Radiology

Chest CT Features of COVID-19 in Rome, Italy

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Summary:

In Rome, Italy, COVID-19 pneumonia is characterized by constant presence of peripheral ground-glass opacities, associated with multilobe and posterior involvement, bilateral distribution, and subsegmental vessel enlargement.

Keys Results:

1. In this prospective study of patients in Rome, Italy, the sensitivity, specificity, and accuracy of CT for COVID-19 were 97%, 56%, and 72%, respectively, using RT-PCR as standard of reference.

2. On chest CT, ground-glass opacities (GGO) were present in 100% of patients with RT-PCR confirmed COVID-19. 93% of patients had multilobe and posterior lung involvement; 91% of patients had bilateral pneumonia.

3. On CT, subsegmental vascular enlargement (more than 3 mm diameter) in areas of lung opacity was observed in 89% of patients with confirmed COVID-19 pneumonia, with unclear etiology.

Abbreviations:

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

COVID-19: Coronavirus Disease 2019

RT-PCR: reverse transcription polymerase chain reaction

GGO: ground-glass opacities

Abstract

Background

The standard for diagnosis of SARS-CoV-2 virus is reverse transcription polymerase chain reaction (RT-PCR) test, but chest CT may play a complimentary role in the early detection of COVID-19 pneumonia.

Purpose

To investigate CT features of patients with COVID-19 in Rome, Italy, and to compare the accuracy of CT with RT-PCR.

Methods

In this prospective study from March 4, 2020, until March 19, 2020, consecutive patients with suspected COVID-19 infection and respiratory symptoms were enrolled. Exclusion criteria were: chest CT with contrast medium performed for vascular indications, patients who refused chest CT or hospitalization, and severe CT motion artifact. All patients underwent RT-PCR and chest CT. Diagnostic performance of CT was calculated using RT-PCR as reference. Chest CT features were calculated in a subgroup of RT-PCR-positive and CT-positive patients. CT features of hospitalized patients and patient in home isolation were compared by using Pearson chi squared test.

Results

Our study population comprised 158 consecutive study participants (83 male and 75 female, mean age 57 y ±17). Fever was observed in 97/158 (61%), cough in 88/158 (56%), dyspnea in 52/158 (33%), lymphocytopenia in 95/158 (60%), increased C-reactive protein level in 139/158 (88%), and elevated lactate dehydrogenase in 128/158 (81%) study participants. Sensitivity, specificity, and accuracy of CT were 97% (60/62)[95% IC, 88-99%], 56% (54/96)[95% IC,45-66%] and 72% (114/158)[95% IC 64-78%], respectively. In the subgroup of RT-PCR-positive and CT-positive patients, ground-glass opacities (GGO) were present in 58/58 (100%), multilobe and posterior involvement were both present in 54/58 (93%), bilateral pneumonia in 53/58 (91%), and subsegmental vessel enlargement (> 3 mm) in 52/58 (89%) of study participants.

Conclusion

The typical pattern of COVID-19 pneumonia in Rome, Italy, was peripherally ground-glass opacities with multilobe and posterior involvement, bilateral distribution, and subsegmental vessel enlargement (> 3 mm). Chest CT sensitivity was high (97%) but with lower specificity (56%).

Introduction

A novel coronavirus, named SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) was identified related to the new emerging viral pneumonia consequently named COVID-19 (Coronavirus Disease 2019). In accordance to the guidelines (3), the reference standard for the diagnosis of SARS-CoV-2 infection is next-generation sequencing or real-time reverse transcription polymerase chain reaction (RT-PCR) methods applied to respiratory tract specimens. However, due to intrinsic limitations (i.e. collection and transportation of samples and diagnostic kit performance), sensitivity of RT-PCR at initial presentation ranges between 60% and 71% (4-7).

As reported by Ai (5), in a cohort of 1014 patients in Wuhan China, the sensitivity, specificity and accuracy of chest CT in the detection of COVID-19 pneumonia were 97%, 25% and 68% respectively using RT-PCR results as reference standard. Similar results were found in other studies, suggesting that CT imaging may be helpful in early detection of interstitial pneumonia in patients with high degree of suspicion for COVID-19 pneumonia (6, 8).

Typical chest CT patterns of COVID-19 viral pneumonia include multifocal bilateral peripheral ground glass areas associated with sub-segmental patchy consolidations mostly sub-pleural and predominantly involving lower lung lobes and posterior segments (8-14).

The aim of this study was to investigate chest CT features of patients with COVID-19 in Rome, Italy, and to compare the diagnostic performance of chest CT with RT-PCR.

Material and Methods

Patient Population and Study Design

This prospective study was approved by our local institutional review board (IRB) and written informed consent was obtained from all study participants. In case of inability of the patients to provide informed consent, it was received from the relatives or the admitting physicians who requested CT examination.

Consecutive patients admitted at the Emergency Department of Sant'Andrea Hospital, were enrolled from March 4, 2020, until March 19, 2020. Inclusion criteria were *(a)* patients with fever and respiratory symptoms, such as cough, and dyspnea; *(b)* patients with mild respiratory symptoms and close contact with a confirmed COVID-19 patient; *(c)* patients with a previously positive test result.

Exclusion criteria were *(a)* chest CT with contrast medium performed for vascular indication (ie, pulmonary embolism, aortic dissection, coronary syndrome) , *(b)* patients who refused chest CT or hospitalization, *(c)* severe motion artifact on chest CT.

Clinical Data

All patients underwent a prescreening questionnaire about COVID-19 symptoms in one of the six dedicated tents for COVID-19 located outside the Emergency Department collecting specific clinical information: fever, cough and dyspnea. Fever was defined with a temperature >37.5°C. Thereafter, specific blood tests (COVID-19 panel, internal disposition) and nasopharyngeal and oropharyngeal swabs were obtained for each patient. To confirm the positivity to SARS-COV2, real-time reverse transcriptase RT-PCR (Charitè, Berlin, Germany) was used (15). All patients received two nasopharyngeal and oropharyngeal swabs at a time interval of 24 hours. Patients were considered negative after two consecutive negative RT-PCR results. Patient demographic characteristics, clinical signs and symptoms, and laboratory results were collected. Symptomatic patients (fever >37.5°C, cough and dyspnea) with positive RT-PCR and positive CT were hospitalized, whereas patients with positive RT-PCR but negative CT (see below) and/or mild symptoms (fever ≤37.5°C, no dyspnea) were discharged for home isolation per our hospital guidelines. Data about hospitalization or home isolation were also collected.

CT Acquisition Technique

As part of our hospital COVID-19 guidelines, after the RT-PCR swabs, all patients underwent chest CT to determine the presence or absence of viral pneumonia. All chest CT acquisitions were obtained with the patients in supine position during end-inspiration without contrast medium injection. Chest CT performed on a 128-slice CT (GE Revolution EVO 64 Slice CT Scanner, GE Medical Systems, Milwaukee, WI, USA) dedicated only to patients with COVID-19 . The following technical parameters were used: tube voltage: 120 kV; tube current modulation 100-250 mAs; spiral pitch factor: 0.98; collimation width: 0.625. Reconstructions were made with convolution kernel BONEPLUS at a slice thickness of 1.25 mm. Decontamination of the room consisted of surface disinfection with 62-71% ethanol or 01% sodium hypochlorite. After each patient chest CT examination, passive air exchange was performed for 40-60 minutes.

CT Image Analysis

DICOM data were transferred onto a PACS workstation (Centricity Universal Viewer v.6.0, GE Medical Systems, Milwaukee, WI, USA). Two radiologists in consensus with 15 and 25 years of thoracic imaging experience evaluated the images using a clinically available dedicated application (Thoracic VCAR v13.1, GE), defining patients as CT-positive when a diagnosis of viral pneumonia was reported.

The following CT features were also recorded (16): *(a)* ground-glass opacities (GGO), (b) GGO pattern, *(c)* GGO location, *(d)* consolidation, *(e)* multilobe involvement, *(f)* bilateral distribution, *(g)* location of consolidation or GGO, *(h)* pulmonary nodules surrounded by GGO, *(i)* interlobular septal thickening, *(j)* air bronchogram, *(k)* halo sign, *(l)* presence of cavitation, *(m)* bronchial wall thickening, *(n)* bronchiectasis, *(o)* perilesional vessel diameter, *(p)* lymphadenopathy (defined as lymph node with short axis > 10mm), *(q)* pleural and *(r)* pericardial effusion.

Statistical Analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS Inc. Chicago, IL). All continuous variables were expressed as medians and ranges and categorical variables as counts and percentages. The diagnostic performance of CT was evaluated with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy considering RT-PCR as the reference standard. CT findings for patients who required hospitalization versus home-isolation were compared by using the Pearson chi-squared test. P values of <0.05 were considered statistically significant. A 95% confidence interval was provided by the Wilson score method.

Results

Patient Population and Clinical Data

Study population comprised 158 consecutive study participants (83 male and 75 female, mean age 57$\pm$17 y, range 18-89). Fever was observed in 97/158 patients (61%). Cough and dyspnea were present in 88/158 (56%) and 52/158 (33%) patients, respectively.

Laboratory blood tests on admission showed lymphocytopenia (defined as lymphocyte count <1.1×10^9/L), with a lymphocyte count of 1.08 $\pm$ 0.47 ×10^9/L in 95/158 cases (60%); increased (>0.50 mg/dL) C-reactive protein (CRP) levels (13.64 $\pm$ 38.68 mg/dL) in 139/158 (88%) patients;

increased (> 220 U/L) lactate dehydrogenase (LDH) levels (339.50 ± 124.15 U/L) in 128/158 (81%) patients. Full results are reported in Table 1.

CT Diagnostic Performance

Sixty-two/158 (39%) patients had positive RT-PCR and 102/158 (64%) patients had positive CT findings. Detailed results are reported in Table 2. Using RT-PCR as reference standard, sensitivity, specificity and accuracy of CT for COVID-19 pneumonia were 97% (60/62)[95% IC, 88-99%], 56% (54/96)[95% IC,45-66%] and 72% (114/158)[95% IC 64-78%], respectively.

CT Image Analysis

To understand the CT features of patients with COVID-19 pneumonia, a sub-analysis was performed considering only study participants with positive RT-PCR testing and chest CT findings. Of 158 study participants, 62 participants were RT-PCR-positive and among these, 60 participants were classified as CT-positive. Considering the exclusion of two study participants due to the presence of severe chest CT motion artifact, 58 study participants were evaluated in this sub-analysis (Figure 1).

GGO were present in 58/58 patients (100%), multilobe involvement (≥ 2 lobes) and posterior involvement were both present in 54/58 (93%) patients, 53/58 (91%) patients had bilateral pneumonia distribution, and peripheral GGO location was observed in 52/58 (89%).

A simultaneous involvement of all five lobes was observed in 43/58 patients (74%). Right lower lobe was the most affected in 53/58 patients (93%), followed by left lower lobe and right upper lobe involved in 51/58 patients (both 91%). Regarding GGO, three patterns were observed in order of frequency as follows: Crazy paving in 23/58 patients (39%), rounded morphology in 19/58 patients (32%) and linear opacities in 16/58 cases (27%).

An enlarged subsegmental vessel, defined as vessel diameter > 3 mm, was observed in 52/58 patients (89%) with mean vessel diameter of 3.9±0.6 mm. Consolidation was observed in 42/58 patients (72%) including 32/58 (55%) with subsegmental involvement. Presence of lymphadenopathy was reported in 34/58 patients (59%). Less frequent findings are shown in Table 3 and Table 4. Examples of chest CT findings are shown in Figures 2 and 3.

Chest CT features were compared between patients who required hospitalization (inpatients, 49 patients) versus those patients who were referred for home isolation (outpatients,

9 patients). There were no significant differences in chest CT findings between these groups (Figure 5, all findings p> 0.06).

Discussion

To date, the majority of results evaluating the use of chest CT for COVID-19 pneumonia were of patient populations in China. We conducted a prospective study at our institution in Rome, Italy comparing chest CT to RT-PCR for COVID-19 infection. Two RT-PCR tests within 24 hours were used to confirm the presence or absence of COVID-19 infection. In 158 study participants, the sensitivity and specificity of chest CT was 97% (60/62) [95% IC, 88-99%] and 56% (54/96) [95% IC,45-66%], respectively. Typical CT features of COVID-19 were ground glass opacities (58/58, 100%), multilobe (>2 lobes) and posterior involvement (both 54/58, 93%) and bilateral pneumonia distribution (53/58, 91%). On CT, subsegmental vascular enlargement (more than 3 mm diameter) in areas of lung opacity was observed in 89% of patients with confirmed COVID-19 pneumonia. There were no significant differences of chest CT features for individuals who with severe disease who were hospitalized versus those referred for mild disease referred for self-isolation, although the study size was small for this comparison (49 vs. 9 patients, respectively).

Our results are in accordance with the systematic review performed by Salehi et al (17) of 919 patients despite some interesting differences: our population showed a higher prevalence of pulmonary consolidations (72% vs 31%), GGO peripheral distribution (89% vs 76%) and ground glass opacities (100% vs 88%), respectively. Our population differs from that of Zhu et al. of 32 patients, where GGO was found in only 47% of patients with COVID-19 (19). Recently, Chung et al analyzed a small population of 21 patients, showing a very low frequency of crazy paving pattern compared to our results (19% vs 39%, respectively) (18). Mediastinal adenopathy was also much more frequent in our population (58%). In general, the patients in our study were somewhat older (mean, 57 years) with more men (52%) described in prior reports.

An interesting chest CT feature was the presence of enlarged subsegmental pulmonary vessels 89% of study participants. This finding was described by Albarello et al in two patients in Italy (20). Bai et al described subsegmental vascular enlargement in 59% of the patients with COVID-19 pneumonia versus those with 22% of those with non-viral pneumonia. (14). Ye et al suggested vascular enlargement may be due to pro-inflammatory factors (16). Subsegmental

vascular enlargement could reflect the hyperemia induced by SARS-CoV-2 infection versus viral pulmonary infections such as SARS and MERS (21) (22, 23).

The diagnostic performance of chest CT in this study was in accordance with recently published data. Using RT-PCR as reference, we report a high sensitivity of 97%, moderate specificity of 56% and accuracy of 72%. This was similar to results from Ai et al reporting a sensitivity of 97%, specificity of 25% and accuracy of 68% in patients from Wuhan China (5).

Several limitations should be addressed. In our setting, clinical and laboratory data were limited due to the urgency of the situation. Patient outcomes were not available at the time of this communication. The size of our patient study was limited.

In conclusion, typical pattern of COVID-19 pneumonia on chest CT in Rome, Italy was characterized by the consistent presence of peripheral ground glass opacities associated with multilobe and posterior involvement, bilateral distribution, and subsegmental vessel enlargement (>3 mm).

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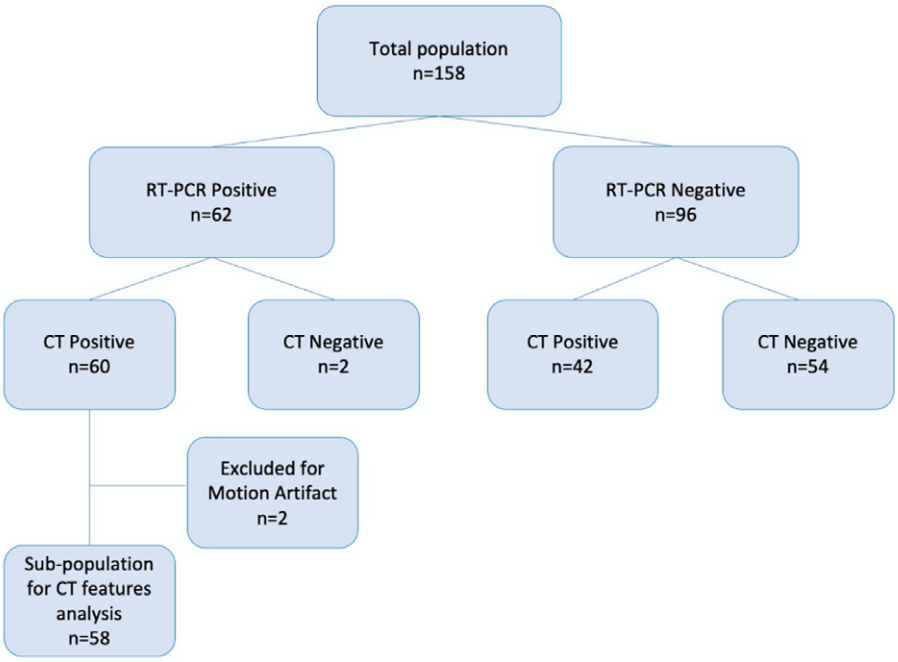

Figure 1: Flow chart of the study.

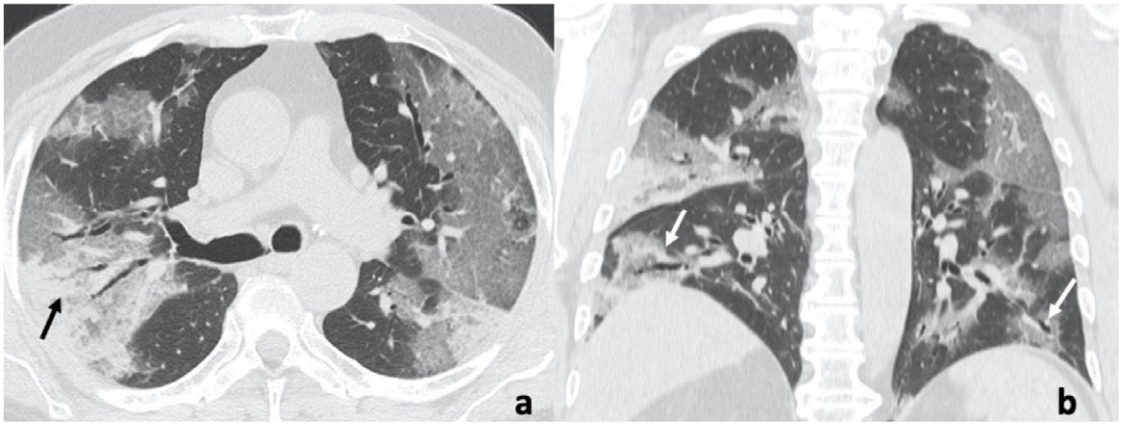

Figure 2: Axial and coronal thin-section unenhanced CT scan of 65-year-old man with unknown exposure history who presented with fever and cough. (a) Chest CT shows diffuse bilateral confluent and predominantly linear ground-glass opacities with a pronounced peripheral distribution and consolidation with air bronchogram (black arrow). (b) Coronal thin-section unenhanced CT scan shows diffuse bronchiectasis of both lower lobes (white arrows).

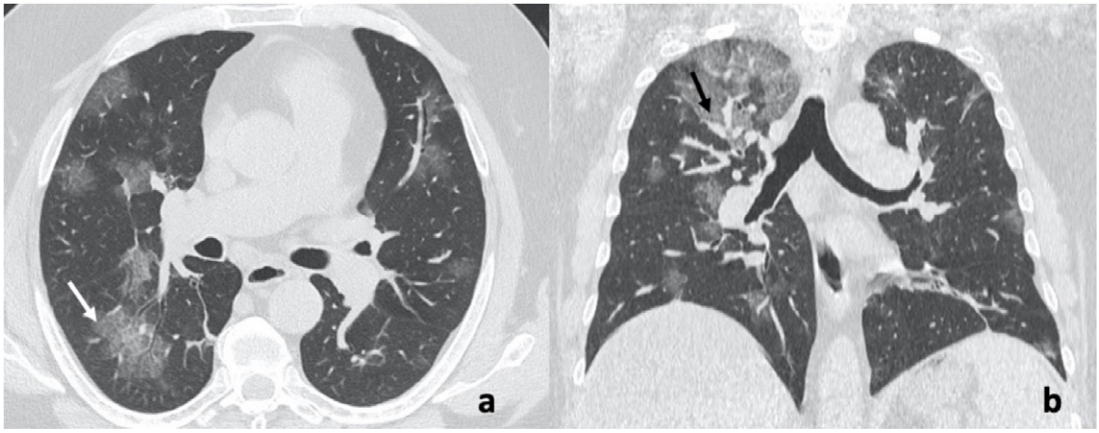

Figure 3: Axial and coronal thin-section unenhanced CT scan of 55-year-old man with history of recent travel to Milan who presented with fever and dyspnea. (a) Scan shows bilateral ground-glass opacities with rounded morphology (white arrow) in both upper and lower lobes, and interlobular/intralobular septal thickening (crazy paving).

(b) Scan shows predominantly apical ground-glass opacities with tubular size increase of segmental and subsegmental vessels (black arrow).

Tables

Table 1: Clinical Data

	Number of patients (n=158)	%
Patient demographics		
Mean age	57±17 y	
Years (range)	18-89	
Total patients	158	100
Male	83	52
Female	75	47
Result of RT-PCR assay		
Positive	62	39
Negative	96	61
Signs		
Fever (>37.5°C)	97	61
Cough	88	56
Dyspnea	52	33
Laboratory test		
C-reactive protein (mg/L; normal range 0.00-0.50)		
Increased	139	88
Normal	19	12
Lactic Acid Dehydrogenase (U/L; range 125-220)		
Increased	128	81
Normal	30	19
Lymphocytes (×10^3/mm^3, normal range 1.5–3.0)		
Increased	13	8
Decreased	95	60
Normal	50	32

Table 2: Diagnostic Performance of chest CT for COVID-19 infection with RT-PCR as the standard of reference

	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
Number	60	54	42	2	60/62	54/96	60/102	54/56	114/158
Percentage					97%	56%	59%	96%	72%
95% CI					88-99%	45-66%	53-64%	87-99%	64-78%

CI confidence interval; TP true positive, TN true negative, FP false positive, FN false negative, PPV positive predictive value, NPV negative predictive value.

Table 3: CT feature in patients with RT-PCR confirmed COVID-19 infection

CT Features Analysis	Patients (N=58)	% (95% CI)
Ground Glass Opacity (GGO)	58	100%
Multilobe involvement (≥ 2 lobes)	54	93% (86-99)
Bilateral distribution	53	91% (83-98)
Posterior Involvement	54	93% (86-99)
GGO location (peripheral)	52	89% (81-97)
Subsegmental vessel enlargement (> 3 mm)	52 (3.9±0.6 mm)	89% (81-97)
Consolidation	42	72% (60-83)
Subsegmental	32	55% (42-67)
Segmental	10	17% (7-26)
Lymphadenopathy	34	58% (45-70)
Bronchiectasis	24	41% (28-53)
Air Bronchogram	21	36% (26-45)
Pulmonary nodules surrounded by GGO	10	17% (7-26)
Interlobular Septal thickening	8	13% (4-21)
Halo sign	7	12% (3-20)
Pericardial Effusion	3	5% (0-10)
Pleural effusion	2	3% (0-7)
Bronchial wall thickening	1	1% (0-3)
Cavitation	0	0%

CI confidence intervals

Table 4: CT feature in patients with RT-PCR confirmed COVID-19 infection

CT Features sub-analysis	Patients (n = 58)	
Number of lobes involved		**% (95% CI)**
0	0	0% (NA)
1	4	6% (0-12)
2	2	3% (0-7)
3	3	5% (0-10)
4	6	10% (2-17)
5	43	74% (62-85)
Frequency of lobe involvement		
Right upper lobe	53	91% (83-98)
Right middle lobe	48	82% (72-91)
Right lower lobe	54	93% (86-99)
Left upper lobe	49	84% (74-93)
Left lower lobe	53	91% (83-98)
GGO pattern		
Crazy Paving	23	39% (26-51)
Rounded morphology	19	32% (19-44)
Linear opacities	16	27% (15-38)

CI confidence interval

Table 5: Comparison of chest CT features in patients hospitalized for COVID-19 pneumonia versus those referred home for self-isolation (mild disease)

CT Features	Inpatients		Outpatients		P value
	n = 49	% (95% CI)	(n = 9)	% (95% CI)	
Ground Glass Opacity (GGO)	49	100%	9	100%	n.a.
Multilobe involvement (≥ 2 lobes)	46	93% (85-100)	8	88% (66-100)	0.58
Bilateral distribution	46	93% (85-100)	7	77% (49-100)	0.11
Posterior Involvement	46	93% (85-100)	8	88% (66-100)	0.58
GGO location (peripheral)	45	91% (82-99)	7	77% (49-100)	0.20
Subsegmental vessel enlargement (< 3 mm)	43	87% (77-96)	9	100%	0.66
Consolidation	37	75% (62-87)	5	55% (22-87)	0.21
Lymphadenopathy	22	44% (30-57)	1	11% (0-31)	0.06