CT Findings in Patients with COVID-19-Compatible Symptoms but Initially Negative qPCR Test

CT-Manifestationen in Patienten mit COVID-19-typischen Symptomen trotz initial negativem qPCR-Test

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ZUSAMMENFASSUNG

Ziel Mittels dieser Studie soll evaluiert werden, ob Patienten mit starkem Verdacht auf eine SARS-CoV-2 Infektion trotz eines bereits erfolgten negativen quantitativen Polymerase-Kettenreaktion (qPCR)-Tests mittels Computertomografie (CT) verlässlich diagnostiziert werden können.

Material und Methoden In dieser retrospektiven Studie wurden 437 Patienten mit Verdacht auf COVID-19, aber initial negativer qPCR und anschließend durchgeführter Thorax-CT zwischen dem 13. März und 30. November 2020 eingeschlossen. Der Referenzstandard zu den CT-Befunden war die qPCR (mindestens 3 aufeinander folgende qPCR-Tests, im Falle eines Infektionsverdachtes durch die CT), um die Sensitivität, Spezifität, den positiven prädiktiven Wert (PPV) und den negativen prädiktiven Wert (NPV) des CT zu bestimmen.

Ergebnisse Die CT erzielte eine Sensitivität von 100 % (95 % Konfidenzintervall [KI]: 65–100), eine Spezifität von 88 % (95 % KI: 84–90), einen PPV von 12 % (95 % KI:6–22), einen NPV von 100 % (95 % KI: 99–100) und eine diagnostische Genauigkeit von 88 % (95 % KI: 84–91).

Schlussfolgerung In diesem speziellen Studiensetting kann die CT trotz initial negativer qPCR eine SARS-CoV-2 Infektion detektieren. Alle Patienten mit einem positiven CT-Befund zeigten einen fortgeschrittenen pulmonalen Befall trotz aktueller negativer qPCR. Die CT kann als diagnostische Methode bei weiterbestehendem klinischen Verdacht auf eine SARS-CoV-2 Infektion trotz negativem qPCR-Test eingesetzt werden und eine Infektion sicher ausschließen.

Kernaussagen:

- Die Low-Dose-Thorax-CT kann infizierte Patienten trotz vorliegendem negativen qPCR-Test erkennen und eignet sich aus diesem Grund, besonders im frühen Krankheitsstadium, als additive diagnostische Methode.
- Die Low-Dose-Thorax-CT kann eine SARS-CoV-2 Infektion in einer Pandemie verlässlich ausschließen.
- Eine zuverlässige Differenzierung zu anderen viralen Parenchymveränderungen ist schwierig.

ABSTRACT

Purpose To assess whether it is possible to reliably detect patients with strong suspicion of COVID-19 despite initially negative quantitative polymerase-chain-reaction (qPCR) tests by means of computed tomography (CT).

Materials and Methods 437 patients with suspected COVID-19 but initially negative qPCR and subsequent chest CT between March 13 and November 30, 2020 were included in this retrospective study. CT findings were compared to results of successive qPCR tests (minimum of 3 qPCR tests if

CT suggested infection) to determine the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CT for diagnosing COVID-19.

Results COVID-19 was diagnosed correctly with a sensitivity of 100 % [95 % confidence interval (CI): 65–100] and a specificity of 88 % [95 % CI: 84–90]. A PPV of 12 % [95 % CI: 6–22] and an NPV of 100 % [95 % CI: 99–100] were determined.

Conclusion CT is able to detect COVID-19 before qPCR in initially negative patients in this special study setting. Similar CT findings in COVID-19 and other atypical pneumonias can lead to high numbers of false-positive patients, reducing the specificity of CT.

Key Points:
- Low-dose chest CT is able to diagnose COVID-19 in symptomatic patients even in cases of an initially negative quantitative PCR result and therefore is a fast support method to detect COVID-19, especially in early disease.
- Low-dose chest CT can reliably exclude COVID-19 in a pandemic setting.
- CT does not always ensure a reliable differentiation from other viral diseases.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has kept the entire world in suspense. The gold standard of COVID-19 diagnosis is quantitative polymerase chain reaction (qPCR). However, the sensitivity of qPCR depends on different factors, such as disease stage, the method of sample acquisition, and the type of test in use [1]. For this reason, the Fleischner society recommends additionally performing a low-dose chest CT examination in patients with clinical presentation and/or medical history indicative of COVID-19 or in patients experiencing an aggravation of symptoms [2]. CT examinations may indicate COVID-19 pneumonia earlier than qPCR in specific cases since they allow independent assessment of the involvement of the lung parenchyma [3, 4]. Typical CT findings of COVID-19 pneumonia are ground-glass opacities, infiltrations, crazy paving pattern, and predominant involvement of the lower lobes and the periphery [3, 5–11]. However, these imaging findings are non-specific and may appear in a similar way in other diseases [9, 12], like other viral pneumonias. In an early stage of a viral infection, imaging patterns caused by different viruses are similar and cannot be distinguished easily by means of CT [13]. Besides in a SARS-CoV-2 infection, ground-glass opacities occur in 75 % of patients with cytomegalovirus, 50–75 % with adenovirus, and up to 25 % with influenza [14]. Consolidations can also occur in 50–75 % of patients with adenovirus and up to 25 % with influenza [14]. Hence, ground-glass opacities and consolidation are typical but not specific for COVID-19.

Since qPCR tests might provide false-negative results and since CT might not allow differentiation between COVID-19 pneumonia and other pneumonias, infection control in a pandemic situation might be challenging, especially in a large hospital and in the case of a high patient volume. Here, it is of utmost importance to identify patients with CT findings typical for COVID-19 pneumonia to a) initiate adequate patient treatment and b) to prevent transmission of infections between patients and between patients and staff. The purpose of this retrospective study was therefore to assess whether low-dose chest CT allows the diagnosis of COVID-19 in symptomatic patients with initially negative qPCR.

Materials and methods

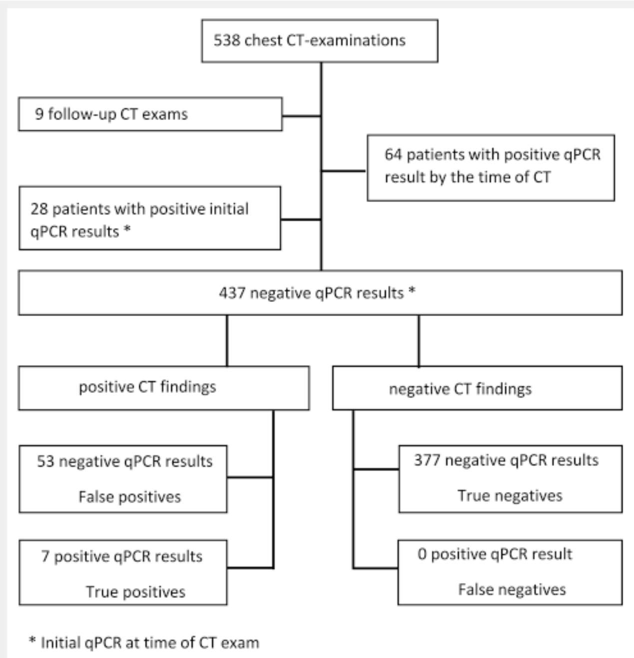
Patient cohort

The institutional review board approved this retrospective study cohort and waived patient informed consent. Approval was granted for analysis of the CT images, medical records, and laboratory data. Patient diagnosis and treatment have not been modified for the purpose of this study. This study includes patients that underwent a chest CT in our department between March 13 and November 30, 2020. Thus, this study covers the period of the entire first wave and the "lockdown light" phase of the second wave (rise of the second wave) in Germany in 2020. Patients were admitted through the emergency department of the hospital or via different hospital units for other elective reasons for admission.

The inclusion criteria were an initially negative qPCR test and suspected SARS-CoV-2-infection based on respiratory symptoms, which included cough, shortness of breath, and/or need for oxygen supply, and a chest CT examination after an initial qPCR test. The exclusion criteria were follow-up examinations and CT examinations following a positive qPCR test result, see ▶ **Fig. 1**. Patients with an initially negative, but subsequently positive qPCR test, without any CT examination during their treatment were not included in this study.

qPCR

At our clinic, patients are tested for suspected COVID-19 at the time of referral using a standardized qPCR method according to a standardized protocol of our virology department [15]. Initial qPCR tests were performed in the emergency room on respiratory tract specimens (nasopharyngeal and oropharyngeal) at the virology department. Further tests were taken at the different hospital units. In our hospital, even in the early pandemic phase, the qPCR tests were usually available after 6–8 hours. Results of the qPCR



▶ **Fig. 1** Overview of the included patients, computed tomography (CT) results, and quantitative polymerase chain reaction (qPCR) results.

▶ **Abb. 1** Überblick über die in die Studie eingeschlossenen Patienten sowie die Ergebnisse der Computertomografie (CT) und quantitativen Polymerasekettenreaktion (qPCR).

tests were available prior to CT acquisition. Patients with suspected infection were isolated from each other in special wards. In cases in which patients were symptomatic for COVID-19, were first-contact persons, and had steadily worsening symptoms with, e. g., increasing oxygen demand and need of intubation or additional suspicion of lung arterial embolism, CT scans were performed prior to the notification of the qPCR results due to emergency care.

In the case of clinical and image morphological suspicion of infection, a patient was admitted as an inpatient. If three subsequent qPCR test results were negative, a patient was treated as non-infected.

Information on the number of qPCR tests, timing of tests, type of testing, and test results was obtained and analyzed by the Department of Virology.

Antibody test

Antibody tests were performed in patients in poor clinical condition with suspected infection despite multiple negative qPCR tests. At the beginning of the pandemic, it was not yet possible to make a statement about the test accuracy of the COVID-19 qPCR test, since no evaluated comparative method was available. Here, in addition to CT examination, antibody tests were also carried out occasionally in order to detect a false-negative qPCR test in the case of antibody detection. The presence of IgA and IgG antibodies directed against corona epitopes was tested by the virology department.

CT acquisition

Due to the radiation exposure during CT examinations and the risk of stochastic and deterministic radiation damage including risk of radiation-induced cancer, CT was not performed as the primary diagnostic method for the detection of infection in our hospital in every patient. Only if patients had clinical indications (e. g., worsening of symptoms resulting in unstable patients, oxygen supply, intubation, and life-threatening diagnoses like pulmonary embolism), CT was performed. Even though we occasionally had many patients with respiratory symptoms in the emergency department, the indication for CT was restrictive.

All included patients were examined on one of three state-of-the art CT scanners (Somatom Definition Edge – scanner A, during day period – or Somatom Definition Flash (scanner B) and Somatom Definition AS (scanner C), during the night and on weekends (all Siemens Healthineers, Forchheim, Germany). Patients were imaged in supine position with elevated arms and in breath-hold technique following maximal inspiration. The scan range was defined from the lung apex to the base. The applied CT protocol parameters were 100–120 kV_p with automatic exposure control. Images were reconstructed iteratively using ADMIRE (scanner A) and SAFIRE (scanner B, C) (both Siemens Healthineers, Forchheim, Germany). According to the national recommendations for the diagnosis of COVID-19, a non-contrast-enhanced chest CT examination was performed. Only in cases with an additional diagnostic question (n = 3, e. g. lung embolism), contrast agents were applied [16].

CT image evaluation

CT images were reviewed in consensus by one resident and two board-certified radiologists. A structured reporting system is used in the institution to evaluate each CT scan according to the same criteria. The following CT criteria were considered: a) lesion characteristics: ground-glass opacities, consolidation, crazy paving pattern, interlobular septal thickening, air bronchogram, bronchiectasis, caverns, pleural thickening and pneumothorax, b) lesion location: left, right, or bilateral lung parenchyma, peripheral or central accentuation. All additional pathologies were described in a “further findings” section.

Based on the literature, DRG, and the RSNA recommendations, the suspicion of an infection was raised in the presence of the following CT patterns [3, 5–8, 10, 11, 17]: ground-glass opacities, consolidation, crazy paving pattern, and bilateral patterns with emphasis on the lung periphery. Consolidations and crazy paving patterns were optional and not necessarily suspicious as long as bilateral, peripherally accentuated ground-glass opacities with a patchy appearance were present. In the presence of non-typical changes, e. g., evidence of bacterial infection such as consolidations in one lobe, tree-in bud phenomenon, peripheral avoidance, ubiquitous mosaic ground-glass patterns with septal thickening and enlarged heart and/or unilateral occurrence, patients were classified as non-infectious. Especially in an early state of infection, unilateral occurrence may also be shown by SARS-CoV-2 infection, as published after this study, but we internally classified unilateral occurrence as unlikely at the time of study [18].

Data collection

CT image data, volumetric CT dose index ($CTDI_{vol}$), dose length product (DLP), and scan length were collected in the local picture archive and communication system (SECTRA Medical, Sweden). Patient weight and height were documented.

The effective dose was calculated using the tube potential-specific conversion factors published by Deak et al. (k_{100kVp} = 0.0144 mSv/(mGy · cm), k_{120kVp} = 0.0145 mSv/(mGy · cm)), using the tissue weighting factors in ICRP publication 103 [19].

Data analysis

Statistical analysis was performed using SPSS version 27 (SPSS Inc. Chicago, IL) and Microsoft Excel 2016 (Redmond, WA, USA). For continuous values, mean and standard deviation with the corresponding ranges (minimum-maximum) are provided. The sensitivity, specificity, positive and negative predictive values (PPV/NPV), and disease prevalence including 95 % confidence intervals (CI) were calculated by applying the contingency table with the Fisher's exact and Wilson-Brown test using qPCR results as the reference with GraphPad Prism 8.0 (GraphPad Software, Inc., San Diego, California, USA). A contingency table with Fisher's exact test as well as Chi-square test was performed to assess differences in CT findings between COVID-19 true-positive, false-positive, and true-negative patients according to the structured report. The level of significance was $p < 0.05$. Tests were adjusted for all pairwise comparisons using Bonferroni correction.

Results

Patient population

A total of 437 examinations were included in the final study cohort (see ▶ **Fig. 1**). Patient characteristics and CT exposure parameters can be found in ▶ **Table 1**.

qPCR results and antibody test results

All included patients were initially negative according to the primary qPCR test. Despite the initially negative qPCR test, subsequent qPCR tests were positive in seven patients. Therefore, the initial qPCR was false-negative in 7/437 (1.6 %) patients.

In 9/437 (2 %) patients, antibody tests were carried out during hospitalization. Two of the tests detected IgA or IgG antibodies.

Diagnostic performance of CT

Of all included patients, 60/437 (14 %) patients had CT findings in accordance with COVID-19. CT detected all of the abovementioned 7/60 (12 %) patients with positive subsequent qPCR tests correctly (CT true positives) (see ▶ **Fig. 2**). In 53/60 (88 %) patients, the qPCR remained negative (CT false positives). In 377/437 (86 %) patients, CT findings were not in accordance with COVID-19 (CT true negatives). There were no false-negative results on CT evaluation.

▶ **Table 1** Chest computed tomography protocol parameters and patient cohort information. For the latter, results are reported as mean ± standard deviation with range in parentheses.

▶ **Tab. 1** Protokolleinstellungen der Thorax-Computertomografie und resultierende Dosiswerte der Patienten. Die Werte sind angegeben in Mittelwert ± Standardabweichung und Bereich in Klammern.

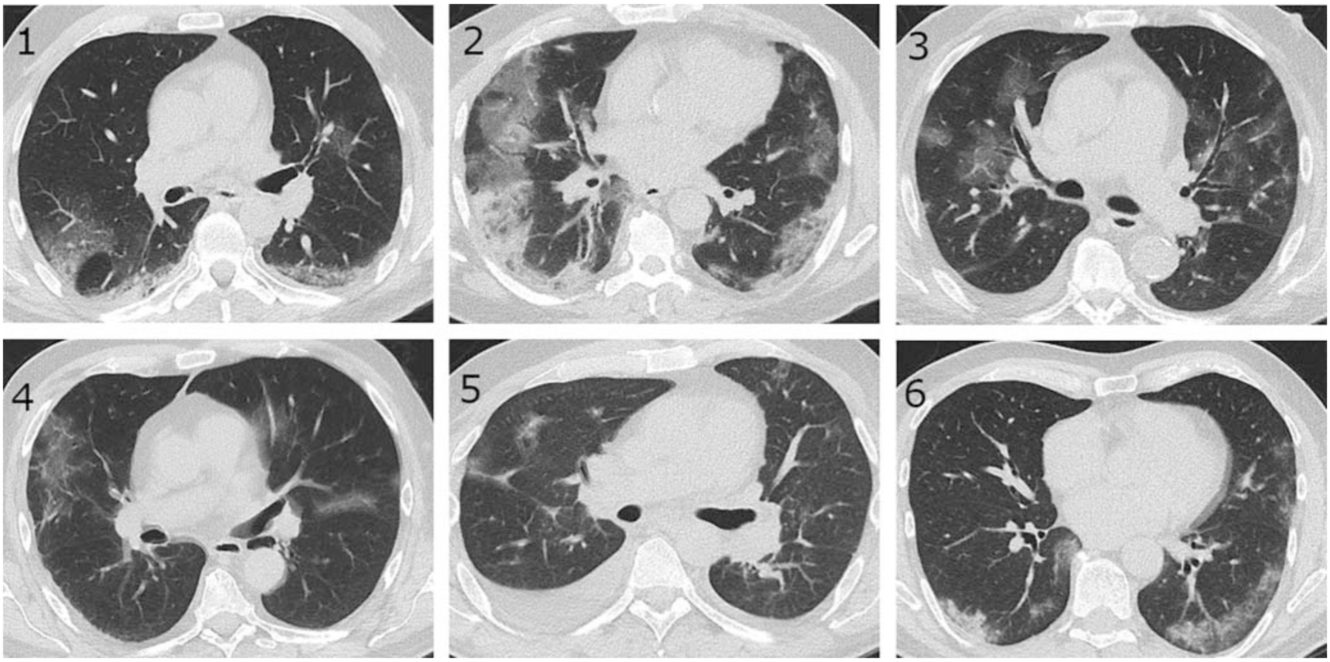
Parameter	Value
Scanner A	79.6 %
Tube potential	100 kVp
Reference tube current-time product [mAs]	60
Automatic exposure control	Semi: 100kVp fixed, CARE Dose 4D
Scanner B	19.7 %
Tube potential	100/120
Reference tube current-time product [mAs]	60/37
Automatic exposure control	CARE kV, CARE Dose 4D
Scanner C	0.7 %
Tube potential	100/120
Reference tube current-time product [mAs]	100/61
Automatic exposure control	CARE kV, CARE Dose 4D
Spiral pitch factor	0.6
Rotation time [s]	0.28
Collimation	128 × 0.6 mm
Total collimation width [mm]	38.4
FOV [cm]	50
Number of patients	437
Age [years]	69.7 ± 15.6 (12–98)
Gender [m/f]	275/162
BMI [kg/m²]	26.2 ± 5.4 (12.8–49.0)
$CTDI_{vol}$ [mGy]	3.1 ± 1.2 (1.3–9.4)
DLP [mGycm]	99.3 ± 39.6 (41.8–315.0)
Effective dose [mSv]	1.4 ± 0.6 (0.6–4.5)
Scan length [cm]	30.2 ± 3.2 (21.0–38.4)

FOV: field of view, DLP: dose length product, $CTDI_{vol}$: volumetric computed tomography dose index, BMI: body mass index.

For the detection of COVID-19 with chest CT, the sensitivity was 100 % [95 % CI: 65–100 %], the specificity was 88 % [95 % CI: 84–90 %], the PPV was 12 % [95 % CI: 6–22 %], and the NPV was 100 % [95 % CI: 99–100 %]. The prevalence of COVID-19 in the cohort was 2 % [95 % CI: 1–3 %]. The PLR equaled 8.11 [95 % CI: 6.31–10.44], whereas the NLR was 0 (see ▶ **Table 2**).

CT findings

CT findings for the total cohort and separated into CT true-positive, true-negative and false-positive patients are presented in



▶ **Fig. 2** Shown are slices of the axial lung windows of 6 patients who tested negative on qPCR at the time of CT. All of these patients had bilateral involvement of COVID-19 with typical lung parenchymal changes (peripheral enhancement, crazy paving pattern, and consolidations within ground-glass opacities). Subsequent qPCR tests performed after CT examination identified these patients as infectious.

▶ **Abb. 2** Axiale Schichten im Lungenfenster von 6 Patienten mit negativem qPCR-Test zum Zeitpunkt der Computertomografie. Bei allen diesen Patienten lagen bipulmonale COVID-19-typische Parenchymveränderungen vor (Betonung in der Peripherie, Crazy Paving Pattern, Konsolidierungen innerhalb der Milchglastrübungen). Nachfolgende qPCR-Tests bestätigten schlussendlich eine Infektion mit SARS-CoV-2.

▶ **Table 2** Diagnostic performance of chest computed tomography with quantitative polymerase chain reaction test result as reference. Results of the Fisher's exact test and Wilson-Brown.

▶ **Tab. 2** Gezeigt wird die diagnostische Genauigkeit der Thorax-Computertomografie im Vergleich zur quantitativen Polymerasekettenreaktion als Referenz. Dargestellt sind die Ergebnisse des Fisher's exact test und Wilson-Brown.

Effect size	Value	95 % CI
Sensitivity [%]	100	65–100
Specificity [%]	88	84–90
Positive likelihood ratio	7.08	4.92–10.19
Negative likelihood ratio	0.14	0.02–0.89
Positive predictive value [%]	12	6–22
Negative predictive value [%]	100	99–100
Disease prevalence [%]	2	1–4

CI: confidence interval.

▶ **Table 3**. After categorization of the patients according to the typical manifestations of COVID-19, some pulmonary findings were significantly more frequent in CT true-positive (CTP) patients compared to CT true-negative (CTN) patients, see ▶ **Table 4**. These were: ground-glass opacities (100 %:51 % (CTP: CTN), p≤ 0.01), consolidation (100 %:46 %, p≤ 0.01), and crazy paving pattern (57 %:6 %, ≤ 0.01). Differences regarding spatial distribution were also notable. Bilateral manifestation (100 %:36 %, p≤ 0.01) as well as emphasis of the peripheral (100 %:20 %, p≤ 0.01) lung lobes were significantly more common in patients with true-positive CT findings. Pleural thickening, bronchiectasis, caverns, pleural and pericardial effusion were seen equally in both groups.

In 206/437 (47 %) patients, CT findings were consistent with pneumonia other than COVID-19. In 53/437 (12 %) patients, no findings on CT were found despite their symptoms.

CT findings of false-positive patients

In total, 53 patients were classified as false positives by CT. In these patients ground-glass opacities were visible in 96 %, consolidations in 87 %, and thickened interlobular septa in 68 % (▶ **Fig. 3**). In some patients, other viral pathogens, such as cytomegalovirus or parenchymal changes due to an underlying disease, were found to be the cause of the parenchymal changes.

CT findings of true-positive patients

The most common manifestations were ground-glass opacities and consolidation (each 100 %), crazy paving pattern, thickened interlobular septa, and air bronchogram (all 57 %). A bilateral manifestation (100 %) was visible with emphasis in the periphery

▶ **Table 3** Major chest computed tomography findings, differentiated regarding the lung manifestations in the entire cohort, in true-positive and in false-positive CT examinations. Patients with true-positive CT examinations are patients with positive qPCR tests.

▶ **Tab. 3** Dargestellt sind die erhobenen Hauptbefunde der Thorax-Computertomografie der Gesamtkohorte, die richtig positiven (TP), die falsch positiven (FP) und die richtig negativen (TN). Die Patienten mit richtig positiven CT-Befunden (TP) sind zugleich auch alle Patienten mit positiver qPCR.

	CT			
	Entire cohort n = 437	TP n = 7	FP n = 53	TN n = 377
Ground-glass opacities (%)	57	100	96	51
Consolidation (%)	52	100	87	46
Crazy paving pattern (%)	11	57	34	6
Thickened interlobular septa (%)	43	57	68	40
Air bronchogram (%)	32	57	60	28
Bronchiectasis (%)	16	0	28	15
Caverns (%)	3	0	2	3
Pleural thickening (%)	21	29	26	20
Pneumothorax (%)	0	0	0	0
Bilateral infestation (%)	43	100	87	36
Emphasis lower lobes (%)	34	57	66	29
Emphasis periphery (%)	28	100	75	20
Emphasis posterior (%)	29	43	72	23
Pleural effusion (%)	35	29	26	36

CT – computed tomography, qPCR – quantitative polymerase chain reaction, TP – true positive, TN – true negative, ns – no significant difference, * – p ≤ 0.01.

(100 %) and lower lobes (57 %) (▶ **Fig. 4, 5**). In all cases, qPCR detected the patients as infected after the second or third test.

CT findings of CT true-positive patients compared to CT false-positive patients

No statistically significant differences in lung manifestations between CT true-positive and false-positive patients were determined, see ▶ **Table 4**.

▶ **Table 4** Results of the contingency tables assessing differences in CT findings between true-negative (TN) and true-positive (TP) CT examinations, between TN and false-positive (FP) CT examinations and between FP and TP CT examinations, according to the structured report and corresponding qPCR results, using a significance level of $p < 0.05$. Tests were adjusted for all pairwise comparisons using Bonferroni correction.

▶ **Tab. 4** Dargestellt sind die Ergebnisse der Kontingenztafeln für den Vergleich der computertomografischen (CT) Befunde zwischen richtig negativen (TN) und richtig positiven (TP), zwischen TN und falsch positiven (FP) und zwischen FP und TP CT-Befunden. Es liegt ein Signifikanzlevel von $p < 0,05$ vor. Die Tests wurden hinsichtlich ihrer mehrfachen Vergleiche Bonferroni-korrigiert.

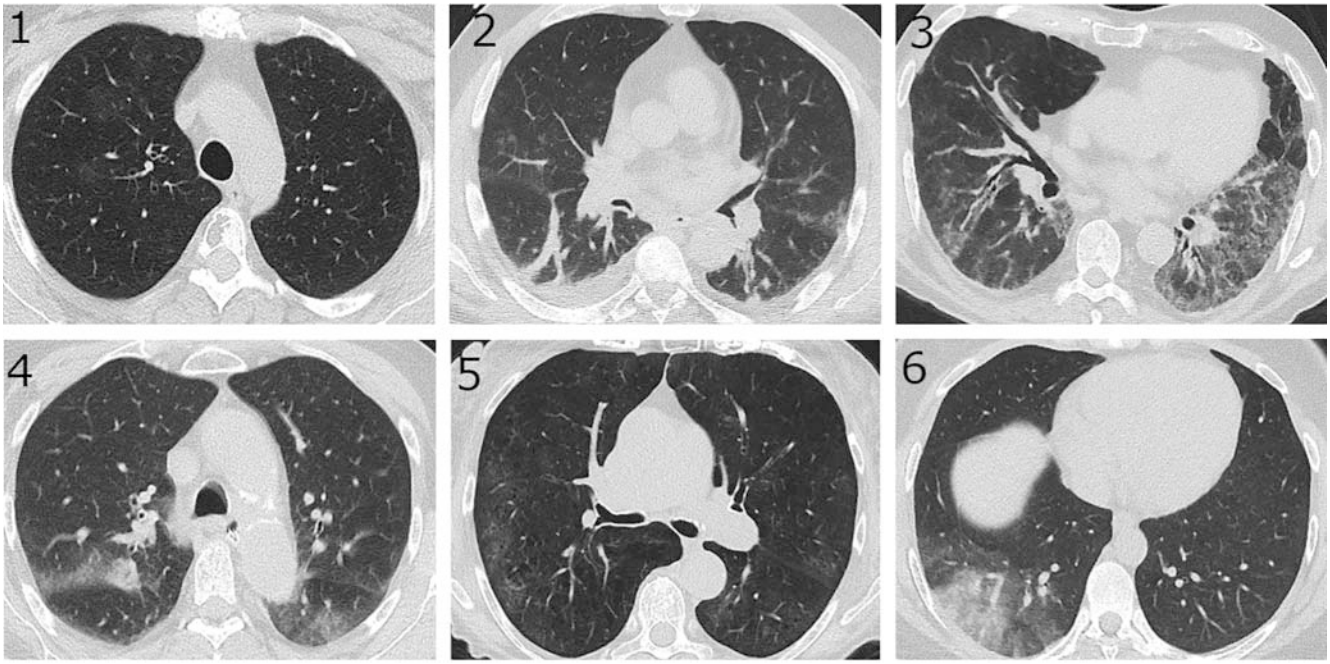
	TN: FP	FP vs. TP	TP: TN
Ground-glass opacities (%)	*		*
Consolidation (%)	*		*
Crazy paving pattern (%)	*		*
Thickened interlobular septa (%)	*		
Air bronchogram (%)	*		
Bronchiectasis (%)	*		
Caverns (%)			
Pleural thickening (%)			
Pneumothorax (%)			
Bilateral infestation (%)	*		*
Emphasis lower lobes (%)	*		
Emphasis periphery (%)	*		*
Emphasis posterior (%)	*		
Pleural effusion (%)			
Pericardial effusion (%)			

CT – computed tomography, qPCR – quantitative polymerase chain reaction, TP – true positive, TN – true negative, FP – false positive, * – significant difference.

Discussion

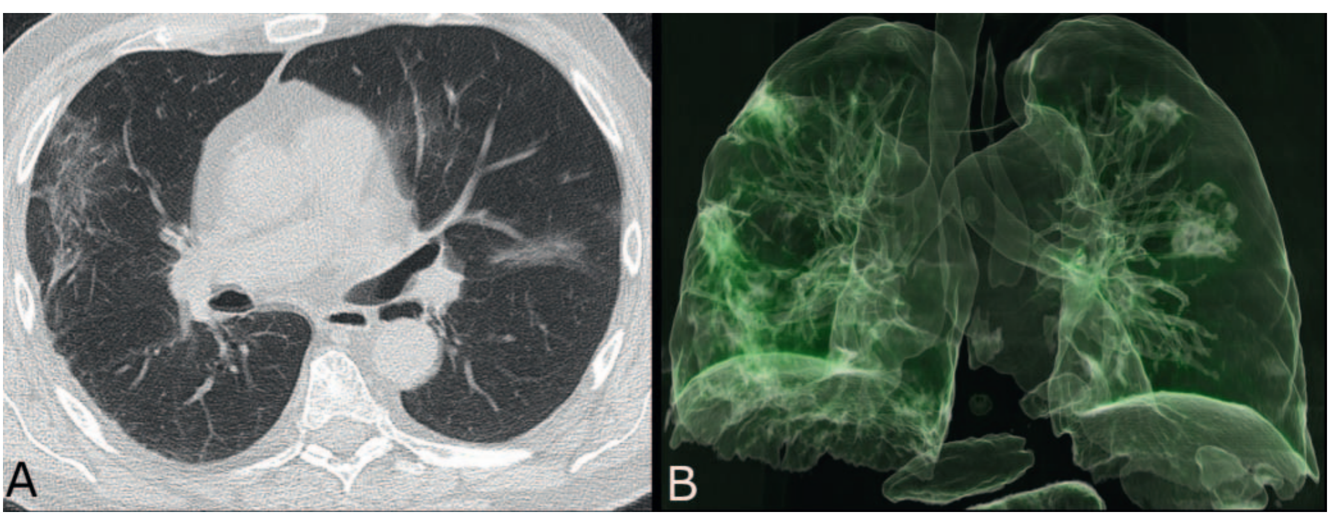
In this special study setting, CT was able to reliably detect the presence of COVID-19 in patients with initially negative qPCR. Patients with initially false-negative qPCR but active SARS-CoV-2 infection showed typical and in some cases already pronounced pulmonary patterns of COVID-19. The study was performed in a tertiary care hospital in a pandemic situation, where fast differentiation between SARS-CoV-2 infected and non-infected patients was necessary to prevent disease transmission within the hospital. Despite a rush of patients, the hospital was able to handle the patients and treat those in need. At the time of the study, no data on the sensitivity and specificity of the qPCR test was available due to the lack of a comparable method. Nevertheless, there were patients in whom infection was ruled out by qPCR but who were still strongly suspected of having an infection (e. g., first-degree contacts, steadily worsening respiratory symptoms with oxygen demand, additional loss of taste and smell, and diarrhea). In these patients, there was a clinically justified indication to perform a CT examination. Therefore, in these cases, we wanted to investigate how likely an infection is to be visible on CT despite a negative qPCR test and whether CT can identify infected patients.

Our data indicate a high sensitivity (100 %) with a moderate specificity of 88 % with respect to diagnosing COVID-19 using CT in patients with initially false-negative qPCR. In a study by Long et al., all patients with initially negative qPCR but subsequently



▶ **Fig. 3** Shown are axial slices of the lung windows of 6 patients who received a false-positive result on CT. All patients had bilateral lung parenchymal changes (patient number 6 also had upper lobe involvement, which is not shown). Ground-glass opacities were predominantly present in these patients. Nevertheless, qPCR tests performed after CT examination did not yield a positive result.

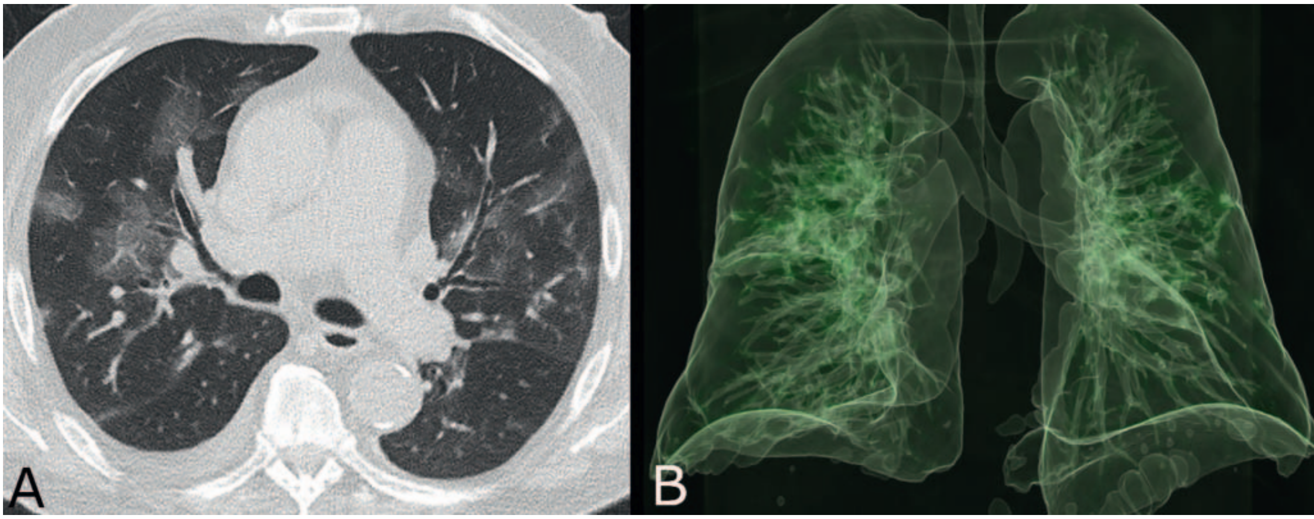
▶ **Abb. 3** Axiale Schichten im Lungenfenster von 6 Patienten mit falsch positivem CT-Befund. Alle diese Patienten zeigten bipulmonale Parenchymveränderungen (Patient Nr. 6 hatte einen Befall beider Oberlappen und des rechten Unterlappens, letzterer hier dargestellt). Die Patienten wiesen überwiegend Milchglastrübungen auf. Nichtsdestotrotz blieben nachfolgende qPCR-Tests negativ.



▶ **Fig. 4** 77-year-old patient with contact to persons infected with coronavirus, suffering from fever, cough, and fatigue. **A, B** The images of the initial computed tomography (CT) examination showed breathing artifacts. However, typical manifestations for coronavirus disease were clearly visible. **B** 3 D view with the function CT Pulmo 3 D (syngo.via, Siemens Healthineers, Forchheim, Germany). Window: 1500 HU, level: –500 HU.

▶ **Abb. 4** 77-jähriger Patient, der unter Fieber, Husten und Müdigkeit litt und Kontakt zu infizierten Personen hatte. **A, B**: Bilder der initialen Computertomografie (CT) zeigen trotz Atemartefakten typische Manifestationen für eine SARS-CoV-2-Infektion. **B** 3D-Darstellung mit der Funktion CT Pulmo 3 D (syngo.via, Siemens Healthineers, Forchheim, Deutschland). Fenster: 1500 HU, Level: –500 HU.

positive qPCR already had positive CT findings for COVID-19 pneumonia at their initial presentation, resulting in an identical sensitivity of 100 % in these six patients [20]. Unfortunately, they do not present any data on the specificity.



▶ **Fig. 5** 74-year-old patient with first negative quantitative polymerase chain reaction test result and positive computed tomography (CT) scan (**A, B**) and in the course also positive qPCR result after tracheal swabbing. **B** 3 D view with the function CT Pulmo 3 D (syngo.via, Siemens Healthineers, Forchheim, Germany). Window: 1500 HU, level: –500 HU.

▶ **Abb. 5** 74-jähriger Patient mit initial negativem qPCR-Ergebnis, positivem Computertomografiebefund (**A, B**) und im Verlauf auch positivem qPCR-Ergebnis nach trachealem Abstrich. VB: 3D-Darstellung mit der Funktion CT Pulmo 3 D (syngo.via, Siemens Healthineers, Forchheim, Deutschland). Fenster: 1500 HU, Level: –500 HU.

Published sensitivities reported by Li et al. (80 %), Bai et al. (70–93 %), Kim et al. (94 %), Fang et al. (98 %), Long et al. (97 %), and Caruso et al. (97 %) [20–25] and specificities reported by Kim et al. (37 %), Caruso et al. (56 %), Li et al. (82 %), and Bai et al. (93–100 %) [21, 22, 25, 26] cannot be compared directly to the cohort presented here. A limitation is the pre-selection of our cohort in which we included only patients with suspected disease who initially had a negative qPCR test result. Patients with an initially positive qPCR result were excluded in contrast to the last-mentioned studies. This reduces the total number of patients as well as the number of SARS-CoV-2-infected patients in our cohort, thereby limiting a comparison with other published studies in terms of infestation pattern and onset of symptoms.

In this study, the suspicion of an infection was assessed based on the literature and the RSNA recommendations [5–8, 17]. Compared to the abovementioned studies [20–25], the presence of the same CT patterns was evaluated (e. g., peripheral distribution, ground-glass opacities, crazy paving pattern, vascular thickening, consolidations). Although there are now different categorization strategies (CO-RADS, RSNA, DRG recommendations), they all assess the same manifestations more or less. We are aware that consensus evaluation with 3 radiologists does not correspond to everyday clinical practice. Since experience was limited at the beginning of the pandemic, it was important for us to make a consensus decision in order to have as few false-negative patients as possible. In this way, we aimed to interrupt a potential chain of infection. One reason for our high sensitivity but moderate specificity could be the internal procedure of strict evaluation of typical pulmonary changes. Nevertheless, our results show no significant difference in the presence of the patterns between true-positive and false-positive patients but significant differences between false-positive and true-negative patients. Therefore, we conclude that the configuration of the parenchymal changes is decisive for the evaluation of the presence of acute infection. For example, ubiquitous ground-glass opacities are less likely to be present at the onset of infection. In contrast, round-shaped ground-glass opacities, which are predominantly found in the periphery and the basal lobes, are more likely to be associated with acute SARS-CoV-2 infection [27, 28]. Nevertheless, other respiratory viral infections may be present and can cause similar parenchymal patterns in comparison to COVID-19. These similar viral parenchymal patterns will probably make it more difficult to diagnose SARS-CoV-2 infection by CT in the future after the pandemic situation when different viral infections are present in the patient population. In addition, preexisting conditions of the lung parenchyma that can lead to a false diagnosis may be present [29]. Especially in cases with mild parenchymal changes, a misinterpretation is possible. Hence, in the case of uncertain CT findings, patients were classified and treated as infected and potentially contagious to ensure that no positive cases were missed. Thus, the sensitivity is increased at the expense of specificity. One source of error could be the swabbing procedure for the qPCR test. Insufficient execution might result in false-negative results. Nevertheless, the number of correct negative swabs as well as the presence of a trained and permanent team in the emergency room show that the swabs were taken correctly and in a qualified manner. One explanation for false-negative qPCR tests discussed in the literature could be the viral load of the sample and the amount of sputum at the time of the test [30]. Especially in the first days of infection, these false-negative results can occur, as studies have already shown [31].

In addition, the pretest probability is a relevant factor. The relatively low number of false-negative findings is related to the low prevalence at our hospital at the time of the study. However, a high local prevalence also means a higher probability of false-negative tests [31].

Clinical Relevance

In conclusion, CT can identify infected patients before qPCR in this particular study setting in which patients with an initially negative qPCR test underwent CT for additional diagnosis in a pandemic situation. Yet, CT cannot perfectly distinguish between COVID-19 and other respiratory infections in a cohort with initially negative qPCR. Especially patients with initially false-negative qPCR who tested positive only after repeated qPCR tests illustrate the necessity for CT examinations in patients with COVID-19-compatible symptoms but negative initial qPCR test. Nevertheless, due to the radiation exposure during CT examinations and the risk of stochastic and deterministic radiation damage including the risk of radiation-induced cancer, CT cannot replace qPCR tests as a screening method. Yet, CT can help to interrupt infection pathways and identify initially false-negative patients to ensure adequate treatment.

Conflict of Interest

The authors declare that they have no conflict of interest.

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