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Original paper

Chest computed tomography of suspected COVID-19 pneumonia in the Emergency Department: comparative analysis between patients with different vaccination status

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Abstract

Purpose: To identify differences in chest computed tomography (CT) of the symptomatic coronavirus disease 2019 (COVID-19) population according to the patients' severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination status (non-vaccinated, vaccinated with incomplete or complete vaccination cycle).

Material and methods: CT examinations performed in the Emergency Department (ED) in May-November 2021 for suspected COVID-19 pneumonia with a positive SARS-CoV-2 test were retrospectively included. Personal data were compared for vaccination status. One 13-year experienced radiologist and two 4th-year radiology residents independently evaluated chest CT scans according to CO-RADS and ACR COVID classifications. In possible COVID-19 pneumonia cases, defined as CO-RADS 3 to 5 (ACR indeterminate and typical) by each reader, high involvement CT score (≥ 25%) and CT patterns (presence of ground glass opacities, consolidations, crazy paving areas) were compared for vaccination status.

Results: 184 patients with known vaccination status were included in the analysis: 111 non-vaccinated (60%) for SARS-CoV-2 infection, 21 (11%) with an incomplete vaccination cycle, and 52 (28%) with a complete vaccination cycle (6 different vaccine types). Multivariate logistic regression showed that the only factor predicting the absence of pneumonia (CO-RADS 1 and ACR negative cases) for the 3 readers was a complete vaccination cycle (OR = 12.8-13.1 compared to non-vaccinated patients, $p \leq 0.032$). Neither CT score nor CT patterns of possible COVID-19 pneumonia showed any statistically significant correlation with vaccination status for the 3 readers.

Conclusions: Symptomatic SARS-CoV-2-infected patients with a complete vaccination cycle had much higher odds of showing a negative CT chest examination in ED compared to non-vaccinated patients. Neither CT involvement nor CT patterns of interstitial pneumonia showed differences across different vaccination status.

Key words: computed tomography, COVID-19, SARS-CoV-2, vaccination, pneumonia.

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Authors' contribution:
A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic on 11 March 2020 [1]. Since then, more than 500 million cases and 6 million deaths have been confirmed by the World Health Organization [2]. The development and administration of a COVID-19 vaccine proved to be effective in limiting COVID-19 pneumonia, even though vaccines are not 100% effective at preventing illness [1,3-5].

Since the beginning of the pandemic outbreak caused by SARS-CoV-2, chest computed tomography (CT) demonstrated high sensitivity [6-8] in recognizing COVID-19 patients while waiting for reverse transcriptase-polymerase chain reaction (RT-PCR) confirmation [9-13], and to predict clinical complications [14-17]. Furthermore, the extent of pneumonia at the initial CT exam has major prognostic value [18].

Some authors recently described differences in pneumonia rates and CT findings between patients with complete or incomplete vaccination cycle [19-22]. However, these studies showed evidence limited to a population vaccinated with inactivated virus vaccine BBV152 viz. Covaxin® (Bharat Biotech) or the non-replicating viral vector vaccine AZD1222 (ChAdOx1) viz. Covishield® (AstraZeneca, University of Oxford) [19-21]. On the other hand, Lee *et al.* reported results on CT findings limited to a small population of partially (n = 64) or completely vaccinated (n = 22) patients [21]. Furthermore, these studies [19-22] showed contrasting results regarding the extent of COVID-19 lung involvement depending on the different vaccination statuses.

This study aimed to identify differences in chest CT according to patient vaccination status (non-vaccinated, vaccinated with incomplete or complete vaccination cycle) in a symptomatic population with a positive SARS-CoV-2 diagnostic test at admission to the Emergency Department (ED).

Material and methods

Population

This was a retrospective observational study using imaging data generated during routine clinical management. The study was performed in accordance with the principles of the Declaration of Helsinki and approved by the Local Ethics Committee, which waived the requirement for informed consent due to the retrospective nature of the study.

All chest CT examinations performed in the ED of our institution in the period between 1 May 2021 and 24 November 2021 were considered eligible regardless of their indication. To be included, their report had to contain the words "COVID", "interstitial", or "CO-RADS". From these, all chest CT examinations repeated in subsequent controls, and all the patients without an antigen or molecular RT-PCR test positive for SARS-CoV-2 on the ED dismissal report were excluded. Finally, cases were excluded when no clear statement was available on whether vaccination was performed.

Data retrieval

For each patient, the following demographic and clinical information was retrieved from ED dismissal reports: gender; age; pre-existent comorbidities (immunological pathology or drug-related immunosuppressive conditions such as oncological or post-transplantation therapies; cardiovascular diseases; respiratory diseases; diabetes; obesity) and the sum of them for each patient (0, 1, or ≥ 2); performed vaccination for SARS-CoV-2 disease; number of doses (1 or 2, since the booster/third vaccine dose had only recently been introduced at the time of the study); vaccine type; days from the last dose; and type (dyspnoea, cough, fever, other), number (1, 2, 3, or more), and duration of symptoms.

CT technique and evaluation

Non-contrast CT scans were performed using 128-slice CT scanners (Siemens, Erlangen, Germany) in a craniocaudal direction in a single breath-hold with helical scans obtained in

A supine position with 100-120 kVp (automatic kV setting based on patient size – "Care kV"), automatic tube current modulation, pitch 1.2, collimation 0.6 mm, and matrix 512 × 512. Images were reconstructed with a slice thickness of 1.5 mm using a Br59 kernel with ADMIRE iterative algorithm (level strength 1).

One radiologist (Reader 1, with 13-year experience) and two 4th-year radiology residents (Readers 2 and 3), with experience of at least 500 COVID-19-positive chest CT readings, independently reassigned CO-RADS score (1 to 5 points-scale) [23] and ACR COVID classification (negative, non-typical, indeterminate, typical) [24,25] to all examinations. The readers also independently evaluated the CT scans according to the following: visual quantification of pulmonary involvement expressed as the percentage of total lung volume and corresponding CT severity score (low involvement < 25%, high involvement ≥ 25%, as proposed by Au-Yong *et al.* [26] and used by Lee *et al.* [21]); CT patterns (presence of ground glass opacities, consolidations, crazy paving areas, mono- or bilateral involvement, mono- or multi-focal involvement); and findings distribution (mainly central, mainly peripheral, or mixed central and peripheral). The main CT pattern when more than one was present (ground glass opacities, consolidations, crazy paving areas) was assigned by the most experienced radiologist (Reader 1). All readers were blinded to the vaccination status of the patients.

Statistical analysis

Demographic and clinical characteristics were compared between non-vaccinated, incompletely vaccinated (1 dose only out of 2 required doses administered), and completely vaccinated patients (complete cycle of 1 or 2 doses required according to the vaccine type) using Pearson's χ^2 test for categorical variables and the Kruskal-Wallis test for independent samples for non-parametric variables.

Overall inter-reader agreement for single categories of CO-RADS and ACR classifications was evaluated using Fleiss' κ. Cohen's quadratic weighted κ was also used to evaluate the agreement between each pair of readers. The κ values were interpreted based on the guidelines provided by Fleiss [27].

The CO-RADS/ACR classifications of the 3 readers were compared between non-vaccinated, incompletely vaccinated, and completely vaccinated patients using Pearson's χ^2 test. Logistic regression was performed to ascertain the effects of vaccination cycle, demographic, and clinical characteristics on the likelihood that the patients will have CO-RADS 1 (ACR negative) assessment for the three readers.

CO-RADS 3 to 5 (ACR indeterminate and typical) were considered as COVID-19 pneumonia; in these cases, CT severity score and CT patterns were compared between non-vaccinated, incompletely vaccinated, and completely vaccinated patients using Pearson's χ^2 test.

Fleiss' κ was used to evaluate the overall inter-reader agreement for each main CT pattern (CT severity score, presence of ground glass opacities, consolidations, crazy paving areas).

SPSS statistical package version 27 (SPSS Inc., Chicago, IL) was used for the analyses, considering a p-value < 0.050 to be statistically significant.

Results

In the selected period, a total of 1515 chest CT examinations were performed in the ED: 349 were first examinations for the suspicion of COVID-19 or interstitial pneumonia, of which 199 CT examinations (13.1% of 1515, 57.0% of 349) were considered eligible given the known vaccination status (non-vaccinated or vaccinated) for COVID-19 (Figure 1).

Of these patients, 111 (56%) were non-vaccinated for SARS-CoV-2 infection and 88 (44%) were vaccinated with at least one dose of the following vaccine types: AZD1222 ChAdOx1 (AstraZeneca, UK), BNT162b2 (Pfizer-BioNTech, USA-Germany), mRNA-1273 vaccine (Moderna, USA), Ad26.COV2.S (Johnson & Johnson-Janssen, Belgium), Gam-COVID-Vac (Sputnik V, Russia), and COVID-19 vaccine BIBP (Sinopharm, China). Of the vaccinated patients, 52 (26%) performed a complete vaccination cycle; for 15 patients (7%) vaccination cycle status was not available; hence, they were subsequently excluded from the analysis.

The population demographic and clinical characteristics are shown in Table 1.

Of the 184 remaining patients, differences in demographic and clinical characteristics of non-vaccinated patients and patients with incomplete or complete vaccination cycle are shown in Table 2. Compared to patients with complete vaccination cycle, non-vaccinated patients showed statistically significant lower median age (56 vs. 74 years old, $p < 0.001$), longer symptomatic time (7 vs. 5 days, $p = 0.002$), lower rates of immunosuppressed condition (6% vs. 19%, $p < 0.001$), cardiovascular disease (32% vs. 81%, $p < 0.001$), respiratory disease (11% vs. 25%, $p = 0.019$), or diabetes (15% vs. 29%, $p = 0.029$). Also, 51% of non-vaccinated patients showed no comorbidities compared to 15% of patients with complete vac-

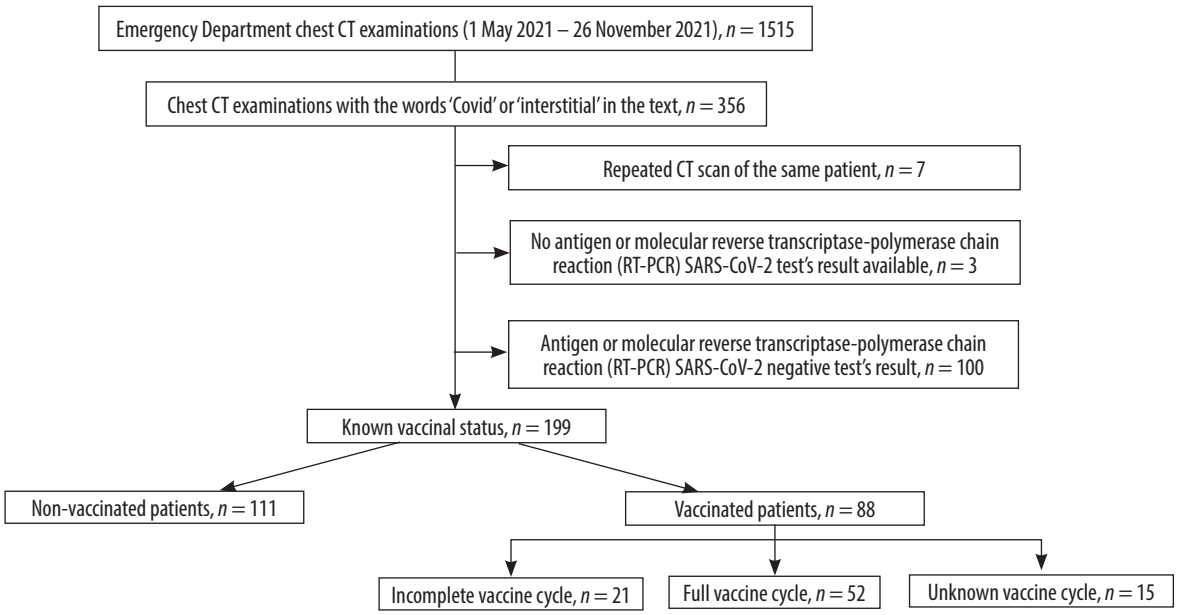

Figure 1. Flow diagram showing patient enrolment in the study

Table 1. Demographic and clinical characteristics of the patients included in the study, $N = 199$

Factor	
Gender, *n* (%)	
Female	83 (42)
Male	116 (58)
Age (years), median, range	63, 20-94
Vaccination cycle, *n* (%)	
No vaccination	111 (56)
Incomplete	21 (11)
Complete*	52 (26)
Not available	15 (7)
Days from last vaccination	
Incomplete vaccination cycle (median)	13
Incomplete vaccination cycle (range)	5-84
Complete vaccination cycle* (median)	129
Complete vaccination cycle* (range)	7-264
Vaccine type, *n* (%)	
BNT162b2 (Pfizer–BioNTech)	34 (39)
AZD1222 ChAdOx1 (AstraZeneca)	27 (31)
mRNA-1273 (Moderna)	6 (7)
Ad26.COV2.S (Johnson & Johnson-Janssen)	4 (4)
Gam-COVID-Vac (Sputnik V)	1 (1)
COVID-19 vaccine BIBP (Sinopharm)	1 (1)
Not available	15 (17)
Symptoms, *n* (%)	
Dyspnoea	98 (49)
Cough	85 (43)
Fever	157 (79)
Other symptoms	7 (3)
1 symptom	71 (36)
2 symptoms	94 (47)
3 or more symptoms	27 (14)
Symptoms duration** (days), median, range	6, 0-30
Comorbidities, *n* (%)	
Immunosuppressed condition***	19 (10)
Cardiovascular disease	99 (50)
Respiratory disease	34 (17)
Diabetes	36 (18)
Obesity	21 (11)
No comorbidities	74 (37)
1 comorbidity	65 (33)
2 comorbidities	37 (19)
3 comorbidities	18 (9)
4 comorbidities	4 (2)
Not available	1 (0.5)

cination cycle ($p < 0.001$), and 17% of non-vaccinated patients showed 2 or more comorbidities vs. 56% of patients with complete vaccination cycle ($p < 0.001$).

Regarding the considered symptoms (fever, dyspnoea, and cough), dyspnoea proved to have a statistically significant correlation ($p < 0.001$) with high CT severity score (high involvement ≥ 25%) for the 3 readers.

CO-RADS and ACR classifications for the 3 readers are shown in Table 3. Regarding the CO-RADS classification, the highest inter-reader agreement according to Fleiss's κ was obtained for CO-RADS 1 (0.944, $p < 0.001$) and the lowest was for CO-RADS 4 (0.273, $p < 0.001$); quadratic weighted κ ranged between 0.818 and 0.866 (excellent agreement, $p < 0.001$) between the 3 couples of readings. Regarding the ACR classification, the highest inter-reader agreement according to Fleiss's κ was obtained for ACR 1 (0.944, $p < 0.001$) and the lowest was for ACR 3 (0.376, $p < 0.001$); quadratic weighted κ ranged between 0.805 and 0.874 (excellent agreement, $p < 0.001$) between the 3 readers.

In the univariate analysis, the CO-RADS 1 rate (ACR negative) was the only characteristic showing significant differences between non-vaccinated patients and patients with completed vaccination cycle for the 3 readers ($p \leq 0.001$, Table 3). In multivariate logistic regression, which included age, gender, vaccination cycle, the 5 pre-existent comorbidities and their sum, and symptom days, the only significant patient condition predicting the absence of pneumonia (CO-RADS 1- and ACR-negative cases) for the 3 readers was the administration of a complete vaccination cycle (OR = 12.8-13.1 compared to non-vaccinated patients, $p \leq 0.032$; Nagelkerke $R^2 = 0.33$-0.36).

In the 149 patients with CO-RADS 3 to 5 (ACR indeterminate and typical) according to Reader 1, neither CT severity score nor CT patterns (ground glass, consolidations, crazy paving areas, laterality, distribution) showed a statistically significant correlation with vaccination status (non-vaccinated patients, patients with incomplete and complete vaccination cycle), with $p \geq 0.136$. No differences in CT pattern prevalence ($p = 0.267$), with the main prevalence of ground glass in 59% ($n = 57$, 95% CI: 49-69%), 76% ($n = 13$, 95% CI: 50-93%), and 81% ($n = 29$, 95% CI: 64-92%), consolidations in 22% ($n = 21$, 95% CI: 14-31%), 18% ($n = 3$, 95% CI: 4-43%), and 8% ($n = 3$, 95% CI: 2-22%), and crazy paving areas in 19% ($n = 18$, 95% CI: 12-28%), 6% ($n = 1$, 95% CI: 0-29%), and 11% ($n = 4$, 95% CI: 3-26%) for non-vaccinated patients, and patients with incomplete and complete vaccination cycle, respectively.

In the 159 patients with CO-RADS 3 to 5 (ACR indeterminate and typical) according to Reader 2, among CT patterns, the presence of consolidations was more frequent in patients with incomplete vaccination cycle (95% vs. 73% of non-vaccinated patients and 64% of patients with complete vaccination cycle, $p \leq 0.044$, without significant difference between the last 2 groups, $p = 0.274$); neither CT severity score nor other CT patterns (ground glass, crazy paving areas, laterality, focality, distribution)

Table 2. Differences in demographic and clinical characteristics of 184 patients with known vaccination cycle (non-vaccinated, incompletely vaccinated, and completely vaccinated patients)

Factor	NV *n* (%) [95% CI]	IV *n* (%) [95% CI]	CV *n* (%) [95% CI]	*p*	NV vs. CV *p*	NV vs. IV *p*	IV vs. CV *p*
Population ($N = 184$)	111 (56) [53-67]	21 (11) [7-17]	52 (28) [22-35]				
Gender							
Female	49 (44) [35-54]	11 (52) [30-74]	17 (33) [20-47]	0.224			
Male	62 (56) [46-65]	10 (48) [26-70]	35 (67) [53-80]				
Age (years), median, range	56, 20-93	67, 29-79	74, 20-92	< 0.001	< 0.001	0.918	0.059
Symptoms							
Dyspnoea	55 (49) [40-59]	10 (48) [26-70]	26 (50) [36-64]	0.983			
Cough	43 (39) [30-49]	10 (48) [26-70]	26 (50) [36-64]	0.36			
Fever	90 (81) [73-88]	15 (71) [48-89]	41 (79) [65-89]	0.602			
Other symptoms	2 (2) [0-6]	1 (5) [0-24]	2 (4) [1-13]	0.48			
1 symptom	45 (41) [31-50]	6 (29) [11-52]	17 (33) [20-47]				
2 symptoms	49 (44) [35-54]	13 (62) [38-82]	23 (44) [31-59]				
3 symptoms	15 (13) [8-21]	1 (5) [0-24]	10 (19) [10-33]				
Symptoms duration (days), median, range	7, 0-30	5, 1-14	5, 0-30	0.002	0.002	≥ 0.483	
Comorbidities							
Immunosuppressed condition	7 (6) [3-13]	2 (10) [1-30]	10 (19) [10-33]	0.043	0.012	≥ 0.311	
Cardiovascular disease	35 (32) [23-41]	11 (52) [30-74]	42 (81) [68-90]	< 0.001	<0.001	0.066	0.014
Respiratory disease	12 (11) [6-18]	5 (24) [8-47]	13 (25) [14-39]	0.048	0.019	≥ 0.103	
Diabetes	16 (15) [9-22]	2 (10) [1-30]	15 (29) [17-43]	0.049	0.029	≥ 0.077	
Obesity	9 (8) [4-15]	3 (14) [3-36]	7 (14) [6-26]	0.485			
No comorbidities	56 (51) [41-60]	8 (38) [18-62]	8 (15) [7-28]	< 0.001	< 0.001	0.299	0.034
1 comorbidity	35 (32) [23-41]	7 (33) [15-57]	15 (29) [17-43]		0.914		
≥ 2 comorbidities	19 (17) [11-25]	6 (29) [11-52]	29 (56) [41-70]		< 0.001	0.219	0.035

showed any statistically significant correlation with vaccination status ($p \geq 0.223$).

In the 155 patients with CO-RADS 3 to 5 (ACR indeterminate and typical) according to Reader 3, CT severity score and other CT patterns (ground glass, consolidations, crazy paving areas, laterality, focality, distribution) showed no statistically significant correlation with vaccination status, with $p \geq 0.089$. The rates of the main CT findings (CT severity score, ground glass, consolidations, crazy paving areas) according to the 3 readers for the 3 vaccination status groups are summarised in Table 4.

According to Fleiss' κ, the overall inter-reader agreement for CT severity score was 0.659, for ground glass opacities it was 0.185, for consolidations it was 0.534, and for crazy paving areas it was –0.058.

Discussion

This study evaluated the admission chest CTs of 199 symptomatic patients with a positive antigen or RT-PCR SARS-CoV-2 test. Among these patients, 56% did not perform any vaccination, while 44% were vaccinated, with 24% of them with an incomplete vaccination cycle.

The absence of pneumonia (classified as CO-RADS 1 or ACR negative) was significantly more frequent (about 13 times) in patients with a complete vaccination cycle compared to non-vaccinated ones, independently of personal characteristics (age and gender) or clinical factors (symptoms and comorbidities). This was remarkable considering that the readers knew that all patients had a positive test for SARS-CoV-2. Also, the result was consistent with literature stating that a complete vaccination status for COVID-19 lowers the disease aggressiveness and, particularly, the pneumonia rate [21]. The rate of CT examinations negative for pneumonia was intermediate in patients with incomplete vaccination cycle, in detail 5% compared to 1% of non-vaccinated and 14-17% of patients with complete vaccination cycle in our study, with no statistically significant differences with the other 2 groups of patients. This result has been reported by the

Table 3. Differences in readers' CO-RADS and ACR classifications according vaccination cycle (non-vaccinated, incompletely vaccinated, and completely vaccinated patients)

		Population *n* (%)	NV *n* (%) [95% CI)	IV *n* (%) [95% CI)	CV *n* (%) [95% CI)	NV vs. CV *p*	IV vs. others *p*
Population	Classification	184 (100)	111 (60) [53-67]	21 (11) [7-17]	52 (29) [22-35]		
Reader 1	1 (ACR negative)	11 (6)	1 (1) [0-5]	1 (5) [0-24]	9 (17) [8-30]	< 0.001	≥ 0.158
CO-RADS	2 (ACR non-typical)	24 (13)	14 (13) [7-20]	3 (14) [3-36]	7 (14) [6-26]	0.88	≥ 0.834
	3 (ACR indeterminate)	18 (10)	8 (7) [3-14]	1 (5) [0-24]	9 (17) [8-30]	0.049	≥ 0.158
	4	30 (16)	22 (20) [13-29]	3 (14) [3-36]	5 (10) [3-21]	0.102	≥ 0.553
	5	101 (55)	66 (59) [50-69]	13 (62) [38-82]	22 (42) [29-57]	0.041	≥ 0.129
	4-5 (ACR typical)	131 (71)	88 (79) [71-86]	16 (76) [53-92]	27 (52) [38-66]	< 0.001	≥ 0.056
Reader 2	1 (ACR negative)	9 (5)	1 (1) [0-5]	1 (5) [0-24]	7 (14) [6-26]	0.001	≥ 0.158
CO-RADS	2 (ACR non-typical)	16 (9)	12 (11) [6-18]	1 (5) [0-24]	3 (6) [1-16]	0.299	≥ 0.394
	3 (ACR indeterminate)	20 (11)	10 (9) [4-16]	3 (14) [3-36]	7 (14) [6-26]	0.386	≥ 0.457
	4	25 (13)	12 (11) [6-18]	5 (24) [17-80]	8 (14)[7-28]	0.407	≥ 0.103
	5	114 (62)	76 (68) [60-77]	11 (52) [30-74]	27 (52) [38-66]	0.041	≥ 0.154
	4-5 (ACR typical)	139 (75)	88 (79) [71-86]	16 (76) [53-92]	35 (67) [53-80]	0.098	≥ 0.454
Reader 3	1 (ACR negative)	9 (5)	1 (1) [0-5]	1 (5) [0-24]	7 (14) [6-26]	0.001	≥ 0.158
CO-RADS	2 (ACR non-typical)	20 (11)	13 (12) [6-19]	2 (9) [1-30]	5 (10) [3-21]	0.001	≥ 0.772
	3 (ACR indeterminate)	31 (17)	18 (16) [10-24]	4 (19) [5-42]	9 (17) [8-30]	0.861	≥ 0.228
	4	25 (13)	15 (13) [8-21]	5 (24) [8-47]	5 (10) [3-21]	0.48	≥ 0.110
	5	99 (54)	64 (58) [48-67]	9 (43) [22-66]	26 (50) [36-64]	0.359	≥ 0.211
	4-5 (ACR typical)	124 (67)	79 (71) [62-79]	14 (67) [43-85]	31 (60) [45-73]	0.928	≥ 0.414

NV – non-vaccinated, IV – incompletely vaccinated, CV – completely vaccinated

Table 4. Rates of the main computed tomography (CT) patterns (CT score, ground glass, consolidations, crazy paving areas) according to the 3 readers for non-vaccinated, incompletely vaccinated, and completely vaccinated patients with CO-RADS 3 to 5 (ACR indeterminate and typical)

	CT pattern	Population *n* (%)	NV *n* (%) [95% CI]	IV *n* (%) [95% CI]	CV *n* (%) [95% CI]	*p*
Reader 1	Population	149 (100)	96 (64) [56-72]	17 (12) [7-18]	36 (24) [18-32]	
CO-RADS 3-5	High CT score (≥ 25%)	75 (50)	52 (54) [44-64]	8 (47) [23-72]	15 (42) [26-59]	0.423
(ACR indeterminate – typical)	Ground glass opacities	136 (91)	85 (89) [80-94]	16 (94) [71-100]	35 (97) [86-100]	0.263
	Consolidations	82 (55)	56 (58) [48-68]	10 (59) [33-82]	16 (44) [28-62]	0.341
	Crazy paving areas	34 (23)	26 (27) [19-37]	1 (6) [0-29]	7 (19) [8-36]	0.136
Reader 2	Population	159 (100)	98 (62) [54-69]	19 (12) [7-18]	42 (26) [20-34]	
CO-RADS 3-5	High CT score (≥ 25%)	70 (44)	47 (48) [38-58]	9 (47) [24-71]	14 (33) [20-50]	0.423
(ACR indeterminate – typical)	Ground glass opacities	159 (100)	98 (100) [96-100]	19 (100) [82-100]	42 (100) [92-100]	1
	Consolidations	117 (74)	72 (74) [64-82]	18 (95) [74-100]	27 (64) [48-78]	0.044*
	Crazy paving areas	43 (27)	29 (30) [21-40]	2 (11) [1-33]	12 (29) [16-45]	0.223
Reader 3	Population	155 (100)	97 (63) [55-70]	18 (12) [7-18]	40 (26) [19-33]	
CO-RADS 3-5	High CT score (≥ 25%)	89 (57)	61 (63) [53-73]	10 (56) [31-79]	18 (45) [29-62]	0.156
(ACR indeterminate – typical)	Ground glass opacities	155 (100)	97 (100) [96-100]	18 (100) [82-100]	40 (100) [91-100]	1
	Consolidations	116 (75)	75 (77) [68-85]	15 (83) [59-96]	26 (65) [48-79]	0.216
	Crazy paving areas	21 (14)	14 (15) [8-23]	0 (0) [0-19]	7 (17) [7-33]	0.181

*Incompletely vaccinated vs. non-vaccinated $p = 0.274$; incompletely vaccinated vs. completely vaccinated $p = 0.012$; non-vaccinated vs. completely vaccinated $p = 0.044$.
NV – non-vaccinated, IV – incompletely vaccinated, CV – completely vaccinated

study of Lee *et al.* (30% of patients with incomplete vaccination cycle compared to 22% of non-vaccinated and 59% of patients with complete vaccination cycle) [21], which instead showed higher rates of CT examinations negative for pneumonia in all groups compared with our study. This difference could be due to a different patient selection because our study included only symptomatic patients (because this was the ED indication for a CT scan). About 8% of asymptomatic patients were included in the study by Lee *et al.* [21], and it might be that the higher rate of mildly symptomatic patients (a low rate of O_2 supply was requested for the whole population) in their study could explain the gap between these studies. On the other hand, our entire population showed about 5-6% of normal initial chest CT, which was comparable to the 5.2% of symptomatic confirmed COVID-19 cases in the study of Leonard-Lorant [28].

Many studies proved that a greater extent of pulmonary involvement at CT scan correlates with higher rates of admission to intensive care units and a worse prognosis for patients [14-16]. In our study, the CT severity score proved to be independent of the vaccination status when patients with typical or intermediate pneumonia (CO-RADS 3 to 5, ACR 3 and 4) were considered. In fact, a high involvement score (≥ 25%) was less frequent in patients with a complete vaccination cycle for the 3 readers; however, no significant differences were found, with CT severity score ≥ 25% showing rate ranges of 42-54%, 33-48%, and 45-63% for each reader (Table 4). This result was concordant with Lee *et al.*, who did not find any difference in lung involvement when SARS-CoV-2 infection developed into interstitial pneumonia [21]. Other studies [19,20,29] reported a significantly greater extent of pulmonary disease in the incompletely vaccinated and non-vaccinated patients compared to the completely vaccinated group, probably due to a different method for assessing lung involvement. In fact, Verma, Joshi, and Ravindra [19,20,29] used the 5-point scale of CT severity score compared to the binary score (< 25% vs. ≥ 25%) proposed by Lee [21] and our study, which did not consider any difference between the highest lung involvement volumes.

Our study showed no difference in common among the 3 readers in the rates of pneumonia classified as CO-RADS 2 to 5 classes (or ACR atypical-indeterminate-typical) between non-vaccinated, incompletely vaccinated, and completely vaccinated patients. This result was confirmed by the study of Lee *et al.* [21], who did not find any significant difference in ACR atypical, indeterminate, or typical rates.

Similarly, no differences in CT patterns between non-vaccinated, incompletely vaccinated, and completely vaccinated patients were shown by the whole panel of readers. Verma *et al.* reported a prevalence of the consolidation pattern, but this result was not confirmed in our study. This was probably due to the difference in inclusion criteria [19] because they did not perform any difference among CO-RADS classification or atypical-indeterminate and typical patterns. Also, it was not possible to exclude that they included non-COVID-19 pneumonia in their evaluation.

The overall agreement between the 3 readers was excellent (quadratic weighted $\kappa > 0.8$) for both CO-RADS and ACR classifications, which was concordant with recent literature [30]. Some differences in CO-RADS 3 or 4 rates for Reader 1, in CO-RADS 5 rates for Reader 2, or CO-RADS 2 rates for reader 3 (Table 3) could be considered as outliers because they were not confirmed by the other 2 readers, and they could be explained by the lower Fleiss' κ values for some categories [31,32]. The decision to consider CO-RADS 3 to 5 as COVID-19 pneumonia was due to the high PPV (70%) previously documented in symptomatic individuals [33].

It must be noted that the time frame of the study was before 26th November 2021, when the "Omicron" Variant of Concern of SARS-CoV-2 was first identified in our country [34]; the decision not to include later cases in this study was to avoid mixing the new SARS-CoV-2 variant as another confounding variable. In this study, the older median age and higher comorbidity rates of patients with complete vaccination cycle compared to incompletely vaccinated and non-vaccinated patients reflected the country's health policies of a vaccination priority for fragile and older patients [35]. The longer median number of days of symptom duration before the ED admission of non-vaccinated compared to vaccinated patients could be due to a attitude of denial towards SARS-CoV-2 disease from some patients of the first group, which was not supported by the results of this study or any evidence in the literature.

The main limitation of our study was the small size of the population with an incomplete vaccination cycle, who showed intermediate results between non-vaccinated patients and patients with complete vaccination cycle. This could have led to rejecting the significance of the differences observed compared to the other 2 groups. Nevertheless, our study included a greater number of completely vaccinated patients with CT examinations than the study of Lee *et al.* [21]. Also, compared to previously published papers [19,20], it evaluated SARS-CoV-2 vaccine types other than BBV152 viz. Covaxin® (Bharat Biotech) or AZD1222 (ChAdOx1) viz. Covishield® (AstraZeneca, University of Oxford). However, subgroup analysis according to the different vaccine types was not possible due to the small number of vaccinated patients per group. A further limitation was the inclusion of patients with positive RT-PCR and positive antigen test; we decided to include these patients because patients in ED were usually tested with the latter one, as there was no time to wait for RT-PCR results. Finally, the new Omicron variants could have changed the CT presentation of the disease when overwhelming older SARS-CoV-2 variants such as the Delta one.

Conclusions

Our study confirmed that symptomatic COVID-19 patients presenting to the ED with a complete vaccination cycle have much higher odds of showing a negative CT chest examination compared to non-vaccinated patients. No differences in lung involvement or CT patterns of interstitial pneumonia were detected between non-vaccinated and vaccinated (completely or incompletely) patients.

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Conflict of interest

The authors report no conflict of interest.

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