Radiology

Chest CT and Hospital Outcomes in Patients with Omicron Compared with Delta Variant SARS-CoV-2 Infection

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Summary

SARS-CoV-2 Omicron variant chest infections are radiologically and clinically less severe than Delta variant infections and are associated with improved hospital outcomes.

Key Results

1. In 106 hospitalized adult patients with Omicron (n=40) and Delta variants (n=66) of SARS-CoV-2, patients with Omicron had lower median chest CT severity scores (CT-SS) (median, 3.5) compared with Delta (median, 11.8) (p<.001).
2. Patients who had received a vaccine booster dose had lower median CT-SS (median, 5) than the unvaccinated patients (median, 11) (p=.03).
3. Bronchial wall thickening was more common with Omicron than Delta SARS-CoV-2 (odds ratio [OR] 2.4, p=.04).

Abbreviations:

CT- SS: chest CT severity score

rt-PCR: reverse transcriptase polymerase chain reaction

ABSTRACT

Background: The SARS-Cov-2 Omicron variant demonstrates rapid spread but with reduced disease severity. Studies evaluating the lung imaging findings of Omicron infection versus non-Omicron variants remain lacking.

Purpose: To compare Omicron and Delta variants of SARS-CoV-2 by their chest CT radiological pattern, biochemical parameters, clinical severity and hospital outcomes after adjusting for vaccination status.

Materials and Methods: Retrospective study of hospitalized adult patients rt-PCR positive for SARS-CoV-2 with CT pulmonary angiography performed within 7 days of admission between December 1, 2021 and January 14, 2022. Blinded radiological analysis with multiple readers including RSNA CT classification, chest CT severity score (CT-SS, range 0 least severe to 25 most severe) and CT imaging features including bronchial wall thickening.

Results: 106 patients (Delta n=66, Omicron n=40) were evaluated (mean age, 58 years ± 18, 58 men). In the Omicron group, 37% (15/40) of CT pulmonary angiograms were categorized as normal compared with 15% (10/66) in the Delta group (p=.016). Using a generalized linear model to control for confounding variables, including vaccination status, Omicron variant infection was associated with a CT-SS that was lower by 7.2 points compared to infection with Delta variant (β=-7.2, 95%CI: -9.9, -4.5; p <.001). Bronchial wall thickening was more common with Omicron than with the Delta variant (odds ratio [OR] 2.4, 95%CI: 1.01, 5.92, p=.04). Vaccination with a booster shot was associated with a protective effect on chest infection compared with the unvaccinated (CT-SS median 5 (IQR 0-11), CT-SS median 11 (IQR 7.5-14), respectively; p = .03). The Delta variant was associated with a higher odds ratio of severe disease (OR 4.6, 95%CI: 1.2, 26, p=.01) and critical care admission (OR 7.0, 95%CI: 1.5, 66, p=.004) than the Omicron variant.

Conclusion: The SARS-COV-2 Omicron variant was associated with fewer and less severe changes on chest CT compared with the Delta variant. Patients with Omicron had greater

frequency of bronchial wall thickening but lower clinical severity and improved hospital outcomes than those with Delta.

INTRODUCTION

A novel SARS-CoV-2 variant designated B.1.1.529 (Omicron) was identified in November 2021 in South Africa and subsequently spread rapidly around the world, accounting for a sudden rise in SARS-COV-2 infections in the UK in December 2021[1]. Patients with Omicron infection have half the odds of hospitalization and of severe disease than those infected with Delta and preceding variants (HR 0.53, 95% CI: 0.50, 0.57)[1,2]. Furthermore, the risk of being admitted to hospital for Omicron infection is 65% lower for vaccinated compared to unvaccinated individuals, although vaccine effectiveness against symptomatic disease with the Omicron variant is lower than that compared with Delta (51% vs 85% 25+ weeks after 2 vaccinations) and wanes rapidly[1]. There is limited data on differential severity and outcomes between variants once patients are admitted to hospital for SARS-COV-2.

A recent study has demonstrated that vaccinated patients with SARS-COV-2 'breakthrough' infections show fewer chest CT findings of pneumonia compared with unvaccinated patients (59% vs 27%)[3]. However, variant status in this study was unknown, and the applicability to other samples of patients may be limited as the vast majority of patients were immunized with a non-mRNA vaccine.

Establishing intrinsic differences in variant virulence, as opposed to reductions in disease severity over time due to population immunity from vaccination or prior infection, is challenging. However, laboratory studies show reduced pathogenesis in animal models[4] and lower replication rates in human lung cells compared with the upper respiratory tract for Omicron versus the Delta variant[5]. These results lend biological plausibility for reduced lung involvement and the risk of severe respiratory outcomes arising directly from the Omicron variant itself.

Multiple studies have shown the degree of parenchymal involvement on CT imaging to associate with disease severity and poor hospital outcomes, including a study that used a 25-point chest CT severity score (CT-SS) of CT pulmonary angiograms[6]. Further studies have evaluated the CT imaging characteristics or 'signature' of SARS-COV-2 infection[7,8], but

studies evaluating the lung imaging findings of Omicron infection versus non-Omicron variants remain lacking.

In this retrospective analysis, we compared the radiological pattern, imaging characteristics and disease severity on initial CT pulmonary angiograms of patients infected with the Omicron variant compared with those infected with the Delta variant, as well as comparing the imaging severity according to vaccination status. We also evaluated the study sample with regard to biochemical parameters, clinical disease severity and hospital outcomes by variant and vaccination status.

MATERIALS AND METHODS

Patients

Data was retrospectively collected on consecutive patients (n=106), admitted to a large tertiary referral center in the UK. Inclusion criteria were hospitalized adult patient (≥ 18 years of age), CT pulmonary angiogram performed within the study time window between December 1, 2021 and January 14, 2022, and a nasal or throat swab which was PCR positive for SARS-CoV-2 within 7 days of admission (Figure 1). Exclusion criteria were technically inadequate or abandoned imaging. The study sample includes patients who were admitted for symptoms of infection as well as those incidentally positive for SARS-CoV-2. CT pulmonary angiography was performed following respiratory deterioration as per our national guidelines[9]. Data was extracted and analyzed using permission granted by the Institutional Review Board HRA and Health and Care Research Wales (HCRW) (IRAS 282670; REC 20/HRA/2546), which waived the requirement for informed consent due to the retrospective nature of the study.

CT protocol

Analysis was performed on the first CT pulmonary angiogram following patient presentation. All scans used one of three CT scanners (Siemens Somatom Drive x2 or GE Revolution GSI). All examinations were performed with 0.625mm slice thickness and section interval and CT

pulmonary angiography protocol (100kV where possible, with 70-100ml of contrast @4ml/s using pump injection, dependent upon body habitus). Images were reviewed in axial plane in lung (W:1500 L:-600), mediastinum (W:350 L:50) and pulmonary vasculature (W:350 L:50) windows.

Imaging Analysis

Radiological Society of North America (RSNA) categorization, assessment for bronchial wall thickening and CT-SS analysis was performed by one radiologist with 15 years of thoracic imaging experience (RB) and 1 radiologist in training (SS) who independently interpreted every imaging study blinded to variant status, clinical information, and other radiologist scoring, within one week. Images were categorized according to the RSNA Expert Consensus Statement into negative, typical, indeterminate or atypical for SARS-COV-2 pneumonia[10]. The dichotomous outcome of bronchial wall thickening was determined following inspection of bronchi throughout all lung lobes. Final RSNA categories and presence/absence of bronchial wall thickening was reached by consensus with a third radiologist (HP, 5 years thoracic imaging experience) in cases of inter-observer discrepancy (n=7 for RSNA categorization, n=26 for bronchial wall thickening). Studies assigned the RSNA categorization of negative, typical or indeterminate (n=100) were evaluated in terms of severity using the semi-quantitative chest CT severity score (CT-SS) as per previous studies[6]. The resulting global CT score was the sum of each individual lobar score, 0 to 25, with the mean score of CT-SS between the two radiologists used for analysis ('Consensus CT-SS'). There was a high level of agreement between observers (weighted Cohen's kappa 0.77, 95%CI: 0.72, 0.83; p <.001).

Further blinded analysis for additional imaging characteristics (as detailed in results table 3) was undertaken by one radiologist with 4 years thoracic imaging experience (LW) and one radiologist with 2 years thoracic imaging experience (CX), with conclusions reached by consensus by a third radiologist with 20 years thoracic imaging experience (FM) in cases of inter-observer discrepancy.

Clinical and biochemical data

Electronic patient records were used to capture patient demographics, vaccination status (typically of an mRNA vaccine or ChAdOx1 for the first two doses, with an mRNA booster where given), comorbidities, immunosuppression status, laboratory findings, in-hospital treatments and clinical outcomes. Date of vaccination was not consistently recorded and could not be included. Oxygen saturation and requirements were used to calculate the WHO ordinal progression score. Patients with severe disease were defined as those patients reaching point 6 or higher during the assessment period[11]. Mortality data was defined by death by 30 days after CT pulmonary angiography; admission to critical care was defined as an admission to either a high dependency unit (HDU) or intensive care unit (ICU) during hospital admission.

PCR and variant status

RT-PCR was performed on Thermo Fisher TaqPath assay. Infections with S gene target failure are used as a surrogate for Omicron status as previously reported[1]. The study was performed prior to the spread of the BA.2 Omicron variant (which does not exhibit S gene target failure).

Statistical analysis

All analyses were conducted in R (version 4.0.5; https://www.r-project.org/). For the primary analysis of CT-SS by variant and vaccination status, Wilcoxon rank-sum test was used to determine differences between scores; median and interquartile range was reported. Multivariable linear regression was used to assess associations controlling for confounding features; full information is given in supplemental materials (Appendix E1). For the analysis of CT imaging characteristics, Fisher's exact test was used to determine differences in proportions between groups, with odds ratio and confidence intervals reported. A logistic regression model was used to control for confounding variables (see Appendix E1) for bronchial wall thickening. For the analysis of 30-day admission to critical care or death, we fitted survival models using Cox proportional hazard regression. Power calculation was performed assuming a reduction of CT-SS of 4 points in Omicron, based on pilot data (alpha 0.05, power 80%). P-value of <.05 was used for significance.

RESULTS

Patient clinical characteristics by variant and vaccination

Data was analyzed from 106 adult patients (Delta n=66, Omicron n=40) (mean age, 58 years ± 18, 58 men) with SARS-CoV-2 infection and CT pulmonary angiograms (Figure 1). BMI and ethnicity were similar across groups. As expected with on-going vaccine roll-out there were differences by variant in vaccination status, with a greater proportion of Delta admissions in patients who were unvaccinated (34/62, 55%, Delta vs 7/32, 22%, Omicron), and a greater proportion of Omicron had received a booster (10/62, 16%, Delta vs 13/32, 41%, Omicron) (Table 1). There was no evidence of a difference in smoking status between variants, or in any comorbidity other than ischaemic heart disease and immunosuppression (Table 1). A greater proportion of those who had received a booster vaccination had active malignancy, COPD, or immunosuppressed status, as well as being on average 20 years older, which would be in keeping with the stage of UK booster roll-out at the time of our study (Table E1).

CT patterns

We evaluated CT findings according to the Radiological Society of North America (RSNA) CT classification of SARS-CoV-2 pneumonia. There were more studies categorized as normal in the patients with Omicron (37%, 15/40) compared with Delta (15%, 10/66) (Fisher exact p=.016). Only 40% (16/40) of the patients with Omicron had typical SARS-COV-2 pneumonia appearances compared with 83% (55/66) of those with Delta ($p < .001$). The indeterminate or atypical patterns comprised a greater proportion of patients with Omicron than Delta (22%, 9/40 vs 1.5%, 1/66) ($p<.001$) (figure 3).

A greater proportion of studies were categorized as normal in the single/double vaccinated or booster vaccinated population (26%, 14/53) compared with unvaccinated (5%, 2/41) (p=.006). Meanwhile, 90% (37/41) demonstrated CT findings typical of SARS-CoV-2 in the unvaccinated group compared with 60% (32/53) in the sample receiving any vaccination

(p=.001). Atypical and indeterminate categories comprised 13% (7/53) in the vaccinated versus 5% (2/41) in the unvaccinated group (p=.29) (figure 3).

Chest CT Severity Score (CT-SS)

Patients with Omicron had a lower median CT-SS (median 3.5, IQR 0-8) than those with Delta (median 11.8, IQR 7.5-15.4), (Wilcoxon rank sum p<.001), (Figure 4A). In an adjusted multivariable linear regression model, controlling for age, smoking status, presence of immunosuppression and vaccination status, Omicron variant infection was associated with a CT-SS that was lower by 7.2 points compared to Delta variant infection (β=-7.2, 95%CI --9.9, -4.5; p <.001) (Table 2).

Vaccination was associated with a lower median CT-SS; unvaccinated patients had a median CT-SS of 11 (IQR 7.5-14) whilst patients who had received a booster vaccine had a median CT-SS of 5 (IQR 0-11.5) (p = .03), (Figure 4B). In adjusted analyses, this association was not present (Table 2).

We repeated our analysis of the impact of variant for each of the vaccine status subgroups. In those who were unvaccinated, the median score CT-SS for patients with Delta was 12 versus 5.5 for those with Omicron (p =.004) while for those who had received one or two vaccinations, the median CT-SS for patients with Delta was 13.5 versus 0 for those with Omicron (p = .046). We saw no evidence of a difference between median CT-SS in patients with Delta compared with Omicron on univariable analysis in those who had been booster vaccinated (5 vs 5 respectively, p > .99), (Figure 4C). After adjusting for age, smoking status and presence of immunosuppression, we again found that patients with Omicron had a lower CT-SS than those with Delta in an unvaccinated and singe/double vaccinated population (unvaccinated β=-7.6 points; 95%CI: -16, -3.3; p=.002; single/double vaccinated β=-9.4 points; 95%CI:-15, -3.9; p=.003), but not in the boosted population (β=-5.8 points; 95%CI: -12, 0.67; p = .095, Table E3).

Finally, we repeated our analysis in only those who had 'typical' findings of SARS-CoV-2 pneumonia, as well as using just one of each radiologist's score (rather than a consensus). In both circumstances a lower CT-SS was noted in those with Omicron (Figures E1 and E2 respectively).

CT imaging characteristics

Bronchial wall thickening was more common in patients with Omicron than with Delta variant, both before (OR, 2.4, 95%CI: 1.01, 5.92; Fisher's exact p=.04, Figure 5) and after adjustment for covariates (adjusted OR 2.8, 95%CI: 1.1, 7.5; p=.04) (Table E4). There were no additional lung CT findings that were more common in Delta versus Omicron variant (Table E5).

Biochemical and clinical severity

Omicron variant infection was associated with higher lymphocyte and monocyte counts compared with Delta variant (figure 6A), while no difference was demonstrated with CRP or platelets (Figure E3). Severe disease (with a WHO score ≥6, requiring non-invasive ventilation or high flow oxygen or more) was associated with Delta versus with Omicron variant (OR 4.6, 95%CI: 1.2, 26; p=.01) (Figure 6B). Critical care admission was also associated with Delta versus Omicron variant (OR 7.0, 95%CI: 1.5, 66; p=.004) (Figure 6C).

High CT-SS correlates with poorer clinical outcomes across both variants

In analyses adjusting for age per the original linear model, a high CT-SS was associated with a composite outcome of admission to critical care or death within 30 days of CT pulmonary angiography (n=27 events, adjusted HR 3.8; 95% CI 1.1-14, p=.04, Table 4). Only one patient with Omicron had a CT-SS of more than 14.

DISCUSSION

The SARS-Cov-2 Omicron variant demonstrates rapid spread but with lower rates of hospital admission and disease severity. Studies evaluating the lung CT findings of Omicron versus non-Omicron variants are lacking. In this report, we examined the CT features and biochemical and clinical outcomes for patients hospitalized with SARS-COV-2 infection of either the Omicron or Delta variant. In patients infected with Omicron variant, more CT pulmonary angiograms were categorized as normal compared with those infected with the Delta variant (37% (15/40) vs 15% (10/66) respectively, p=.016). Omicron variant infection was associated with a CT-SS that was lower by 7.2 points compared to Delta infection (β=-7.2, 95%CI: -9.9, -4.5; p <.001) in an adjusted multivariable linear regression analysis. Bronchial wall thickening was more common with Omicron than with the Delta variant (OR 2.4, 95%CI: 1.01, 5.9; p=.04). Patients who had vaccination with a booster shot had less severe disease on CT versus unvaccinated patients (CT-SS median 5 (IQR 0-11.5), CT-SS median 11 (IQR 7.5-14), respectively; p = .03). The Delta variant was associated with more severe disease (OR 4.6, 95%CI: 1.2, 26.0, p=.01) and critical care admission (OR 7.0, 95%CI: 1.5, 66.2, p=.004) than the Omicron variant. We also identified that Omicron variant infection was associated with both higher lymphocyte and monocytes counts in the peripheral blood. Lower levels of these parameters have been associated with more severe disease[12,13] and so this finding is consistent with Omicron causing less severe illness.

Previous reports have shown vaccination to reduce the relative risk of hospitalization in Delta than Omicron infection[1,14]. Within this context, our results suggest that infection with Omicron variant is intrinsically less severe than Delta variant infection, as evidenced by the significant difference in severity amongst the unvaccinated during our study period and robust findings from the generalized linear model across the entire sample. The persistence of effect in just the ‘typical’ subgroup suggests that the lower CT-SS scores in patients with Omicron are not simply explained by a greater proportion of normal scans. The fact that a large and significant difference continued to be observed regardless of whether the scores were taken from an

experienced or trainee radiologist indicates the utility and relevance of these findings for everyday clinical practice. Further, the high proportion of scans negative for pneumonia in those with Omicron suggests reduced utility of CT as a diagnostic tool in the context of this variant, whilst the wide range of CT-SS scores in just 'typical' cases demonstrates a range of severity within this category, suggesting that CT-SS provides substantially more information rather than simple classification.

We were also able to show that a cut-off CT-SS of 14, as previously described[6], is able to accurately predict critical care admission or death within 30 days for this study sample, further validating this previous finding and demonstrating the utility of CT pulmonary angiogram findings in the radiological assessment of SARS-CoV-2 pneumonia.

Our study had a number of limitations. First, over the study period, case rates and vaccination status showed fluctuations, with differences noted in the underlying demographics of those who had received a booster vaccination; comparisons with regard to different levels of vaccination status are therefore limited. Vaccination efficacy varies not only according to variant type but also the time since vaccination, vaccination type and percentage population vaccinated, variables we were unable to control for in our study. Second, we were unable to establish the frequency of previous infection with SARS-CoV-2 within our study sample. Omicron is associated with a higher rate of reinfection[15] and it is possible that a larger proportion of Omicron cases, compared to Delta, represented reinfections and this may have contributed to the reduced severity of Omicron infections. Third, detection of bronchial wall thickening is subjective and also reduced in those with higher CT-SS due to background ground glass opacification, potentially leading to a reduction in the number of patients with Delta identified to have bronchial wall thickening. Fourth, threshold to imaging may differ between variants. Finally, our study sample contained patients with SARS-CoV-2, however, not all were admitted for SARS-CoV-2, therefore outcome data should be interpreted with caution.

In conclusion, in this small series of hospitalized patients rt-PCR positive for SARS-CoV-2 with CT pulmonary angiography performed within 7 days of admission, we found that the Omicron variant infection is less likely to be associated with SARS-CoV-2 pneumonia, and that, when pneumonia does occur, it is less severe on chest CT. In agreement with chest CT patterns, Omicron infection was associated with reduced clinical and biochemical markers of severity and improved hospital outcomes.

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TABLES

Table 1. Summary of Patient Characteristics

Characteristic		Delta (n=66)	Omicron (n=40)	p-value
Age (years)		56 (18)	62 (19)	.07
Sex	Women	34 (52%)	14 (35%)	.11
	Men	32 (48%)	26 (65%)	.11
Ethnicity	Other	19 (29%)	6 (15%)	.16
	White	47 (71%)	34 (85%)	.16
Vaccination Status	unvaccinated	34 (55%)	7 (22%)	.002
	single or double vaccinated	18 (29%)	12 (38%)	.49
	booster vaccinated	10 (16%)	13 (41%)	.01
	missing	4	8	
Smoking Status	Current smoker	4 (6.1%)	5 (12%)	.29
	Ex-smoker	15 (23%)	14 (35%)	.18
	Never smoked	47 (71%)	21 (52%)	.06
Any Comorbidity		30 (45%)	25 (62%)	.09
Hypertension		17 (26%)	13 (32%)	.46
Diabetes Mellitus		6 (9.1%)	8 (20%)	.11
Ischaemic Heart Disease		4 (6.1%)	10 (25%)	.01
Active malignancy or within past 5 years		7 (11%)	7 (18%)	.31
Asthma		8 (12%)	6 (15%)	.67
COPD		7 (11%)	6 (15%)	.55

Medical condition-induced immunosuppression		9 (14%)	13 (32%)	.02
BMI (kg/m2)		31 (10)	29 (8)	.17
	missing	11	4	
Drug-induced immunosuppression		4 (6.1%)	4 (10%)	.47
Any drug prescribed to treat COVID-19		49 (74%)	23 (57%)	.07
Vasopressors		2 (3.0%)	0 (0%)	.53
Dexamethasone		47 (72%)	23 (57%)	.12
	missing	1	0	
Remdesevir		29 (44%)	17 (42%)	.88
Tocilizumab		34 (52%)	7 (18%)	<.001
Ronapreve		12 (18%)	1 (2.5%)	.02

Data provided is mean (SD) for age and BMI, or n (%) for all other variables. Statistics performed with either Wilcoxon rank sum test (age, BMI) or Fisher's exact test (all other variables). Ethnicity category 'other' includes: Asian – any other Asian background, Asian or Asian British – Bangladeshi, Asian British – Pakistani, Black or Black British – African, Black or Black British – Caribbean, Chinese, Not stated, Other - not known. Ethnicity category 'White' includes: White - any other white background, White – British, White – Irish. For detailed ethnicity data see Table E2. COPD - chronic obstructive pulmonary disease.

Table 2. Univariable and Multivariable Linear Regression Models for the Association between CT-SS and Listed Variables

	Univariable Models			Multivariable Model		
Variable	β coefficient	95% CIs	P value	β coefficient	95% CIs	P value
Omicron variant (ref: Delta)	-6.8	-9.3 - -4.3	<.001	-7.2	-9.9 - -4.5	<.001
Age	-0.083	-0.16 - -0.01	.03	-0.055	-0.13 - 0.021	.16
Current smoker (ref: Never smoked)	-3.5	-8.2 - 1.2	.15	-1.7	-6 - 2.6	.44
Ex-smoker (ref: Never smoked)	1	-2.1 - 4.1	.52	3.1	0.36 - 5.8	.03
Presence of immunosuppression	1.2	-1.9 - 4.3	.46	5.6	2.5 - 8.7	<.001
Single or double vaccinated (ref: unvaccinated)	-1.8	-4.9 - 1.3	.29	-1.3	-4 - 1.4	.37
Booster vaccinated (ref: unvaccinated)	-3.9	-7.4 - -0.37	.03	-3.6	-7.3 - 0.12	.06

All listed variables were included as covariates in the multivariable model, which was determined by backwards selection with an exit p value >0.1 (see Appendix E1).

Table 3. Univariable and Multivariable Cox Proportional Hazard Models for the Relationship between High CT-SS (>=14) and Admission to Critical Care or Death (n events = 27)

Variable	Univariable Model			Multivariable Model		
	HR	95% CIs	P value	HR	95% CIs	P value
High CTSS Score (>=14)	3.4	1.4 - 7.9	.006	3.8	1.1 - 14	.04
Omicron variant (ref: Delta)	0.54	0.18 - 1.6	.27	0.64	0.094 - 4.3	.64
Age	0.99	0.97 - 1.0	.65	0.99	0.96 - 1	.71
Current smoker (ref: Never smoked)	0.57	0.075 - 4.3	.59	1.2	0.13 - 10	.90
Ex-smoker (ref: Never smoked)	0.82	0.32 - 2.1	.69	1.1	0.35 - 3.6	.85
Presence of immunosuppression	1.4	0.57 - 3.5	.46	2.4	0.63 - 9.1	.20
Single or double vaccinated (ref: unvaccinated)	1	0.34 - 3.0	.99	0.56	0.15 - 2.1	.38
Booster vaccinated (ref: unvaccinated)	0.53	0.11 - 2.4	.41	0.51	0.07 - 3.7	.51

All listed variables were included as covariates in the multivariable model.

FIGURES

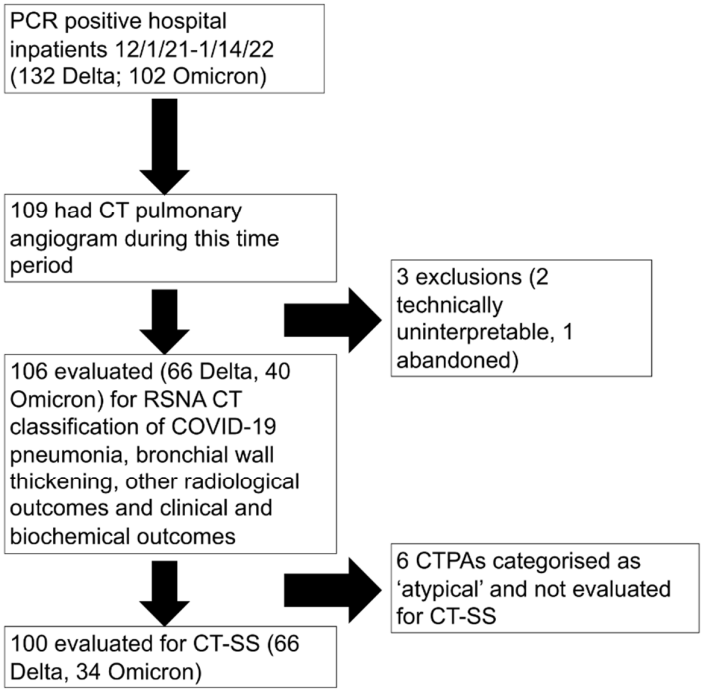
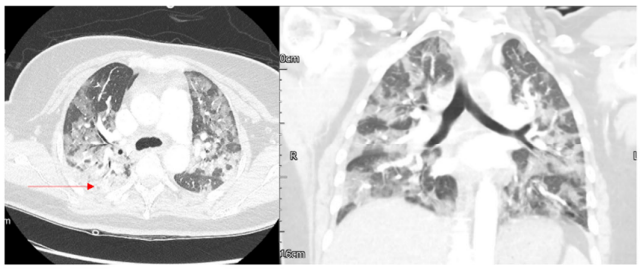
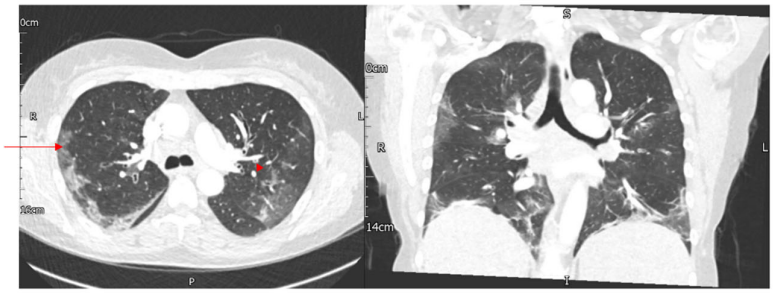


Figure 1. *Flowchart of study patients. CT-SS – Chest CT Severity Score, RSNA – Radiological Society of North America.*



A



B

Figure 2. Example cases. (*A*) *Axial and coronal CT images on lung window in a 33-year-old woman with Delta SARS-CoV-2 pneumonia without critical care admission. Chest CT images show bilateral multifocal patchy ground-glass and consolidation with both central and peripheral distribution, with more confluent consolidation in the posterior segment of right upper lobe (arrow), with overall global mean CT severity score of 23. Bronchial wall thickening is absent.* ***(B)*** *Axial and coronal CT images on lung window in a 59-year-old woman with Omicron SARS-CoV-2 pneumonia without critical care admission. Chest CT images show bilateral multifocal peripheral ground-glass opacities (arrow) with predominantly peripheral distribution, with overall global mean CT severity score of 10. Bronchial wall thickening is present (arrowhead).*

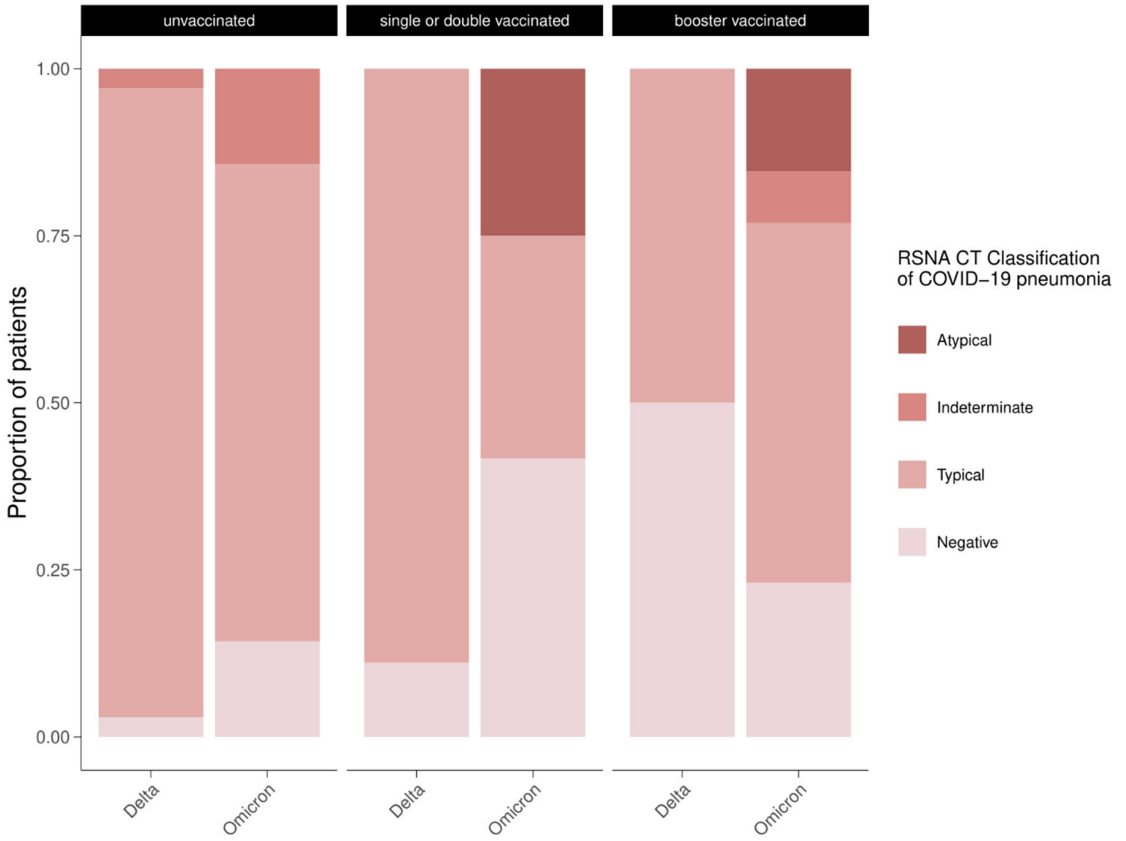
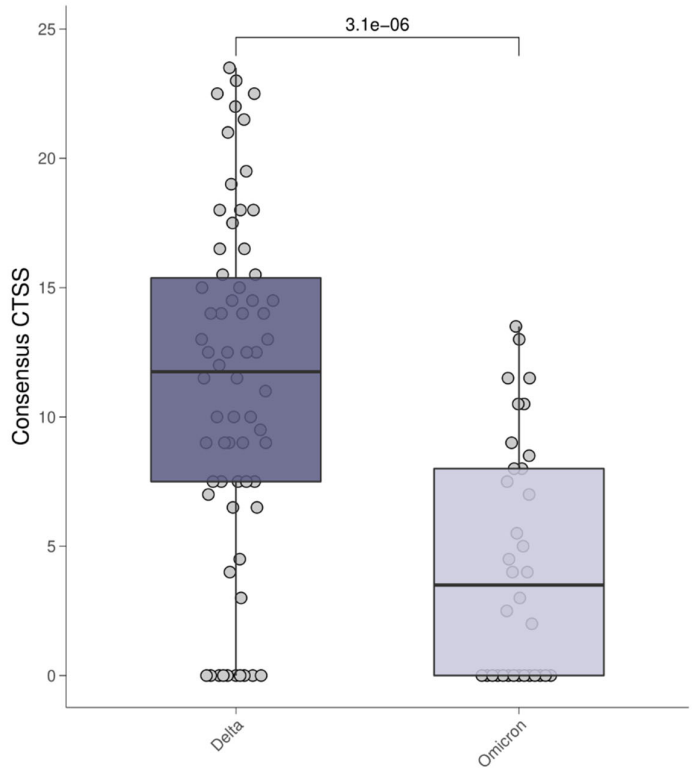
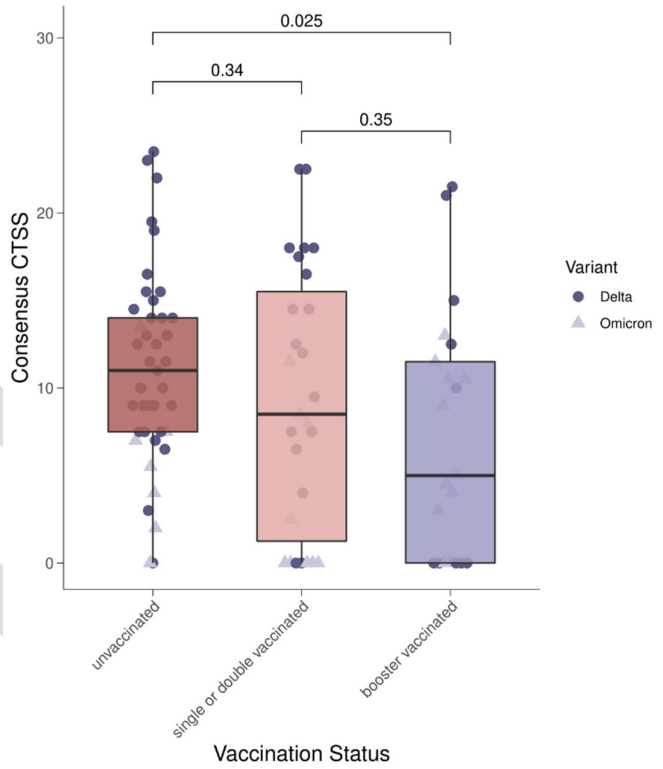


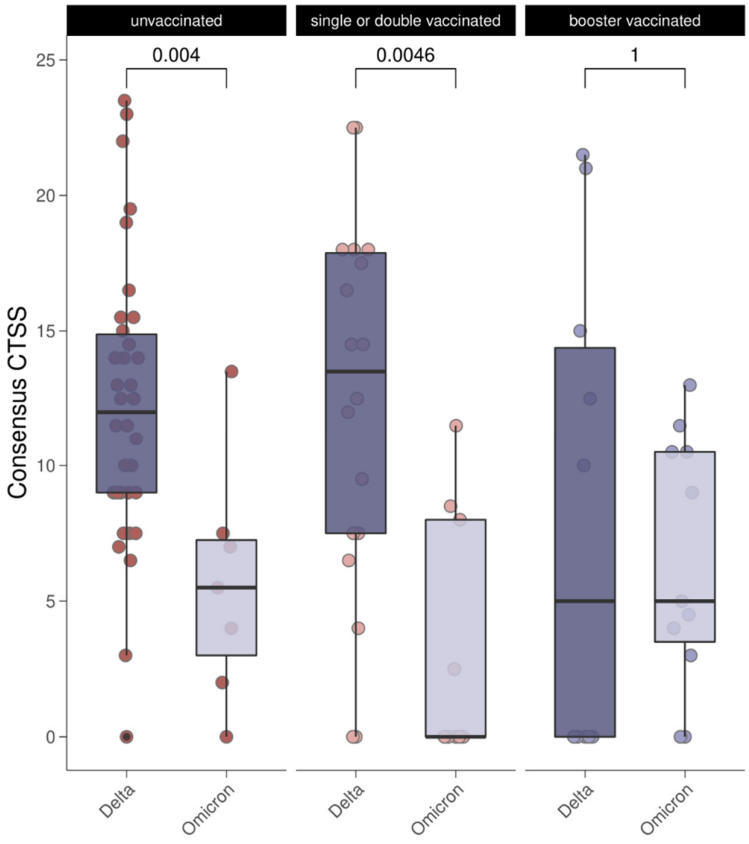
Figure 3. *Proportion of patients with each category of the RSNA CT classification of SARS-COV-2 pneumonia by variant, separated by vaccine status.*


3.1e−06
Consensus CTSS
25
20
15
10
5
0
Delta
Omicron

A


0.025
0.34
0.35
Consensus CTSS
30
20
10
0
Variant
Delta
Omicron
unvaccinated
single or double vaccinated
booster vaccinated
Vaccination Status

B



C

Figure 4*. **(A)** Consensus CT-SS by variant status. **(B)** Consensus CT-SS by vaccination status. **(C)** CT-SS by variant status with the study sample faceted on vaccination status. P values with Wilcoxon rank sum test.*

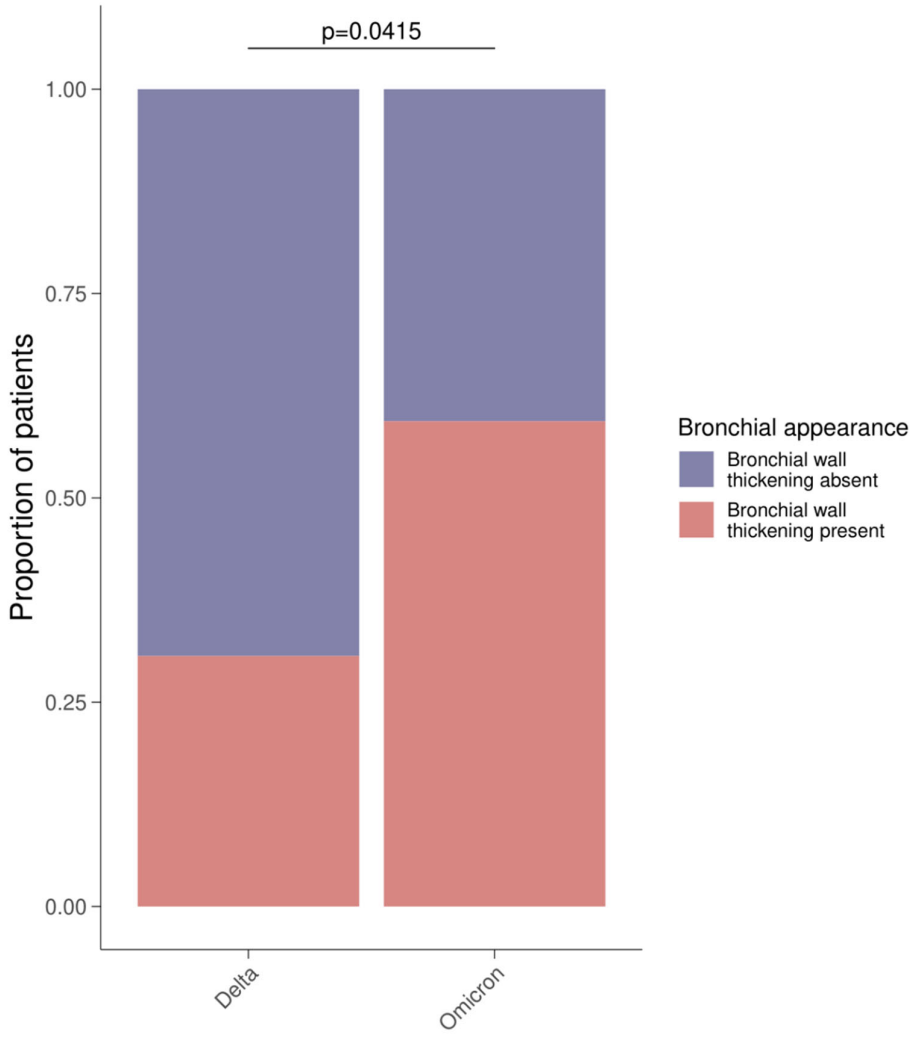
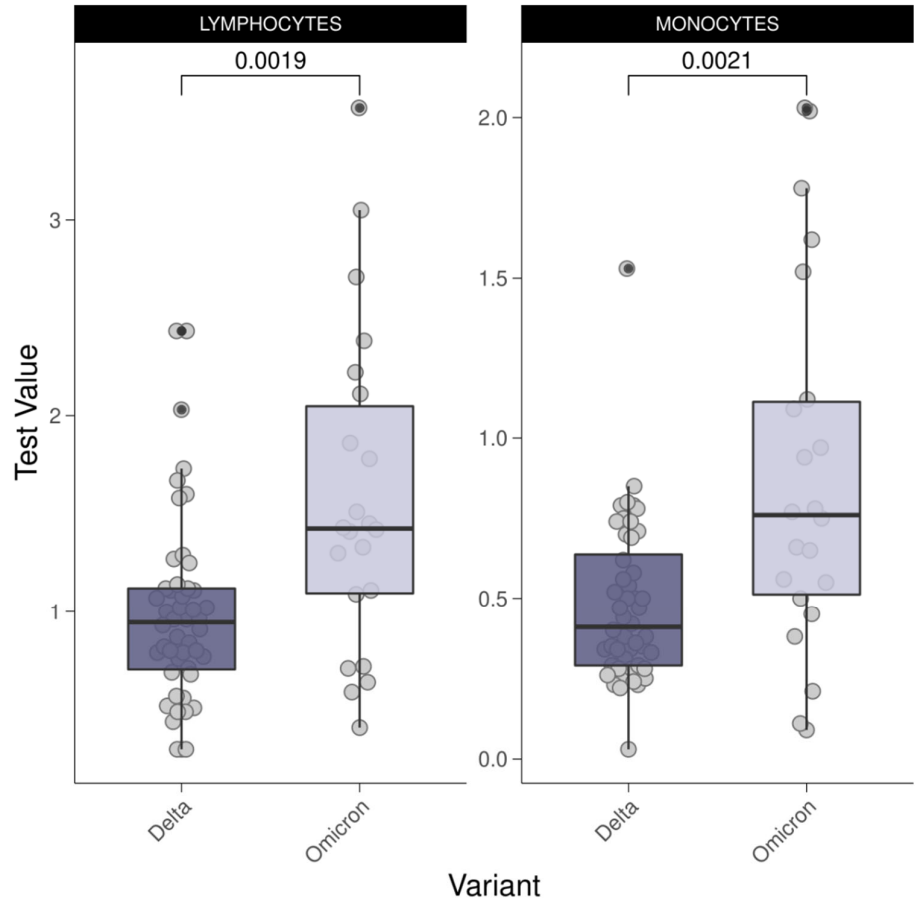
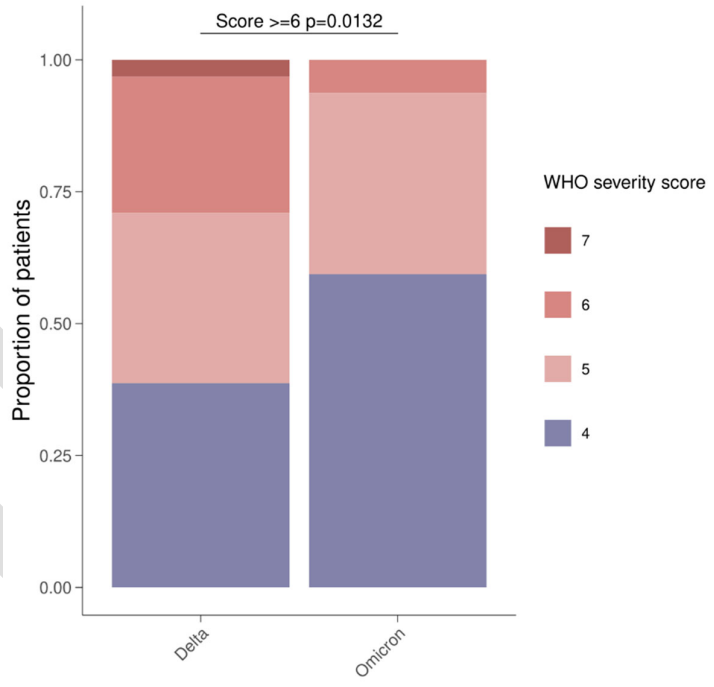


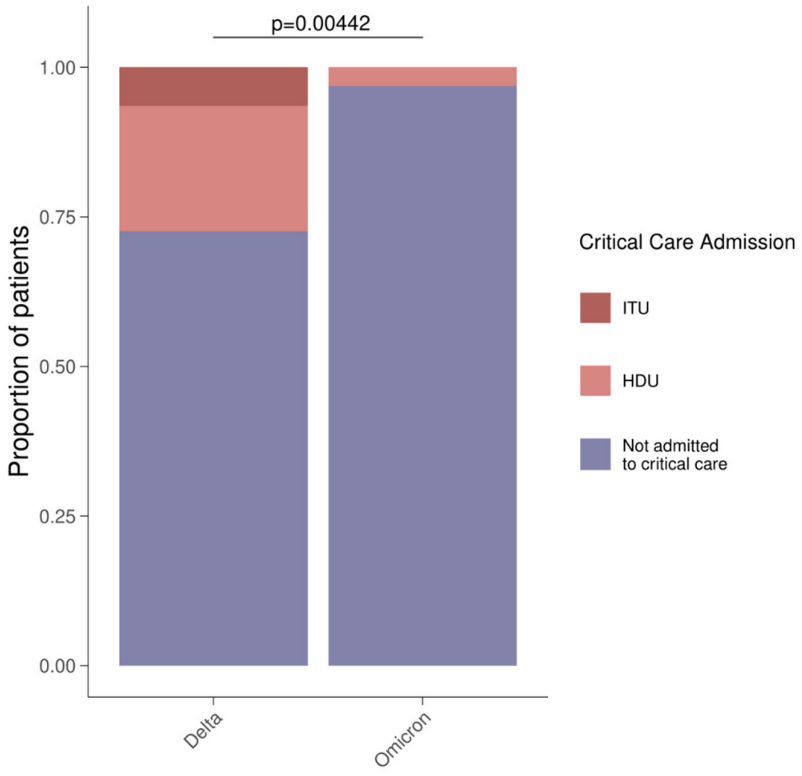
Figure 5. *The proportion of patients with bronchial wall thickening by variant and vaccination status. P values by Fisher's exact test.*


LYMPHOCYTES
MONOCYTES
0.0019
0.0021
Test Value
Variant
Delta
Omicron

A


Score >=6 p=0.0132
Proportion of patients
WHO severity score
7
6
5
4
Delta
Omicron

B



C

Figure 6. *(A) Differences in lymphocytes and monocytes by variant.* ***(B)*** *Proportion of patients with WHO ordinal score by variant.* ***(C)*** *Proportion of patients admitted to critical care by variant. Statistics are with Wilcoxon rank sum (A) or Fisher's exact test (B, C).*

Appendix E1

Supplementary Methods

Statistical analysis

For the primary analysis of CT-SS by variant and vaccination status, multivariable linear regression was used to assess associations between CT-SS and patient age, sex, ethnicity, smoking status, presence of any comorbidity, presence of immunosuppression and vaccination status. Models were fitted using backwards elimination with an exit p value of >0.10. We pre-specified inclusion of vaccination status and variant in all models to allow testing of differences between variants and vaccine status. The final multivariable model included the covariates age, smoking status, immunosuppression and vaccination status:

glm(Consensus CT-SS ~ Variant + Age + Smoking Status + Presence of immunosuppression + Vaccination status)

Univariable and multivariable coefficients and p values are given in Table 2 and Table E6. For regression analysis only complete cases were considered (na.action=na.omit). Despite a prior hypothesis that there could be an interaction between variant and vaccination status, there was no statistical evidence for this (interaction p value >0.15, Table E7) and so no interaction term included in the final model.

For the analysis of bronchial wall thickening we fitted a logistic model, using a similar approach, but pre-specified the inclusion of smoking status and COPD diagnosis alongside vaccination status in the multivariable model as these are known to affect bronchial wall thickness[16,17]. No other co-variates found to be significant on backwards elimination leaving a final model of:

glm(Bronchial wall thickening ~ Variant + Smoking Status + COPD + Vaccination status, family='binomial')

Univariable coefficients and p values given in Table E8 with the multivariable model in Table E4.

For the analysis of 30-day admission to critical care or death, we fitted survival models using Cox proportional hazard regression. We used same covariates selected in the primary analysis of CT-SS by variant.

Supplemental Tables

Table E1. Summary of Patient Characteristics by Vaccination Status

Characteristic		Unvaccinated (n=41)	single or double vaccinated (n=30)	booster vaccinated (n=23)	p-value
Delta		34 (83%)	18 (60%)	10 (43%)	.004
Omicron		7 (17%)	12 (40%)	13 (57%)	.004
Age (years)		51 (15.8)	52 (17.3)	71 (15.6)	<.001
Sex	Women	19 (46%)	19 (63%)	3 (13%)	.001
	Men	22 (54%)	11 (37%)	20 (87%)	.001
Ethnicity	Other	11 (27%)	10 (33%)	3 (13%)	.2
	White	30 (73%)	20 (67%)	20 (87%)	.2
Smoking Status	Current smoker	3 (7.3%)	4 (13%)	1 (4%)	.6
	Ex-smoker	10 (24.4%)	8 (27%)	9 (39%)	.6
	Never smoked	28 (68.3%)	18 (60%)	13 (57%)	.6
Any Comorbidity		16 (39%)	16 (53%)	15 (65%)	.12
Hypertension		7 (17%)	9 (30%)	8 (35%)	.2
Diabetes Mellitus		3 (7.3%)	5 (17%)	5 (22%)	.2
Ischaemic Heart Disease		3 (7.3%)	3 (10%)	5 (22%)	.2

Active malignancy or within past 5 years		1 (2.4%)	4 (13%)	7 (30%)	.004
Asthma		7 (17%)	5 (17%)	1 (4.3%)	.4
COPD		3 (7.3%)	2 (6.7%)	7 (30%)	.025
Medical condition-induced immunosuppression		3 (7.3%)	6 (20%)	12 (52%)	<.001
Drug-induced immunosuppression		1 (2.4%)	3 (10%)	3 (13%)	.2
Any drug prescribed to treat COVID-19		32 (78%)	18 (60%)	17 (74%)	.2
Vasopressors		0 (0%)	1 (3.3%)	0 (0%)	.6
Dexamethasone		32 (78%)	17 (57%)	17 (74%)	.14
Remdesevir		16 (39%)	15 (50%)	11 (48%)	.6
Tocilizumab		20 (49%)	13 (43%)	8 (35%)	.6
Ronapreve		8 (20%)	3 (10%)	1 (4.3%)	.2

Table E2. Detailed Ethnicity Data

Ethnicity	**Number of patients**
Asian - any other Asian background	2
Asian or Asian British - Bangladeshi	1
Asian or Asian British - Pakistani	2
Black or Black British - African	1
Black or Black British - Caribbean	1
Chinese	2
Not stated	12
Other - not known	4
White - any other white background	13
White - British	65
White - Irish	3

Table E3. Multivariable Linear Regression Models for the Association between CT-SS and Listed Variables within Each Vaccination Group

Unvaccinated			
	β coefficient	95% CIs	P value
Omicron variant (ref: Delta)	-7.6	-12 - -3.3	.0017
Age	0.017	-0.099 - 0.13	.77
Current smoker (ref: Never smoked)	0.58	-5.9 - 7	.86
Ex-smoker (ref: Never smoked)	4	0.08 - 7.9	.06
Presence of immunosuppression	2	-4.1 - 8.1	0.53
Single or double vaccinated			
	β coefficient	95% CIs	P value
Omicron variant (ref: Delta)	-9.4	-15 - -3.9	.003
Age	-0.057	-0.24 - 0.12	.54
Current smoker (ref: Never smoked)	-0.3	-7.7 - 7.1	.94
Ex-smoker (ref: Never smoked)	2.3	-5.1 - 9.7	.56
Presence of immunosuppression	4.8	-0.69 - 10	.10
Booster vaccinated			
	β coefficient	95% CIs	P value
Omicron variant (ref: Delta)	-5.8	-12 - 0.67	.10
Age	-0.097	-0.31 - 0.12	.40
Current smoker (ref: Never smoked)	-3.4	-18 - 11	.65
Ex-smoker (ref: Never smoked)	3.6	-2.3 - 9.5	.25
Presence of immunosuppression	7.2	0.54 - 14	.052

Table E4. Multivariable Logistic Regression for the Association between Variant and Bronchial Wall Thickening

	OR	95% CIs	P value
Omicron variant (ref: Delta)	2.8	1.1 - 7.5	.036
Current smoker (ref: Never smoked)	2.6	0.52 - 15	0.25
Ex-smoker (ref: Never smoked)	1.1	0.38 - 3	0.88
COPD	1.5	0.35 - 6.2	0.6
Single or double vaccinated (ref: unvaccinated)	0.81	0.27 - 2.3	0.71
Booster vaccinated (ref: unvaccinated)	1.60	0.49 - 5.3	0.43

All variables are included in the model.

Table E5. Additional Radiological Features by Variant

Category	Parameter	Delta	Omicron	P value
Extent	Multifocal	54 (96%)	22 (88%)	.17
	Diffuse	2 (3.6%)	2 (8.0%)	NA
	Focal	0 (0%)	1 (4.0%)	NA
Location	Peripheral	14 (25%)	7 (28%)	.79
	Mixed	42 (75%)	17 (68%)	.59
	Central	0 (0%)	1 (4.0%)	NA
	Posterior	11 (20%)	6 (24%)	.77
Alveolar	Ground glass opacity	27 (48%)	13 (52%)	.81
	Consolidation	4 (7.1%)	5 (20%)	NA
	Linear opacity	15 (27%)	5 (20%)	.51
	Nodule	2 (3.6%)	3 (12%)	NA
	Cavitation/cystic change	0 (0%)	0 (0%)	NA
Interstitial	Septal thickening	7 (12%)	6 (24%)	.21
	Crazy paving	3 (5.4%)	0 (0%)	NA
Signs	Halo	2 (3.6%)	0 (0%)	NA
	Reverse halo	1 (1.8%)	2 (8.0%)	NA
Airways related	Mucous plugging	8 (12%)	7 (18%)	.44
	Tree in bud nodularity	1 (1.5%)	0 (0%)	NA
Vascular	Pulmonary embolus	2 (3.0%)	3 (7.5%)	NA
	Subsegmental vascular engorgement	0 (0%)	1 (2.5%)	NA

All studies were scored for 'Airways related' and 'Vascular' categories (n=66 Delta and n=40 Omicron). Studies assigned the RSNA categorization of 'negative' were not scored for the

remaining categories (n=56 Delta, n=25 Omicron). Data presented is n (%). P values generated with Fisher's exact test.

Table E6. Univariable Linear Regression for the Association between CT-SS and Listed Variables

Variable	**β coefficient**	**95% CIs**	**P value**
White ethnicity (ref: other ethnicities)	-3.1	-6.2 - 0.036	.05
Presence of comorbidity	-0.55	-3.3 - 2.2	.69
Men (ref: Women)	0.046	-2.7 - 2.8	.97

Table E7. Multivariable Linear Regression for the Association between CT-SS and Variant Including Interaction Term for Vaccination and Variant

	β coefficient	**Std. Error**	**P value**
Omicron variant (ref: Delta)	-6.6	2.5	.01
Single or double vaccinated (ref: unvaccinated)	0.1	1.8	.95
Booster vaccinated (ref: unvaccinated)	-4.2	2.2	.06
Omicron variant* single or double vaccinated	-2.4	3.5	.50
Omicron variant* booster vaccinated	5	3.6	.17

These variables were not included in the multivariable analysis because when combined with all variables, Wald p value was >0.10 (see Supplementary Methods).

Table E8. Univariable Regression Models for the Association between Variant and Bronchial Wall Thickening

	Estimate	**Std. Error**	**P value**
Omicron variant (ref: Delta)	0.25	0.096	.011
Age	0.0028	0.0026	0.28
Sex: Men	0.077	0.096	.43
Ethnicity: White	0.1	0.11	.38
Ex-smoker (ref: current smoker)	-0.29	0.19	.13
Never smoked (ref: current smoker)	-0.3	0.17	.09
Presence of comorbidity	0.083	0.096	.39
Presence of immunosuppression	0.015	0.11	.89
COPD	0.25	0.14	.09
Asthma	-0.21	0.14	.14
Single or double vaccinated (ref: unvaccinated)	0.041	0.11	.72
Booster vaccinated (ref: unvaccinated)	0.32	0.12	.01

No statistical difference for interaction was identified (bottom row).

Supplemental Figures

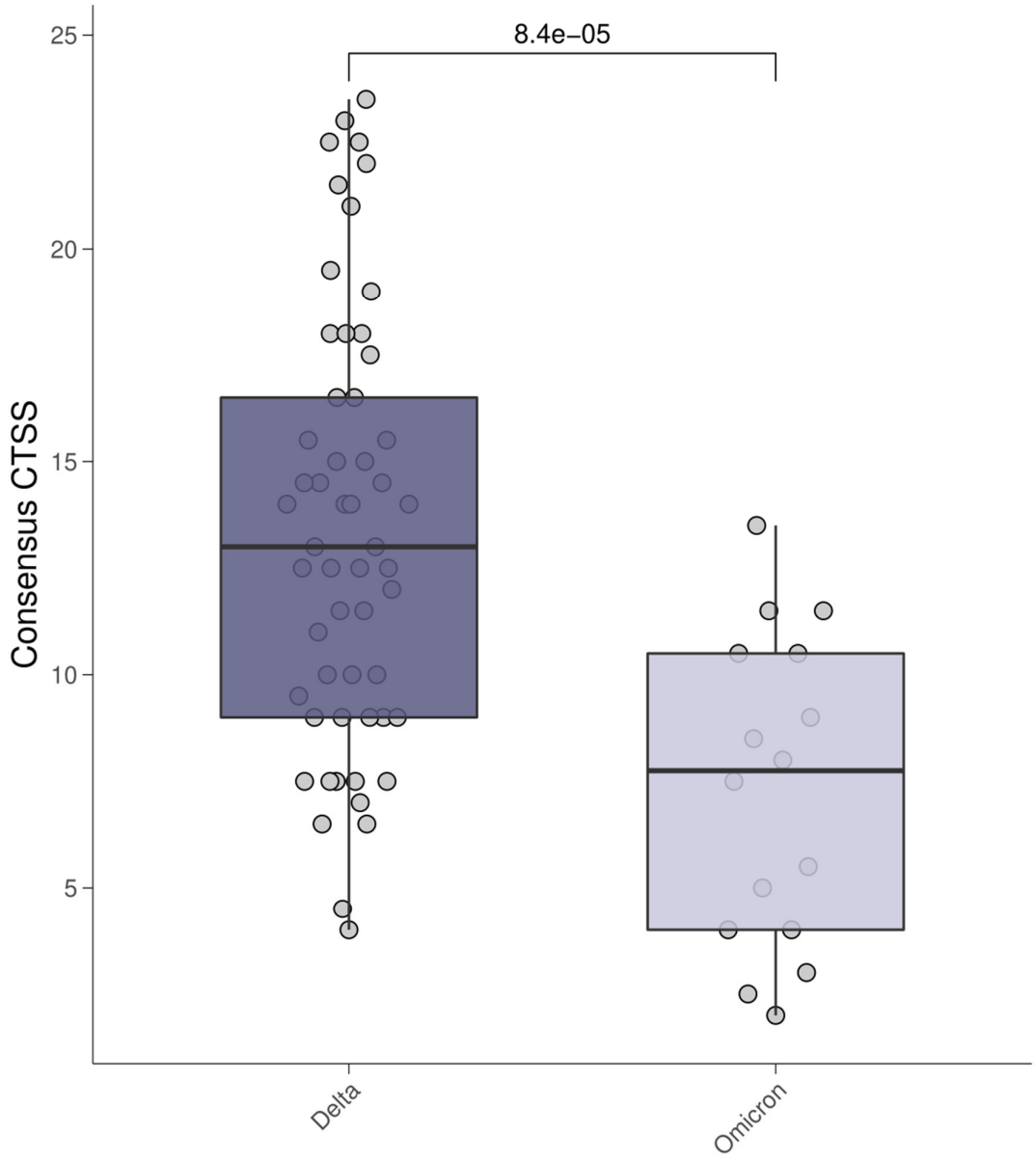
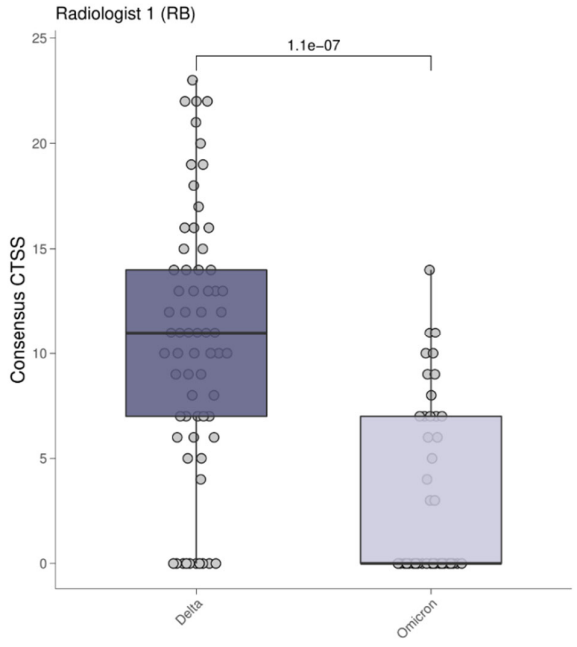
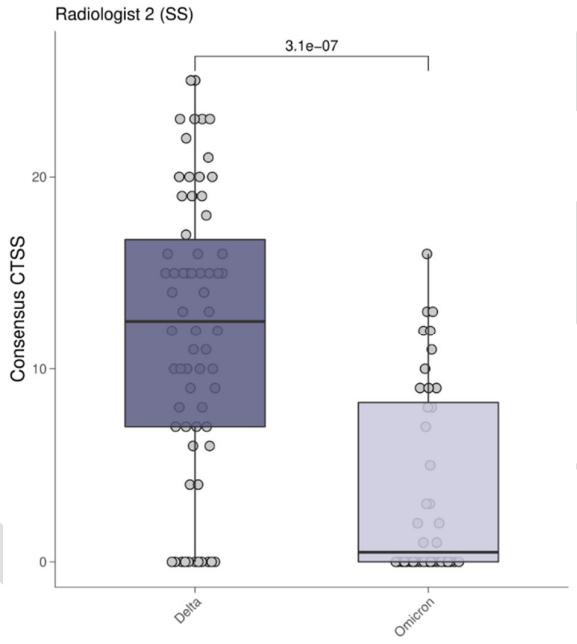


Figure E1: *Consensus CT-SS by variant only in those studies categorized as 'typical' for SARS-CoV-2 pneumonia as per the RSNA expert consensus statement. Statistics with Wilcoxon rank sum test.*



A



B

Figure E2: *CT-SS by variant using the scores taken solely from Radiologist 1* ***(A)*** *or Radiologist 2* ***(B)****. Statistics with Wilcoxon rank sum test.*

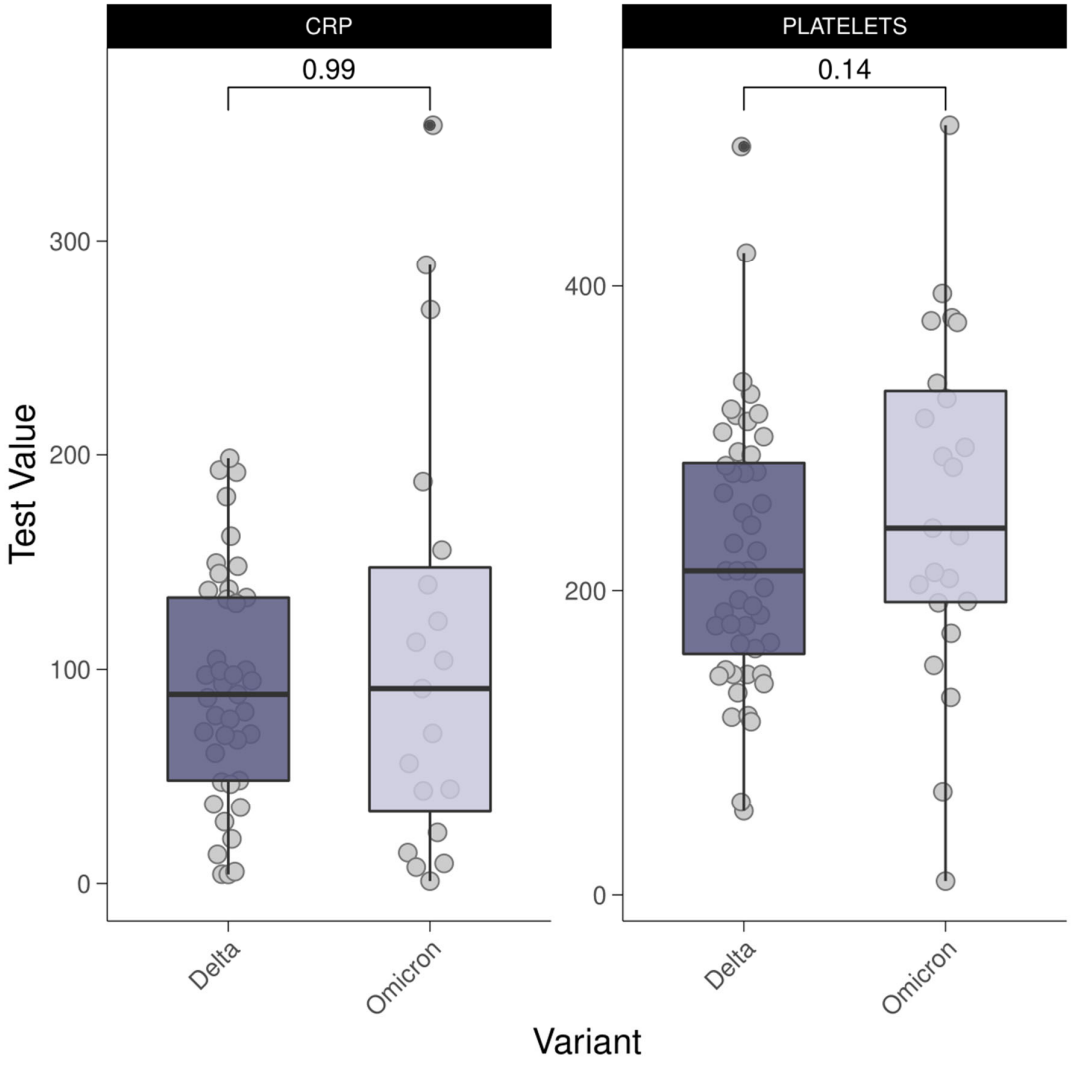


Figure E3: *C-reactive protein (CRP) and Platelets by variant. Statistics with Wilcoxon rank sum test.*