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Comparison of chest computed tomography findings of RT-PCR negative and RT-PCR positive cases in COVID-19 patients

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Abstract

Objective: The purpose was to compare the results of the RT-PCR test, with the findings of Chest CT and to determine the features of CT for the diagnosis of COVID-19 and how to approach RT-PCR negative patients.

Material method: Chest CT findings of 569 COVID-19 diagnosed patients, followed up at the pandemic wards between March and June 2020 were retrospectively examined. Patients were grouped according to RT-PCR results, gender, and age.

Results: 284 (49%) were RT-PCR (+), 285 (50.8%) were RT-PCR (−) of total 569 patients. 11 (1.9%) of RT-PCR (+) had no involvement in Chest CT while all the RT-PCR (−) patients were CT (+). The distribution of lesions in CT were; 544 (95.6%) bilateral, 553 (97.2%) multilobar, 557 (98%) peripherally 151 (26.5%) posteriorly localized. The most common findings were; 539 (94.7%) ground-glass opacity (GGO), 365 (64.1%) consolidation, 160 (28.1%) crazy paving interlobular septal thickening. CO-RADS mean value was 5.4 ± 0.7. GGO and reticulation in RT-PCR (−) patients were significantly higher (p < 0.05). No significant difference was observed, in CT findings for gender. Only the findings of crazy paving interlobular septal thickening and reticulation in 18–64 age group were significantly higher than that in 65–94 age group, 105 (24.8%)–55 (37.9%), 19 (4.5%)–17 (11.7%) respectively (p < 0.05).

Conclusion: The typical findings of COVID-19 pneumonia in Chest CT are: GGO, consolidation and crazy paving in bilateral, peripheral, posterior localization. CT plays an essential role for diagnosis, isolation and treatment in cases of COVID-19 and RT-PCR negative test should be verified by CT.

1. Introduction

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) is a beta corona virus that causes COVID-19 (Coronavirus-19 Disease) infection. It is the 7th corona virus found to infect humans after the coronavirus SARS-CoV-1, which caused the SARS (Severe Acute Respiratory Syndrome) outbreak in China in 2002, and the coronavirus that caused MERS (Middle East Respiratory Syndrome) infection that started in Jordan in 2012. The transmission of SARS-CoV-2 virus is through droplets that spread around during speech, coughing and sneezing. The first case of COVID-19 was reported in China in December 2019. In March 2020, the World Health Organization announced SARS-CoV-2 infection as a pandemic, and as of February 20, 2021, the number of cases worldwide was close to 111 million and more than 2 million people died. Due to the lack of effective antiviral therapy and the fact that vaccination studies that have just begun, early diagnosis and isolation of patients play a crucial role in controlling the epidemic. RT-PCR (real-time reverse transcription polymerase chain reaction of viral nucleic acid) testing for COVID-19 diagnosis is accepted as the reference standard by the T.R. Ministry of Health. As the RT-PCR test requires special equipment, difficulties exist such as collecting and transporting samples, obtaining the results of which are in the range of several hours to a few days, and nasopharyngeal samples giving between 30 and 60% positive results during the first clinical admission. RT-PCR test,
laboratory findings and Chest CT (Chest Computed Tomography) should be evaluated together for the diagnosis of COVID-19 infection. The low sensitivity of the RT-PCR test causes the diagnosis and treatment of many COVID-19 patients to be delayed and continue to infect the community due to the high transmission of the virus. Chest CT is an easy-to-apply, rapidly concluded diagnostic method used in the diagnosis of pneumonia. Chest CT has high sensitivity to show areas of peripheral posterior distribution of GGO, interlobular septal thickening and consolidation in which lower lobes specific to COVID-19 are predominantly involved in which clinically suspected, RT-PCR negative, early-stage patients. The incubation period of SARS-CoV-2 infection is about 5 days (2–14 days), the onset of symptoms is about 10 days (8–16 days) after getting infected. In some studies, the detection of radiological findings earlier than symptom onset has shown the importance of radiological imaging in diagnosing the cases, isolating them from healthy people and initiating the early treatment process. Chest CT’s important role in detecting COVID-19 infection in early stages, has changed treatment protocols in many parts of the world. Although, it is discussed that radiology units constitute a source of contamination due to Chest CT in the period when the hospital burden increases, the prognosis of infection is tried to be estimated by making quantitative measurements of the patient’s lung involvement by visual scoring using artificial intelligence and Chest CT regression models in some centers.

2. Materials and methods

This retrospective study was conducted at Istanbul Health Sciences University, Sisli Hamidiye Effaf Training and Research Hospital, after receiving the approval of the T.C. Ministry of Health and the corporate ethics committee (Date: April 22, 2020, Issue: 2736). The patients who were admitted to the emergency department of our hospital between March and June 2020, with symptoms of fever, dry cough, dyspnea, loss of smell taste and with a pre-diagnosis of COVID-19 pneumonia, who had undergone both RT-PCR test and Chest CT were screened. Among them, the data of 569 patients (313 males, 256 women), who were followed up at the pandemic wards according to the Department of Public Health Turkish Ministry of Health COVID-19 Field Guide were evaluated. Patients <18 age, pregnant women, those with >2 days between RT-PCR test and Chest CT, or with motion artifacts on Chest CT were not included in the study. According to the RT-PCR and CT results of the patients at the time of admission; it was defined as CT (+) CT (+), based on the findings which were compatible or incompatible with COVID-19 pneumonia on Chest CT. Later, the distribution, the localization, the characteristics of Chest CT features and CO-RADS (COVID-19 Reporting and Data System) score were compared. CO-RADS, developed by Dutch radiologists, categorizes the level of suspicion of COVID-19 pneumonia by the use of CT scans and are scored 0 to 6; 1 shows CT findings with “very low probability”, 2 “low probability”, 3 “uncertain”, 4 “high probability” and 5 “very high probability”, while 6 shows “RT-PCR(+)” cases. Chest CT findings were also examined according to the gender of the patients and the age groups between 18-64 and 65-94. Ground-glass opacity, consolidation, crazy paving image, interlobular septal thickening, vascular enlargement (subsegmental vessel diameter > 3 mm), air bronchogram, bronchiectasis, bronchial wall thickening, reticulation, subpleural lines/curvilinear opacity, nodule, halo sign, reverse halo sign (pulmonary nodule surrounded by GGO), pleural thickening and lymphadenopathy (lymph node with a diameter of ~10 mm on the short axis); CT features such as peripheral (peripheral 1/3 residual area of the lung), central distribution, posterior localization were recorded. Demographics, accompanying diseases and Chest CT images were examined from hospital computer records and the Picture Archiving and Communication System (PACS). RT-PCR test was performed using nasopharyngeal/oropharyngeal swabs (Bio speedy SARS CoV-2 Double Gene RT qPCR Kit; Bioeksen) kit. Chest CT was performed in the supine position, during end-inspiration, without IV contrast administration. Patients were given a 100 kV (peak) (kV[p]) and 20 effective milliampere-second (eff mA-s) protocol in the form of unenhanced Chest CT, using the 512 × 512pixel image matrix, 2 mm thin sections were taken in the axial image. Mediasten window adjustment (width, 400 HU; level, 100 HU) and lung window adjustment (width, 1500 HU; level, –500 HU) were used in this study. Tomography findings were evaluated by 2 experienced radiologists and consensus was reached for CO-RADS value.

2.1. Statistical method

In the descriptive statistics of the data, mean, standard deviation, median, lowest, highest, frequency and ratio values were used. The distribution of variables was measured by Kolmogorov-Smirnov test. Independent sample t-test and Mann-Whitney U test were used in the analysis of quantitative independent data. In the analysis of qualitative independent data, Chi-Square testing, when Chi-Square testing conditions were not met, Fischer test was used. SPSS 27.0 program was used in the analysis.

2.2. Results

The data of 569 in-patients between the ages of 18 and 94, who were followed up at the pandemic wards, during March 11,2020 and May 30,2020 were retrospectively examined in this single-centered study. Patients who were detected with SARS-CoV-2 PCR(+) or/and SARS-CoV-2 IgM/G (+/-) or who have the symptoms that are radiologically compatible with COVID-19 but are unexplained by other diagnoses are included. The study group consisted of 256 (45%) female and 313 (55%) male. 284 (49%) patients tested (+) for RT-PCR, while 285 (50.08%) tested (−) for RT-PCR. The mean age of the patients was 55 ± 15.3 (female 55.7 ± 17.05male 54.2 ± 14.03). The most common accompanying diseases were hypertension in 188 (33%) and diabetes in 124 (21.8%) patients, while 228 (40.1%) patients had no accompanying diseases. A total of 558 (98.1%) patients had lung involvement in CT, while 11 (1.9%) had no CT involvement. Distribution of lesions in CT was 544 (95.6%) bilateral and 553 (97.2%) multilobar; 14 (2.5%) unilateral and 5 (0.9%) unilateral. Localization of lesions was 557 (97.8%) peripheral, 151 (26.5%) posterior and 35 (5.8%) central. The most common radiological findings were 539 (94.7%) GGO, 365 (64.1%) consolidation, 160 (28.1%) crazy paving interlobular septal thickening. The mean value of CO-RADS was 5.4 ± 0.7.

The demographic and radiological characteristics of the patients are shown in Table 1.

In the group with RT-PCR(+), lung involvement in CT, bilateral multilobar distribution of lesions and peripheral posterior localization rate were found to be significantly lower (p < 0.05), compared to those in the group with RT-PCR(−). In both groups, unilateral unilobar distribution and central localization rate did not differ significantly (p > 0.05). In CT images, GGO and reticulation were found to be significantly lower in RT-PCR(+) group than in RT-PCR(−) group (p < 0.05). Similarly, the two groups did not differ with respect to radiological images such as consolidation, crazy paving, interlobular septal thickening, vascular enlargement, air bronchogram, bronchiectasis, subpleural lines, nodule halo finding, reverse halo sign, pleural thickening, lymphadenopathy (p > 0.05). The CO-RADS value in the group with RT-PCR(+) was found to be significantly higher than in the group with RT-PCR(−) (p < 0.005) (Table 2). CT Characteristics and Features of Table 2 are shown in Figs. 1 and 2.

When we grouped and examined Chest CT findings by gender, there was no significant difference between the two groups in terms of lung involvement, distribution, localization and characteristics of lesions in CT (p > 0.05) (Table 3).

When we grouped patients as 18–64 years old and 65–94 years old, there was no significant difference in lung involvement in CT was found.
3. Discussion

SARS-CoV-2 binds to the ACE-2 receptor, causing damage to the pulmonary interstitium and later parenchyma. RT-PCR test is standard for confirming diagnosis, but it takes time for the test to conclude; sampling errors, inadequate viral material can delay diagnosis. Sensitivity of the test is between 37 and 71%. The reliability of this test depends on the quality of nasopharyngeal samples, the time the samples were taken, the sensitivity of the RT-PCR test kit used. Recently published mortality studies examining the early periods of the outbreak have shown that, cases with RT-PCR(-) that have not been diagnosed with COVID-19 are nonnegligible.

The Fleischner Society does not recommend the use of Chest CT for triage in asymptomatic or mild clinical cases in April 2020 report. However, in moderately severe cases of COVID-19 where respiratory status is impaired, they recommend CT regardless of the RT-PCR result. In a study of 1014 cases, patients were analyzed based on Chest CT findings and RT-PCR test. RT-PCR's sensitivity was reported as 60–70% and CT's sensitivity was 97%. In regions with high incidence in the rapidly spreading COVID-19 pandemic; contact history, clinical symptoms, typical Chest CT findings and dynamic CT changes of the RT-PCR (−) cases should be evaluated together. Considering the time as short as 9 days from symptom onset to the development of ARDS (acute respiratory distress syndrome), the importance of a method that yields results in minutes such as Chest CT is undeniably useful for COVID-19 pneumonia diagnosis.

RSNA (Radiological Society of North America) categorizes COVID-19 Chest CT into 4 categories as “typical”, “indeterminate”, “atypical” and “negative” in reporting. RT-PCR (−) patients with “typical” findings or CO-RADS 4–5 in CT, should be isolated until repeated tests rule out COVID-19 or alternative diagnoses are found explaining the symptoms (24). In other words, CO-RADS should be evaluated together with the clinical and laboratory findings. In our study, CO-RADS was found to be higher in the RT-PCR(+) group than RT-PCR(−) cases (5.8 ± 0.7, 4.9 ± 0.4) respectively. While all RT-PCR(−) patients had CT involvement, 11 (3.9%) of 284 RT-PCR (+) patients had no CT involvement. CT performed within the first 2 days after the onset of symptoms may not reveal any lesions. RSNA states that, the number of CT reports as “atypical” or “negative” in RT-PCR(+) patients is too high to be neglected. As patients with RT-PCR(+) CT (−) can be carriers of SARS-CoV-2 and their isolation is mandatory due to their importance in the spread of infection. In the study of Liu T et al., 3 RT-PCR(+) people living in the same house were examined and their clinical characteristics and CT involvement were found to be completely different. A normal Chest CT is not enough to exclude the possibility of COVID-19 pneumonia.

In their study conducted at the beginning of the outbreak, Guan W et al. observed instantaneous involvement in 86.2% of 975 Chest CT and found that the most common radiological finding was ground glass opacity with 56.4%.

| Table 1 | Demographic and radiological characteristics of patients. |
|---------|----------------------------------------------------------|
| Age     | Min–max | Median | Mean ± SD/n/ % |
| Age group |        |        |               |
| 18–64   | 18,0 – 94,0 | 55,0 | 55,0 ± 15,3 |
| 65–94   | 424 | 74,5% |
| Gender |        |        |               |
| Female  | 145 | 25,5% |
| Male    | 313 | 55,0% |
| Comorbidities | (-) | (+)   |               |
| (-)    | 228 | 40,1% |
| (+)    | 341 | 59,9% |
| Chronic pulmonary diseases |        |        |               |
| Hypertension | 54 | 9,5% |
| Cardiovascular diseases | 188 | 33,0% |
| Diabetes mellitus | 84 | 14,8% |
| Chronic kidney diseases | 124 | 21,8% |
| Neurological diseases | 21 | 3,7% |
| Psychiatric diseases | 13 | 2,3% |
| Chronic hepatitis | 4 | 0,7% |
| Rheumatologic diseases | 14 | 2,5% |
| Malignancy | 3 | 0,5% |
| CT Involvement | (-) | (+)   |               |
| Bilateral | 11 | 1,9% |
| Multilobar | 558 | 98,1% |
| Unilateral | 544 | 95,6% |
| Unilobar | 14 | 2,5% |
| Localization |        |        |               |
| Peripheral | 557 | 98,0% |
| Central | 33 | 5,8% |
| Posterior | 151 | 26,5% |
| Radiological findings |        |        |               |
| Ground-glass opacity | 539 | 94,7% |
| Consolidation | 365 | 64,1% |
| Crazv paving pattern, interlobar septal thickening | 365 | 64,1% |
| Vascular enlargement | 160 | 28,1% |
| Air bronchogram | 79 | 13,9% |
| Bronchiectasis, bronchial wall thickening | 1 | 0,2% |
| Reticulation | 36 | 6,3% |
| Subpleural lines, curvilinear opacity | 13 | 2,3% |
| Nodule, halo sign | 5 | 0,9% |
| Reverse halo sign | 2 | 0,4% |
| Pleural thickening | 1 | 0,2% |
| Lymphadenopathy | 1 | 0,2% |

| CO-RADS | 0,0 – 6,0 | 5,0 | 5,4 ± 0,7 |

(p > 0.05). In the 65–94 age group, the rate of crazy paving interlobar septal thickening and reticulation was found to be significantly lower than in the 18–64 age group (p < 0.05) (Table 4).
Comparison of demographic characteristics and CT features between groups RT-PCR(+) and RT-PCR(−) results.

|                        | RT-PCR(+) | RT-PCR(−) | P       |
|------------------------|------------|------------|---------|
|                        | Mean ± SD/n/| Mean ± SD/n/| <       |
| Age                    | Median     | Median     | t       |
| Age group              |            |            |         |
| 18–64                  | 55.7 ± 14.8| 55.0 ± 14.8| 0.275   |
| 65–94                  | 215 ± 75.7 | 69 ± 24.3  | 0.516   |
| Gender                 |            |            | X²      |
| Female                 | 142 ± 50.0 | 142 ± 50.0 | 0.017   |
| Male                   | 76 ± 26.7  | 69 ± 24.3  | 0.070   |
| Comorbidities (−)      |            |            | X²      |
| Comorbidities (+)      |            |            |         |
| Chronic pulmonary disease | 24 ± 13.7 | 24 ± 13.7 | 0.398   |
| Hypertension           | 104 ± 59.4 | 104 ± 59.4 | 0.070   |
| Cardiovascular disease | 41 ± 23.4  | 41 ± 23.4  | 0.827   |
| Diabetes mellitus      | 56 ± 32.0  | 56 ± 32.0  | 0.232   |
| Chronic kidney disease | 10 ± 5.7   | 10 ± 5.7   | 0.994   |
| Neurological diseases  | 7 ± 4.0    | 7 ± 4.0    | 0.122   |
| Psychiatric diseases   | 7 ± 4.0    | 7 ± 4.0    | 0.774   |
| Chronic hepatitis      | 3 ± 1.7    | 3 ± 1.7    | 0.314   |
| Rheumatologic diseases | 8 ± 4.6    | 8 ± 4.6    | 0.584   |
| Malignancy             | 2 ± 1.1    | 2 ± 1.1    | 0.624   |
| CT involvement (−)     | 11 ± 3.9   | 11 ± 3.9   | 0.001   |
| (+)                    | 273 ± 96.1 | 273 ± 96.1 |         |
| Distribution           |            |            | X²      |
| Bilateral              | 264 ± 93.0 | 264 ± 93.0 | 0.002   |
| Multilobar             | 271 ± 95.4 | 271 ± 95.4 | 0.011   |
| Unilateral             | 9 ± 3.2    | 9 ± 3.2    | 0.276   |
| Unilobar               | 2 ± 0.7    | 2 ± 0.7    | 0.656   |
| Localization           |            |            |         |
| Peripheral             | 273 ± 96.1 | 273 ± 96.1 | 0.000   |
| Central                | 19 ± 6.7   | 19 ± 6.7   | 0.364   |
| Posterior              | 64 ± 22.5  | 64 ± 22.5  | 0.031   |
| Radiological findings  |            |            |         |
| Ground-glass opacity   | 259 ± 91.2 | 259 ± 91.2 | 0.000   |
| Consolidation          | 173 ± 60.9 | 173 ± 60.9 | 0.109   |
| Cavernous pattern, interlobular septal thickening | 79 ± 27.8 | 79 ± 27.8 | 0.873   |
| Vascular enlargement   | 41 ± 14.4  | 41 ± 14.4  | 0.704   |
| Air bronchogram        | 1 ± 0.4    | 1 ± 0.4    | 0.499   |
| Bronchietasis, bronchial wall thickening | 8 ± 2.8 | 8 ± 2.8 | 0.126   |
| Reticiuation            | 12 ± 4.2   | 12 ± 4.2   | 0.040   |
| Subpleural lines, curvilinear opacity | 5 ± 1.8 | 5 ± 1.8 | 0.404   |
| Nodule, halo sign      | 2 ± 0.7    | 2 ± 0.7    | 0.656   |
| Reverse halo sign      | 0 ± 0.0    | 0 ± 0.0    | 0.00     |
| Pleural thickening      | 0 ± 0.0    | 0 ± 0.0    | 1000     |
| Lymphadenopathy        | 0 ± 0.0    | 0 ± 0.0    | 1000     |
| CO-RADS                 | 5 ± 0.7    | 5 ± 0.7    | 0.000    |

In our study group, both the RT-PCR(+) and the RT-PCR(−) patients' CT images were predominantly bilateral, multilobar involvement; GGO, consolidation and crazy paving image were observed in peripheral posterior localization. The RT-PCR(−) patients had more GGO and reticulation than the RT-PCR(+) group. We interpreted this finding such that the RT-PCR negative cases are still at an early stage. GGO are early consolidation findings in symptomatic cases.

Although COVID-19 is seen in all age groups, it mostly affects the middle age group. The average age of the group we studied was 55 ± 15.3. In many COVID-19 studies, male gender dominance has been shown. Our study group consisted of 55% male and 45% female patients. 60% of RT-PCR(−) cases were male and 40% were female patients. In our study, crazy paving interlobular septal thickening and reticulation were observed with a higher rate in the 18-64 age group than in the 65-94 age group. The crazy paving is an advanced stage (5–8 days) finding: caused by the interlobular septal thickening superimposed on the GGO. Consolidations seen in COVID-19 pneumonia are also bilateral, multifocal and tend to be located in the peripheral subpleural area. Nodule, halo finding, pleural thickening, lymphadenopathy are rare radiological findings in COVID-19 pneumonia, and which were found to be rare in our study as well (5 0.9%-1 0.2%-1 0.2%). Heshui Shi et al., in their study grouped patients individually according to whether Chest CT was performed before or after the onset of symptoms and in the asymptomatic group, before detecting abnormalities in the laboratory values, they observed lung involvement in the CT of the 81 patients. They also indicated that in the asymptomatic group, CT findings progressed from focal unilateral involvement to bilateral GGO and/or consolidation within 1–3 weeks. S. Inui et al. reported predominantly ground-glass opacities in asymptomatic RT-PCR(+) cases and consolidation findings in symptomatic cases. Although bilateral ground glass opacities are considered as characteristic of COVID-19 pneumonia, similar radiological findings can be seen in pneumonia caused by other beta coronaviruses, rhinoviruses, influenza. However, RSNA suggests that these findings can be reported as “compatible with COVID-19 pneumonia” rather than “viral pneumonia” in the pandemic environment. There are some limitations to our study: Repeated RT-PCR results of patients and dynamic changes in CT were not examined due to the
patient overload at the Emergency Department, the time between the onset of symptoms to the RT-PCR test or CT is unclear. Prospective studies including clinical outcome of patients are needed for better understanding COVID-19.

4. Conclusion

The data of 569 patients who were followed up with Covid-19 diagnosis were examined in the city, which is the most populated one in the country and is the center of the epidemic. RT-PCR (−) and RT-PCR (+) patient numbers were almost equal. The patients had similar average age and accompanying disease, depending on gender. The female patients in the RT-PCR(+) group were significantly higher than in the RT-PCR(−) group.

Typical radiological findings of COVID-19 such as bilateral, peripheral, posterior localization GGO and consolidation were seen in Chest CT of patients and these were in compliance with the literature. When RT-PCR(−) and (+) cases are compared, the higher incidence of GGO in RT-PCR(−) led us to think that these patients are at early-stage. Furthermore, the higher incidence of crazy paving interlobular septal thickening and reticulation seen at 18–64 age group could be explained in terms of greater number of patients and the different stages of infection.

The world has been fighting the COVID-19 infection, which is transmitted by respiratory droplets and direct contact, and it can cause severe pneumonia, with a mortality rate of about 2% since December 2019. Nonspecific clinical findings and symptoms, asymptomatic carriers and the high infectivity of the virus mandate the use of specific diagnostic methods for rapid diagnosis and patient isolation in COVID-19 pneumonia.

Author contributions

The authors confirm contribution to the paper as follows: Study Design: M. Arzu Özkaraflı, Hüseyin Özkurt. Data collection: Üğur Yanc, M. İleriş Bardaç, İşıl Kibar Akıllı. Analysis and interpretations of results: M. Arzu Özkaraflı, Hüseyin Özkurt, Draft manuscript
| CT features of. | 18-64 age group | 65-94 age group | P  |
|----------------|-----------------|----------------|----|
| CT involvement |                 |                |    |
| (−)            |                  |                |    |
| 6              | 2,3%            | 5              | 1,6%| 0,233 X² |
| (+)            | 418             | 163,3%         | 140 | 44,7%    |
| Radiological findings |               |                |    |
| Ground-glass opacity |          |                |    |
| 405            | 95,5%           | 134            | 92,4%| 0,149 X² |
| Consolidation   | 266             | 62,7%          | 99  | 68,3%    |
| Crazzy pving pattern, interlobular septal thickening | | | |
| 105            | 24,8%           | 55             | 37,9%| 0,002 X² |
| Vascular enlargement |          |                |    |
| 61             | 14,4%           | 18             | 12,4%| 0,553 X² |
| Air bronchogram | 1               | 0,2%           | 0   | 0,0%     |
| Bronchiectasis, bronchial wall thickening | | | | |
| 8              | 1,9%            | 3              | 2,1%| 0,891 X² |
| Reticulation   | 19              | 4,5%           | 17  | 11,7%    |
| Subpleural lines, curvilinear opacity  | 10              | 2,4%           | 3   | 2,1%     |
| Nodule, halo sign | 5               | 1,2%           | 0   | 0,0%     |
| Reverse halo sign | 1               | 0,2%           | 1   | 0,7%     |
| Pleural thickening | 0               | 0,0%           | 1   | 0,7%     |
| Lymphadenopathy | 0               | 0,0%           | 1   | 0,7%     |

X² - Chi-square test (Fisher test).

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Declaration of competing interest

No potential conflict of interest relevant to this article was reported.

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