (medium 10 vs 15, $p < 0.001$). Compared with the initial CT, the CT scores of the last CT exams in deceased group were significantly increased (medium 21.5 vs 8.5, $p = 0.001$).

Other major CT findings including pleural effusion, pericardial effusion, and pleural thickening were also evaluated. Compared with deceased patients, recovered patients were more likely to have pericardial effusion (20[43%] vs 7[13%], $p = 0.001$). Whereas the occurrence rates of pleural thickening in deceased patients were significantly higher than those of the recovered patients (40[77%] vs 14[30%]). There was a significant difference in pericardial effusion and pleural thickening between the severe phase and improved phase for the recovered group (both $p < 0.001$).

Discussion

This retrospective study aimed to determine the value of pulmonary circulation in the assessment of the severity and tendency of severe and critical patients with COVID-19 pneumonia through chest CT images. Our study comprehensively described the major differences in pulmonary circulation on chest CT images between deceased patients and recovered patients with COVID-19. The severe phases and the improved phases of COVID-19 patients in the recovered group were also evaluated and compared. We found that evaluation in the diameters of pulmonary veins on chest CT images might be a useful tool for determining the severity and tendency of COVID-19. Furthermore, the dilation of PV was a predictor of poor clinical outcomes.

COVID-19 has caused far more infections and deaths than severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) due to its high infectivity, which have mortality rates of 9.6% [14] and 34.4% [15], respectively. Because no specialized drugs have been found to treat severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the main treatment is timely symptomatic and supportive treatment [16]. Among patients with COVID-19, especially those who are severely and critically ill, SARS-CoV-2 primarily affects the lungs, it also affects multiple organs, such as the cardiovascular system [17]. However, to our knowledge, no study has been performed to evaluate pulmonary circulation on chest CT in COVID-19 pneumonia patients.

In our study, the diameters of pulmonary vein of the deceased patients were larger than recovered patients in the severe phase ($p < 0.001$), and compared with the initial CT, PVs were more dilated on the

last CT before death in the deceased patients (all $p < 0.05$), which may indicate that the dilation of pulmonary vein in severe and critical patients with COVID-19 are at higher risk of death. Furthermore, construction of a ROC curve yielded an optimal cut-off value of the PV diameters for prediction of survival. We proposed that the dilation of PV was a predictor of poor clinical outcomes. The dilation of PV is seen in pulmonary congestion caused by increased pulmonary venous return and left heart insufficiency [18,19]. Pulmonary inflammation leads to congestion of the lung tissue, which has been reported in the early studies. Severe and critically patients have severe pulmonary infections, manifested by abnormal laboratory and radiographic findings, such as higher levels of WBC and h-CRP; more ground-glass opacities, consolidation and higher total CT scores. Therefore, obvious congestion might increase PV regurgitation, leading to the enlargement of PV. In recovered patients, the reduction of PV diameter accompanied by lower total CT score in the improved phase compared with in the severe phase, indicates the reduced of pulmonary circulation reflux and the absorption and improvement of pulmonary inflammation. In addition, the main target organ of the COVID-19 infection is the lung, and some recent studies have reported it could also cause myocardial damage [17,20]. Mechanistically, SARS-CoV-2, binds to the transmembrane angiotensin-converting enzyme 2 (ACE2), and then enters type 2 pneumocytes, macrophages, pericytes and cardiomyocytes [17]. High expression of ACE2 in pericytes could lead to development of microvascular dysfunction. ACE2 expression is up-regulated in failing human hearts, suggesting a plausible explanation for a higher infectivity of virus and a higher mortality in patients with heart failure. The significant increase of myocardial enzyme spectrum indicates that the myocardium is involved [5]. In our study, compared with the recovered patients, the deceased patients showed the significant increase of high-sensitivity troponin, lactic dehydrogenase and NT-proBNP, which was consistent with relevant reports and suggested myocardial injury and cardiac dysfunction [21]. Mechanisms underlying myocardial injury remain unclear. It is worthy of attention whether they reflect systemic or local process and ischaemic or inflammatory process. Also, since ACE2 (a homologue of ACE) is expressed in cardiomyocytes, direct cardiomyocyte infection by SARS-CoV-2 may be a possibility [17, 22]. Pulmonary congestion indirectly indicated left heart insufficiency, which is usually manifested as blurred hilar shadows and dilated PVs on CT images. CT examination clearly showed the hilar structure, so it has a unique advantage in determining whether the lesion involves the hilum. In our study, 36 cases (69%) of 52 deceased patients and 20 cases (42.55%) of 47 recovered patients shown hilar involvement on chest CT images ($p=0.009$). Some attempts to treat COVID-19 cardiac injury have done, the detection of pulmonary circulation, especially pulmonary vein, might help identify a subset of patients at greater risk of COVID-19 complications and successful therapies. Therefore, the changes of PVs might indirectly reflect the activity of pulmonary inflammation and cardiac insufficiency. This new radiological evidence provided an innovative new method compared with previous investigations in the assessment of the severity of severe and critical patients with COVID-19.

The representative chest CT findings of patients with COVID-19 were peripheral and/or subpleural ground-glass opacities or consolidation for common patients [1]. Furthermore, in severe and critical COVID-19 pneumonia patients, more and more ground-glass attenuation and airspace consolidation as well as involvement of multiple lung lobes and high CT scores were common chest CT finding [23], which was

similar in our study. Traditionally, more and more larger lesions on CT images indicates that the lung inflammation was more serious. However, we posed a hypothetical question which pulmonary manifestations of severe and critical COVID-19 pneumonia might be related to myocardial injury and cardiac insufficiency, especially accompanied by dilated PVs.

This study has the following limitations: Firstly, it was a retrospective study. Secondly, there was a small sample size of COVID-19, thus some conclusions are preliminary. More powerful studies with pooled data from multiple centers is needed in our subsequent studies. Thirdly, no lung biopsy or autopsy was performed to reflect the histopathological changes.

In conclusion, the retrospective study suggests that chest CT should be considered as a quick and effective method to assess the changes in pulmonary circulation and the progression of COVID-19 pneumonia. Evaluation of changes in pulmonary circulation by chest CT images might be considered as a useful tool for determining the severity and tendency of COVID-19. The changes of PVs might indirectly reflect the activity of pulmonary inflammation and cardiac insufficiency. Pulmonary manifestations of severe and critical COVID-19 pneumonia might be related to myocardial injury and cardiac insufficiency, especially accompanied by dilated PVs. In this way, the evolution of the patient's condition could be detected in time, and targeted treatment can be adopted, so as to improve the prognosis of patients and reduce the risk of death of severe patients, especially critical patients.

Declarations

Acknowledgements

We express our gratitude to Professor David A. Lynch (the Department of Radiology, National Jewish Health, Denver) and Qihang Chen (Department of Radiology, Beijing Hospital) for consultation on CT images.

Funding

No

Guarantor

The scientific guarantor of this publication is Hanxiong Guan

Compliance with ethical standards Conflict of interest

The authors of this article declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry

No complex statistical methods were necessary for this paper.

Informed consent

SARS-Cov-2 is a continuing public health outbreak investigation globally. Therefore, written informed consent was waived by the Institutional Review Board.

Ethical approval

This study was approved by the Ethics of Committees of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (IRB ID:TJ-C0200108).

Study subjects or cohorts overlap:

No.

Methodology

- retrospective
- observational
- performed at one institution

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Tables

Table 1: Clinical characteristics of COVID-19 patients (N = 99)

	All patients <i>N</i> = 99	Recovered cases <i>N</i> = 47	Dead cases <i>N</i> = 52	<i>P</i>
Age, years	60.53±15.00	50.23±13.01	68.02±12.61	2.11*10 ⁻⁸ *,a
<45	16(16.2%)	14(29.8%)	2(3.8%)	2.72*10 ⁻⁶ *,c
45-70	59(59.6%)	31(66.0%)	28(53.8%)	
>70	24(24.2%)	2(4.3%)	22(42.3%)	
Sex				
Male	69(69.7%)	28(59.6%)	41(78.8%)	0.062 ^c
Female	30(30.3%)	19(40.4%)	11(21.2%)	
Initial Symptoms	<i>N</i> = 59	<i>N</i> = 46	<i>N</i> = 13	
Fever	51(86.4%)	41(89.1%)	10(76.9%)	0.3567 ^d
Shortness of breath	11(18.6%)	9(19.6%)	2(15.4%)	1.00 ^d
Cough	11(18.6%)	9(19.6%)	2(15.4%)	1.00 ^d
Diarrhea	4(6.8%)	4(6.8%)	0	0.5664 ^d
Fatigue	5(8.5%)	2(4.3%)	3(23.1%)	0.06595 ^d
Comorbidities	<i>N</i> = 98	<i>N</i> = 46	<i>N</i> = 52	
Glycuresis	13(13.3%)	5(10.9%)	8(15.4%)	0.719 ^c
Cerebrovascular disease	1(1.0%)	0	1(1.9%)	1.000 ^d
History of operation	16(16.3%)	6(13.0%)	10(19.2%)	0.580 ^c
Chronic lung disease	13(13.3%)	3(6.5%)	10(19.2%)	0.121 ^c
Chronic kidney disease	6(6.1%)	1(2.2%)	5(9.6%)	0.210 ^d
Heart disease	10(10.2%)	4(8.7%)	6(11.5%)	0.746 ^d
Hematopathy	1(1.0%)	0	1(1.0%)	1.000 ^d
Cancer	2(2.0%)	0	2(3.8%)	0.497 ^d
Others	13(13.3%)	7(15.2%)	6(11.5%)	0.812 ^c
Underlying Disease	<i>N</i> = 97	<i>N</i> = 46	<i>N</i> = 51	
Hypertension	34(35.1%)	14(30.4%)	20(39.2%)	0.489 ^c

Note: Quantitative data were presented as mean ± standard deviation (minimum-maximum), while the counting data were presented as count (percentage of the total). The continuity variable is denoted by Median (IQR) or mean (SD), and Mann-Whitney U test or t test is adopted. The classification variable is represented by n (%), and the chi-square test or Fisher's test is adopted.

Table2: Laboratory findings of COVID-19 patients (N = 99)

Laboratory Investigations	N	All patients	N	Recovered cases	N	Dead cases	P
WBC (×10 ⁹ /L)	97	6.67(4.51-11.8)	45	5.18(3.72-8.14)	52	9.35(5.42-13.43)	1.10*10 ^{-3*} ,b
<5.18		32(33.0%)		23(51.1%)		11(21.1%)	9.30*10 ^{-4*} ,c
5.18-10.19		33(34.0%)		15(33.3%)		16(30.8%)	
>10.19		32(33.0%)		7(15.6%)		25(48.1%)	
Creatinine(umol/L)	96	76.5(61.2-100.2)	45	67(56-77)	51	88(66-114.5)	1.23*10 ^{-4*} ,b
<65.7		32(33.3%)		21(46.7%)		11(21.6%)	1.36*10 ^{-4*} ,c
65.7-86		33(34.4%)		19(42.2%)		14(27.4%)	
>86		31(32.3%)		5(11.1%)		26(51.0%)	
Urea(mmol/L)	97	5.41(3.7-9.2)	46	4.17±1.47	51	9(5.8-13.4)	2.76*10 ^{-10*} ,b
<4.4		32(33.0%)		26(56.5%)		6(11.8%)	1.11*10 ^{-9*} ,c
4.4-7.7		33(34.0%)		19(41.3%)		14(28.4%)	
>7.7		32(33.0%)		1(2.2%)		31(60.8%)	
Monocyte (×10 ⁹ /L)	98	0.41(0.26-0.63)	46	(0.47(0.25-0.63)	52	0.40(0.28-0.61)	0.5982 ^b
<0.32		32(32.65%)		13(28.3%)		19(36.54%)	0.6053 ^c
0.32-0.56		34(34.70%)		16(34.8%)		18(34.61%)	
>0.56		32(32.65%)		17(36.9%)		15(28.85%)	
Lymphocyte (×10 ⁹ /L)	97	0.66(0.49-0.92)	41	0.71(0.53-1.09)	56	0.635(0.44-0.84)	0.1461 ^b
<0.54		31(31.9%)		11(26.8%)		20(35.7%)	0.1476 ^c
0.54-0.84		34(35.1%)		12(29.3%)		22(39.3%)	
>0.84		32(33%)		18(43.9%)		14(25%)	
Platelet (×10 ⁹ /L)	97	159(112-228)	46	189(140-259)	51	137(88-182)	8.22*10 ^{-4*} ,b
<125		31(31.96%)		9(19.6%)		22(43.14%)	3.30*10 ^{-2*} ,c
125-201		35(36.08%)		18(39.1%)		17(33.33%)	
>201		31(31.96%)		19(41.3%)		12(23.53%)	
Eosnoohils(×10 ⁹ /L)	98	0(0-0.01)	46	0(0-0.0175)	51	0(0-0.01)	0.2113 ^b
Neutrophils(×10 ⁹ /L)	97	5.34(2.98-10.67)	45	3.86(2.56-5.91)	52	8.46(4.09-12.61)	2.28*10 ^{-4*} ,b
<3.71		32(33.0%)		21(46.7%)		11(21.15%)	4.37*10 ^{-4*} ,c
3.71-8.46		32(33.0%)		18(40%)		15(28.85%)	
>8.46		33(34.0%)		6(13.3%)		26(50%)	
GFR(ml/min/1.73m ²)	97	91(68.7-105.9)	46	101.3(90.2-111.2)	51	74.3(48.8-95.5)	4.72*10 ^{-6*} ,b
<77.2		32(33.0%)		6(13.0%)		26(51.0)	9.87*10 ^{-5*} ,c
77.2-102		33(34.0%)		17(37.0)		16(31.4%)	
>102		32(33.0%)		23(50.0%)		9(17.6%)	
Cystatin c(mg/L)	52	1.242(0.3567-2.129)	32	0.9460(0.7857-1.106)a	20	1.7795(0.5251-3.0339)	1.475*10 ^{-3*} ,d
High-sensitivity troponin(pg/mL)	76	14.4(4.8-46.3)	30	4.400(2.475-8.825)b	46	551.8(-1247.09-2352.69)a	7.593*10 ^{-5*} ,c
Lactic dehydrogenase(U/L)	95	369.0(264.0-569.0)	44	310.1(197.69-422.31)a	51	519.0(385.5-818.0)b	3.932*10 ^{-8*} ,c
hs-CRP(mg/L)	96	59.1(31.5-131.3)	45	36.00(13.60-63.10)b	51	105.8(51.3-165.8)b	4.78*10 ^{-4*} ,c
DD2(ug/mL FEU)	95	1.260(0.445-4.910)	45	0.530(0.370-0.970)b	50	4.325(2.010-22.000)b	1.196*10 ^{-8*} ,c
NT-proBNP(pg/mL)	72	2055.08(-3856.00-7966.27)	28	191.29(-71.35-453.92)a	44	3287.84(-4097.91-10673.59)a	2.606*10 ^{-9*} ,c

Note: WBC : white blood cell , LDH : lactic dehydrogenase, hs-CRP : high-sensitivity C-reactive protein , NT-proBNP: N-terminal proB-type natriuretic peptide

Table 3: CT review of COVID-19 patients between the deceased patients and the recovered patients in the severe phase (N = 99)

		Recovered cases N = 47	Dead cases N = 52	P
PV	RSPV	12.92(8.36-17.97)	13.885(9.81-18.17)	0.026
	RIPV	10.78(7.25-15.74)	12.61(7.25-15.74)	0.000
	LSPV	11.29(8.07-14.38)	12.965(9.34-15.2)	0.000
	LIPV	10.23(7.16-12.91)	11.355(5.34-15.77)	0.015
	PA	25.97(19.74-37.94)	31.05(19.8-39.7)	0.000
	P/A	0.82(0.62-1.30)	0.85(0.62-1.02)	0.070
Imaging findings	Pleural Effusion	7 (15%)	7 (13%)	1.000
	Pericardial Effusion	20 (43%)	7 (13%)	0.001
	Pleural Thickening	14 (30%)	40 (77%)	0.000
	Hilar Involvement	20 (43%)	36 (69%)	0.009
CT score	RU	3 (0 - 5)	4 (1 - 5)	0.000
	RM	2 (0 - 4)	3.5 (0 - 5)	0.003
	RI	3 (0 - 5)	4 (1 - 5)	0.000
	LU	3 (0 - 5)	4 (1 - 5)	0.001
	LI	3 (0 - 5)	4 (1 - 5)	0.131
	Total	15 (3 - 22)	19.5 (5 - 25)	0.001

Note: PV: Pulmonary Vein; PA: Pulmonary Artery; RSPV: Right Superior Pulmonary Vein; RIPV: Right Inferior Pulmonary Vein; LSPV: Left Superior Pulmonary Vein; LIPV: Left Inferior Pulmonary Vein; P/A: main pulmonary artery diameter/ aortic diameter; P/A: main pulmonary artery diameter/ aortic diameter

Table 4: CT review of COVID-19 patients between the deceased patients and the recovered patients in two phase

		Recovered cases N = 47			Deceased cases N = 12		
		CT#1	CT#2	P	CT#1	CT#2	P
PV	RSPV	12.92(8.36-17.97)	11.58(7.52-16.67)	0.000	12.125(9.69-14.41)	14.46(12.91-15.33)	0.000
	RIPV	10.78(7.25-15.74)	9.51(5.07-12.8)	0.000	11.595(8.41-13.84)	13.625(9.85-14.42)	0.003
	LSPV	11.29(8.07-14.38)	10.33(7.07-12.81)	0.000	12.17(9.34-13.74)	13.79(11.02-15.2)	0.005
	LIPV	10.23(7.16-12.91)	9.51(6.25-12.23)	0.000	11.17(9.03-13.74)	12.465(9.85-14.5)	0.021
	PA	26.11(19.74-37.94)	25.44(17.63-39.99)	0.014	27.95(24.8-33.5)	30.55(27.1-39.7)	0.004
	P/A	0.82±0.62-1.30	0.79±0.55-1.23)	0.168	0.87(0.77-1.10)	0.88(0.79-1.02)	0.329
Imaging findings	Pleural Effusion	7 (15%)	1 (2%)	0.149	0 (0%)	2 (17%)	1.000
	Pericardial Effusion	20 (43%)	10 (21%)	0.000	1 (8%)	0 (0%)	1.000
	Pleural Thickening	14 (30%)	15 (32%)	0.000	1 (8%)	8 (67%)	0.273
	Hilar Involvement	20 (43%)	3 (6%)	0.070	1 (8%)	9 (75%)	0.546
CT score	RU	3 (0 - 5)	2 (0 - 4)	0.000	2 (0 - 4)	4 (3 - 5)	0.002
	RM	2 (0 - 4)	1 (0 - 4)	0.000	1.5 (0 - 4)	4 (2 - 5)	0.001
	RI	3 (0 - 5)	2 (0 - 4)	0.000	1.5 (0 - 5)	5 (1 - 5)	0.002
	LU	3 (0 - 5)	2 (0 - 4)	0.000	1.5 (0 - 4)	4 (3 - 5)	0.002
	LI	3 (0 - 5)	2 (0 - 4)	0.000	2.5 (0 - 4)	4.5 (1 - 5)	0.001
	Total	15 (3 - 22)	10 (1 - 20)	0.000	8.5 (0 - 20)	21.5 (13 - 25)	0.001

Note: For Recovered cases: #1: the CT in the severe phase; #2: the CT in the recovered phase

For Deceased cases: #1: the initial CT; #2: the last CT for dead patients

Note: PV: Pulmonary Vein; PA: Pulmonary Artery; RSPV: Right Superior Pulmonary Vein; RIPV: Right Inferior Pulmonary Vein; LSPV: Left Superior Pulmonary Vein; LIPV: Left Inferior Pulmonary Vein; P/A: main pulmonary artery diameter/ aortic diameter; RU: the right upper lobe; RM: the right middle lobe; RI: the right inferior lobe; LU: the left upper lobe; LI: the left inferior lobe

Table 5: ROC results of PV diameter in COVID-19 patients between the deceased patients and the recovered patients in the severe phase (N = 99)

	RSPV	RIPV	LSPV	LIPV
cut-off	13.33	12.84	12.25	11.28
AUC	0.629	0.709	0.743	0.661
P Value	0.027	<0.0001	<0.000	0.006
95%CI	0.517-0.741	0.607-0.812	0.648-0.839	0.553-0.768
Sensitivity	0.673	0.462	0.673	0.519
Specificity	0.596	0.915	0.745	0.809

Note: PV: Pulmonary Vein; PA: Pulmonary Artery; RSPV: Right Superior Pulmonary Vein; RIPV: Right Inferior Pulmonary Vein; LSPV: Left Superior Pulmonary Vein; LIPV: Left Inferior Pulmonary Vein; AUC : area under the

Figures

Figure 1

(a) and (b) HRCT findings in a 54-year-old man with severe COVID-19 pneumonia who did not survive. HRCT scan shows bilateral areas of extensive ground-glass opacities and consolidation in most lobes. Besides, the diameter of the right inferior pulmonary vein (RPV) was 13.34mm. The dilation of RPV was found. (c) and (d) HRCT findings in a 61-year-old man with severe COVID-19 pneumonia who survived and recovered. HRCT scan showed bilateral areas of extensive ground-glass opacities and consolidation in most lobes and the diameter of the right inferior pulmonary vein was 9.85 mm.

Figure 2

HRCT findings in a 57-year-old woman with severe COVID-19 pneumonia who was deceased. (a) and (b) At presentation (day 10 after the onset of initial symptoms), there were several mixed ground-glass opacity and consolidation lesions, which were located peripheral and subpleural region. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 10.81mm and 8.83mm, respectively. (c) and (d) Day 18 after the onset, the images exhibited showed diffuse lesions in most lobes (white lung). Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 14.23mm and 11.18mm, respectively, which were more dilated compared with the initial CT. Four days later, the patient died.

Figure 3

HRCT findings in a 40-year-old man with severe COVID-19 pneumonia who survived and recovered. (a) and (b) In the severe phase (day 9 after the onset of initial symptoms), the images exhibited showed diffuse mixed ground-glass opacity and consolidation lesions. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 14.24mm and 10.33 mm, respectively . (c) and (d) Day 42 after the onset, the lesions were absorbed. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 9.11mm and 7.78 mm, respectively, and the diameters of pulmonary vein was significantly smaller than those in the severe phase. The patient was discharged two day later. Figure 3. HRCT findings in a 40-year-old man with severe COVID-19 pneumonia who survived and recovered. (a) and (b) In the severe phase (day 9 after the onset of initial symptoms), the images exhibited showed diffuse mixed ground-glass opacity and consolidation lesions. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 14.24mm and 10.33 mm, respectively . (c) and (d) Day 42 after the onset, the lesions were absorbed. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 9.11mm and 7.78 mm, respectively, and the diameters of pulmonary vein was

significantly smaller than those in the severe phase. The patient was discharged two day later. Figure 3. HRCT findings in a 40-year-old man with severe COVID-19 pneumonia who survived and recovered. (a) and (b) In the severe phase (day 9 after the onset of initial symptoms), the images exhibited showed diffuse mixed ground-glass opacity and consolidation lesions. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 14.24mm and 10.33 mm, respectively . (c) and (d) Day 42 after the onset, the lesions were absorbed. Meanwhile, the diameter of the right inferior pulmonary vein (RPV) and left inferior pulmonary vein (LPV) were 9.11mm and 7.78 mm, respectively, and the diameters of pulmonary vein was significantly smaller than those in the severe phase. The patient was discharged two day later.