BMJ Open Respiratory Research

Lung volume measurement using chest CT in COVID-19 patients: a cohort study in Japan

Shiro Otake,[1] Yusuke Shiraishi,[2] Shotaro Chubachi ,[1] Naoya Tanabe ,[2] Tomoki Maetani,[2] Takanori Asakura,[3] Ho Namkoong,[3] Takashi Shimada,[1] Shuhei Azekawa,[1] Kensuke Nakagawara,[1] Hiromu Tanaka,[1] Takahiro Fukushima,[1] Mayuko Watase,[4] Hideki Terai,[1] Mamoru Sasaki,[5] Soichiro Ueda,[5] Yukari Kato,[6] Norihiro Harada ,[6] Shoji Suzuki,[7] Shuichi Yoshida,[7] Hiroki Tateno,[7] Yoshitake Yamada,[8] Masahiro Jinzaki,[8] Toyohiro Hirai,[9] Yukinori Okada,[10,11] Ryuji Koike,[12] Makoto Ishii,[13] Naoki Hasegawa,[14] Akinori Kimura,[15] Seiya Imoto,[16] Satoru Miyano,[17] Seishi Ogawa,[18,19] Takanori Kanai,[20] Koichi Fukunaga[1]

To cite: Otake S, Shiraishi Y, Chubachi S, *et al*. Lung volume measurement using chest CT in COVID-19 patients: a cohort study in Japan. *BMJ Open Respir Res* 2024;**11**:e002234. doi:10.1136/bmjresp-2023-002234

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjresp-2023-002234).

Received 6 December 2023
Accepted 9 April 2024

For numbered affiliations see end of article.

Correspondence to
Dr Shotaro Chubachi;
bachibachi472000@z6.keio.jp

ABSTRACT

Objective This study aimed to investigate the utility of CT quantification of lung volume for predicting critical outcomes in COVID-19 patients.

Methods This retrospective cohort study included 1200 hospitalised patients with COVID-19 from 4 hospitals. Lung fields were extracted using artificial intelligence-based segmentation, and the percentage of the predicted (%pred) total lung volume (TLC (%pred)) was calculated. The incidence of critical outcomes and posthospitalisation complications was compared between patients with low and high CT lung volumes classified based on the median percentage of predicted TLC_{ct} (n=600 for each). Prognostic factors for residual lung volume loss were investigated in 208 patients with COVID-19 via a follow-up CT after 3 months.

Results The incidence of critical outcomes was higher in the low TLC_{ct} (%pred) group than in the high TLC_{ct} (%pred) group (14.2% vs 3.3%, p<0.0001). Multivariable analysis of previously reported factors (age, sex, body mass index and comorbidities) demonstrated that CT-derived lung volume was significantly associated with critical outcomes. The low TLC_{ct} (%pred) group exhibited a higher incidence of bacterial infection, heart failure, thromboembolism, liver dysfunction and renal dysfunction than the high TLC_{ct} (%pred) group. TLC_{ct} (%pred) at 3 months was similarly divided into two groups at the median (71.8%). Among patients with follow-up CT scans, lung volumes showed a recovery trend from the time of admission to 3 months but remained lower in critical cases at 3 months.

Conclusion Lower CT lung volume was associated with critical outcomes, posthospitalisation complications and slower improvement of clinical conditions in COVID-19 patients.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The measurement of lung volume using chest CT has been reported to be a simple and useful indicator of various lung diseases.

⇒ However, few reports have examined lung volume in COVID-19 patients.

WHAT THIS STUDY ADDS

⇒ CT-derived lung volume measurement has significant value as an easily assessable indicator for predicting the severity of COVID-19.

⇒ CT-derived lung volume can identify populations at risk of COVID-19 sequelae by evaluating residual lung volume reduction.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Longitudinal studies should examine the association between CT-derived lung volume and the symptoms of long COVID.

INTRODUCTION

The first case of COVID-19 occurred in October 2019; since then, 764 473 623 cases and 6915273 deaths have been reported worldwide.[1] Although initially feared as an unidentified pathogen, comprehensive research has been conducted on a global scale, resulting in advances in vaccines and therapeutic agents, thereby improving prognosis.[2–4] However, the virus persists with mutations, and the epidemic remains unrelenting in various regions of the world.[5]

Chest CT is extensively used to diagnose COVID-19 and predict its severity.[6 7] The measurement of lung volume using chest CT has been reported to be a simple and useful indicator of various lung diseases, including chronic obstructive disease (COPD) and idiopathic pulmonary fibrosis (IPF), where CT-derived lung volume correlates with pulmonary function test results.[8–11] Recent studies have indicated its usefulness in

assessing disease activity, especially IPF because it enables the evaluation of longitudinal lung volume reduction resulting from lung fibrosis.[12 13] COVID-19 manifests as ground glass opacities and consolidation shadows during the acute phase, which may improve or lead to fibrotic lesions over time.[14 15] Fibrotic scarring following acute inflammation may also reduce lung volume in patients with COVID-19 pneumonia. However, few reports have examined lung volume in COVID-19 patients,[16–19] and only one report has specifically investigated its association with severity.[17]

COVID-19 causes long-term lung sequelae.[20] Chest CT serves as a valuable tool for assessing structural sequelae of the lungs, and many studies using qualitative evaluation by radiologists have confirmed the presence of residual opacities at the 3-month time point following COVID-19 diagnosis, particularly in severe cases.[21–24] Therefore, CT-derived lung volume measurements may be advantageous for evaluating long-term lung fibrosis in COVID-19 patients.[16] However, the frequency of patients with a long-term reduction in lung volume and clinical characteristics has not been previously reported.

Based on this background, we hypothesised that automated quantification of lung volume using chest CT would be useful for predicting the severity of COVID-19 and the pulmonary sequelae at 3 months. Therefore, using the world's largest sample size of CT analysis data in a multicentre, long-term patient cohort, we aimed to (1) compare detailed clinical characteristics, such as the relationship between lung volume and critical outcomes and complications during hospitalisation and (2) examine the 3-month course of lung volume, clinical characteristics and predictive factors in patients with residual lung volume loss.

METHODS

Study design and settings

Data for all COVID-19 cases used for the present secondary analysis of a multicentre retrospective study were obtained by the Japan COVID-19 Task Force.[4] All patients who participated in the present study provided written or oral informed consent. The Japan COVID-19 Task Force collected clinical information on patients with COVID-19 aged >18 years who were diagnosed by PCR or antigen testing from four hospitals nationwide in Japan. Of the 1410 patients identified, 210 were excluded due to a lack of CT imaging or height data; thus, 1200 patients were included in the baseline chest CT analysis. The characteristics of the excluded cases are described in online supplemental table 1. Among all patients, there were 102 critical cases, of these, 20 cases (19.6%) were critical at the time the CT was taken and 82 cases (80.4%) subsequently became critical. Of these, 208 patients for whom CT data were available at 3 months were included in the 3-month CT analysis (online supplemental figure 1).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data collection

The following information was extracted from the electronic case record form: age, sex, height, weight, clinical signs and symptoms, laboratory findings on admission, comorbidities and treatment details. Critical outcomes were defined as the need for oxygen supplementation via high-flow oxygen therapy, mechanical ventilation, extracorporeal membrane oxygenation or death.[2] The follow-up period for the outcomes was throughout the hospitalisation period. All laboratory tests were performed according to the clinical care needs of the patients. Symptoms and signs were not only considered at the time of referral and admission but also throughout the hospitalisation period. Laboratory results were collected within 48 hours of the initial visit or admission. The attending physicians at each facility reviewed and evaluated the chest CT images for qualitative pneumonia.[25] A team of respiratory clinicians reviewed the data. If core data were missing, the clinician was contacted for data collection. Missing or absent data on patient background were noted as unknown.

CT acquisition

All CT images were obtained after full inspiration. Images of the entire lung, with a slice thickness of 1–5 mm, were reconstructed using standard kernels. The CT scanners used were the SOMATOM series (Siemens Healthineers), Aquilion series (Canon Medical Systems), Revolution series (GE Healthcare), Discovery series (GE Healthcare) and BrightSpeed (GE Healthcare). All CT images were taken within 48 hours of admission.

AI-based image analysis

Segmentation of pneumonia and the total lung capacity on CT (TLC_{ct}) were calculated on full-inspiratory CT using a SYNAPSE VINCENT volume analyzer (Fujifilm Medical, Tokyo, Japan),[25] and the predicted TLC_{ct}% was calculated based on the predicted values.[26] Representative images of the TLC_{ct} are shown in online supplemental figure 2.

Statistical analysis

Data are presented as the mean±SE. Data were compared among groups using a t-test and χ^2 test. Receiver operating characteristic (ROC) curve analysis was performed to determine the appropriate TLC_{ct}% predicted cut-off values for various outcomes: critical, oxygen requirement, invasive mechanical ventilation (IMV) requirement and mortality. To evaluate the relationship between TLC_{ct} and each outcome, we performed a logistic regression analysis as a multivariate analysis adjusted for known severity

risk factors: age, sex, body mass index (BMI), hypertension, diabetes mellitus, cardiovascular disease, hyperuricaemia, COPD and chronic kidney disease.[27–29 30] Statistical significance was set at p<0.05. Data were analysed using JMP V.16 software (SAS Institute).

RESULTS

Comparison of clinical characteristics between high and low TLC_{ct} groups

The distribution of the TLC_{ct} (%pred) on admission is shown in online supplemental figure 3. Patients were divided into two groups according to the median value, with the top 1/2 defined as high TLC_{ct} (%pred) (≧67.1%, n=600) and the bottom 1/2 as low TLC_{ct} (%pred) (<67.1%, n=600). A comparison of the clinical characteristics between the two groups is shown in online supplemental table 2. The low TLC_{ct} (%pred) group exhibited a higher proportion of men, a higher BMI, a higher incidence of hypertension and chronic kidney disease, and a lower incidence of asthma than the high TLC_{ct} (%pred) group. The low TLC_{ct} (%pred) group exhibited a higher frequency of lower respiratory symptoms, a lower frequency of upper respiratory symptoms, tachycardia, hyperthermia, tachypnoea and lower SpO_2 than the high TLC_{ct} (%pred) group (online supplemental table 3). In the low TLC_{ct} (%pred) group, leucocyte, aspartate aminotransferase, alanine transaminase, blood urea nitrogen, lactate dehydrogenase (LDH), ferritin, KL-6, HbA1c, D-dimer, procalcitonin and C reactive protein (CRP) levels were higher and lymphocyte and albumin levels were lower than those in the high TLC_{ct} (%pred) group (online supplemental table 4).

Critical cases exhibited a lower TLCct(%pred) than non-critical cases. (51.4% vs 67.7%, p<0.0001) (figure 1A). ROC curves showed that the optimal cut-off for TLC_{ct} for predicting critical outcomes was 51.1 (area under the curve, AUC 0.77, sensitivity 53.9%, specificity 85.8%) (figure 1B). Multivariable analysis adjusted for known poor prognostic factors showed that TLC_{ct} was independently associated with critical outcomes. Also, unadjusted univariate analysis for each variable is shown in online supplemental figure 4. In addition, TLC_{ct} predicted oxygen and IMV requirements (online supplemental figures 5 and 6). Also, lung volume was lower in critical cases, both with and without qualitative pneumonia. Multivariable analysis adjusted for AI-based

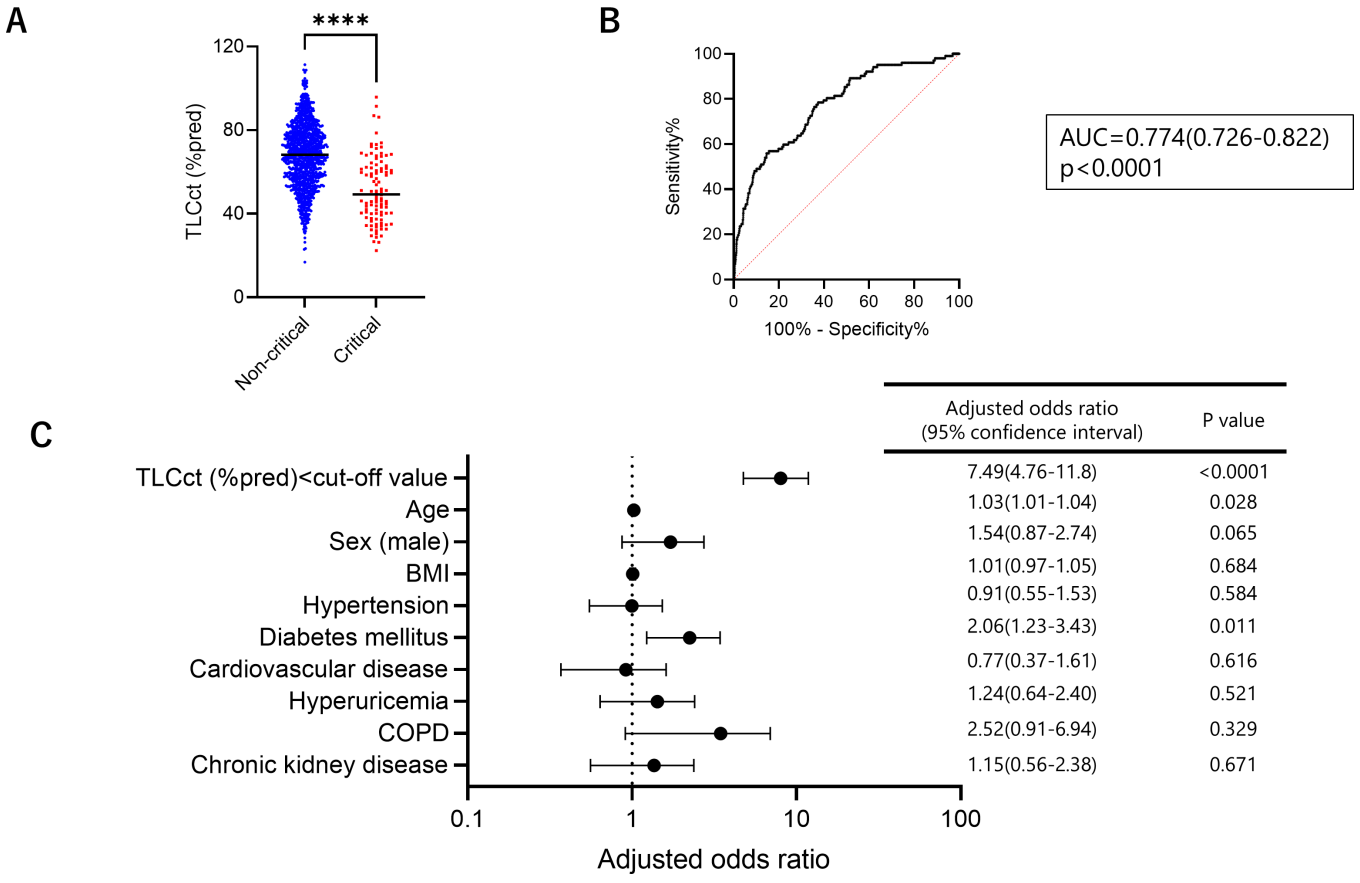

Figure 1 Relationship between critical outcomes and TLC_{ct} (%pred). (A) Comparison of TLC_{ct} (%pred) according to disease severity. (B) ROC curve of TLC_{ct} (%pred) in predicting critical outcomes. (C) Forest plot showing multivariate logistic regression analysis to evaluate the relationship between each variable and critical outcome. ****p<0.0001. AUC, area under the curve; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ROC, receiver operating characteristic; TLCct (%pred): total lung capacity on CT (%predicted).

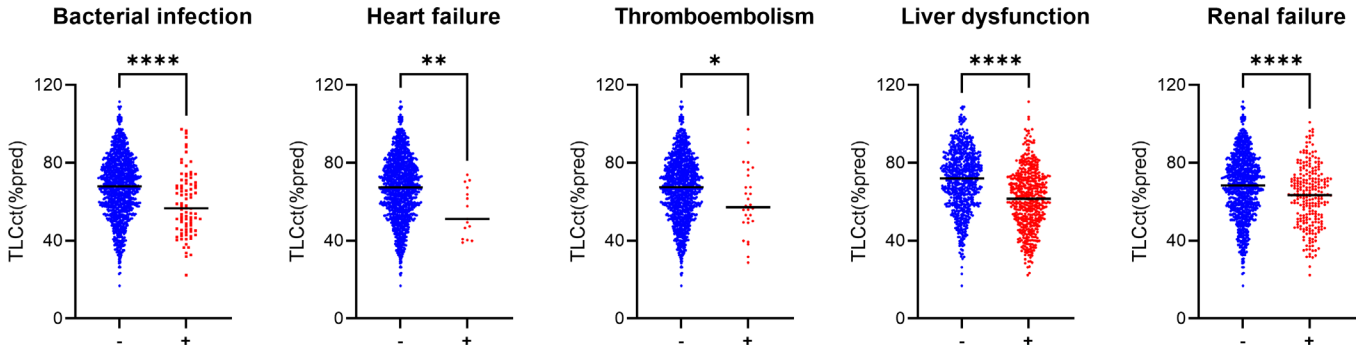

Figure 2 Comparison of the incidence of posthospitalisation complications between high and low TLC_{ct} (%pred) groups. Patients were divided into two groups according to the median TLCct value (%pred). *p<0.05, **p<0.01, ****p<0.0001. TLCct (%pred), total lung capacity on CT (%predicted).

pneumonia volume or the presence of qualitative pneumonia showed an independent association between TLC_{ct} and critical outcomes (online supplemental figure 7). Compared with the CURB-65, an existing severity prediction score, the AUC in the ROC curve was higher in TLCct(%pred) (online supplemental figure 8). Then we performed the following sensitivity analyses. In multivariable analysis including the variables found to differ at baseline characteristics (online supplemental table 2), and it was shown that TLC independently predicted critical outcomes. In addition, we excluded cases that were critical at the time the CT was taken and analysed the association between TLCct (%pred) and critical outcomes. TLCct (%pred) was significantly lower in critical cases, and TLCct (%pred) still independently predicted critical outcomes in multivariable analysis including known severity risk factors (online supplemental figure 9).

Association between complications during hospitalisation and TLCct(%pred)

Comparisons of the TLCct(%pred) with and without complications during hospitalisation are shown in figure 2. The cases with bacterial infection exhibited lower TLC_{ct} (%pred) than cases without bacterial infection (58.81% vs 67.42%, p<0.0001). The same applies to cases with and without heart failure (54.68% vs 66.88%, p=0.0037), thromboembolism (59.62% vs 66.97%, p=0.0174), liver dysfunction (61.25% vs 70.84%, p<0.0001) and renal dysfunction (62.66% vs 67.78%, p<0.0001).

Association between the clinical outcomes and TLCct(%pred), stratified epidemic waves

The epidemic waves were categorised around the prevalent virus variants as the 1st–3rd wave (conventional variant), 4th wave (alpha variant), 5th wave (delta variant) and 6th–7th wave (omicron variant).[31] The critical cases exhibited a lower TLCct(%pred) than non-critical cases for all epidemic waves (1st–3rd waves, 69.39% vs 54.78%, p<0.0001; 4th wave, 69.43% vs 53.03%, p<0.0001; 5th wave, 60.66% vs 47.49%, p<0.0001; and 6th–7th waves, 58.48% vs 47.92%, p=0.0024) (figure 3).

Comparison of clinical characteristics between high and low TLC_{ct} groups at 3 months

The distribution of TLC_{ct} (%pred) at 3 months is shown in online supplemental figure 10. The patients were divided into two groups at the median (71.8%) and then

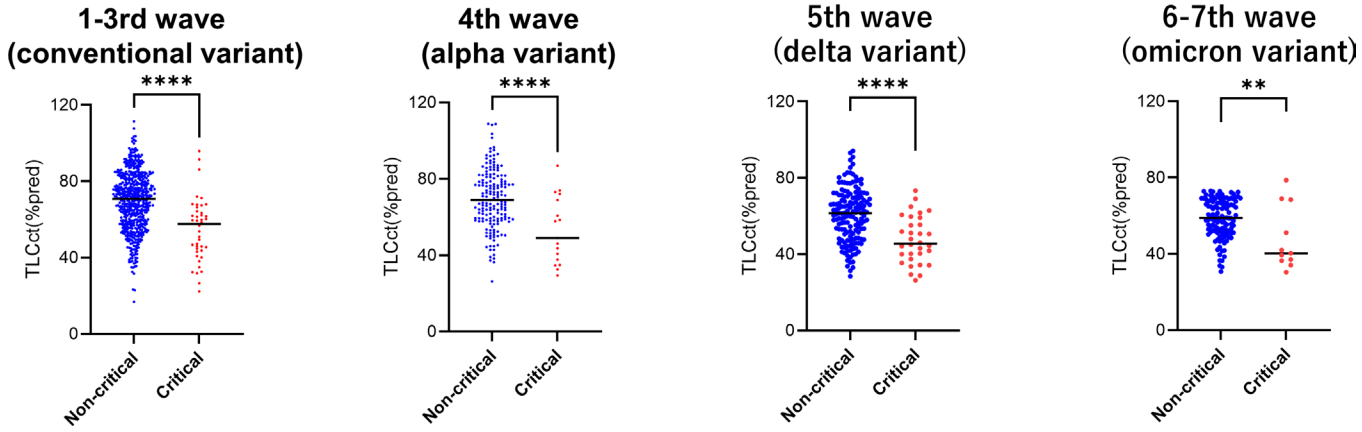

Figure 3 Relationship between critical outcome and TLC_{ct} (%pred) adjusted for epidemic waves in Japan. Patients were divided into two groups according to the median TLCct value (%pred). **p<0.01, ****p<0.0001. TLCct (%pred), total lung capacity on CT (%predicted).

Table 1 Comparison between clinical outcomes of high and low TLC_{CT} groups, as per 3-month CT analysis

	All (n=208)	High TLC_{CT} (%pred) (n=104)	Low TLC_{CT} (%pred) (n=104)	P value
Outcome				
Critical, n (%)	28 (13.3)	7 (6.7)	21 (19.8)	0.0075
Supplementary oxygen, n (%)	119 (56.4)	50 (47.6)	69 (65.1)	0.0125
Mechanical ventilation, n (%)	13 (6.2)	1 (1)	12 (11.3)	0.0026
Mortality, n (%)	1 (0.5)	1 (1)	0 (0)	0.314
Complications				
Bacterial infection, n (%)	25 (12)	7 (6.7)	18 (17.1)	0.0315
Heart failure, n (%)	2 (1)	0 (0)	2 (1.9)	0.159
Thromboembolism, n (%)	10 (4.8)	6 (5.9)	4 (3.8)	0.487
Liver dysfunction, n (%)	126 (60.9)	57 (55.3)	69 (66.4)	0.118
Renal failure, n (%)	48 (23.1)	21 (20.4)	27 (25.7)	0.362

Data are presented as n (%).
TLC_{CT}, total lung capacity on CT.

compared in terms of baseline clinical characteristics (online supplemental table 5). During the 3-month CT analysis, the low TLC_{ct} (%pred) group exhibited a higher proportion of men and a higher incidence of hypertension, chronic kidney disease, diabetes mellitus and hyperuricaemia. After admission, the low TLC_{ct} (%pred) group in the 3-month CT analysis exhibited a higher incidence of critical outcomes, oxygen requirement, IMV requirement and bacterial infection (table 1). The longitudinal changes in TLC_{ct} (%pred) stratified by patients with and without critical outcomes are shown in figure 4. Overall, lung volumes showed a recovery trend from the time of admission to 3 months, but they were still lower in critical cases at 3 months (p<0.0001). When restricting the analysis to cases with a 3-month follow-up, 73.6% of those with low lung volumes on admission maintained this classification after 3 months (online supplemental figure 11). In addition, there was a trend towards more severe cases in the group with a larger absolute value of change than those with a lower value of change (online supplemental table 6).

DISCUSSION

To the best of our knowledge, this is the largest study to demonstrate the utility of lung volume measurement using chest CT in COVID-19 patients, and it is also the first to investigate the clinical characteristics of patients with decreased lung volumes after the acute phase. This study demonstrated that CT-derived lung volume can predict critical outcomes and complications during hospitalisation. Additionally, the longitudinal analysis revealed a higher incidence of decreased lung volume at 3 months in patients with critical outcomes. These findings revealed that CT-derived lung volume measurement holds significant value as an easily assessable indicator for predicting the severity of COVID-19. Furthermore, this tool identifies populations at risk of COVID-19 sequelae by evaluating residual lung volume reduction.

In this study, CT-derived lung volume on admission was associated with multiple outcomes, such as critical outcome, oxygen requirement, IMV requirement and death. It was associated with critical outcomes independently of AI-based pneumonia and pneumonia

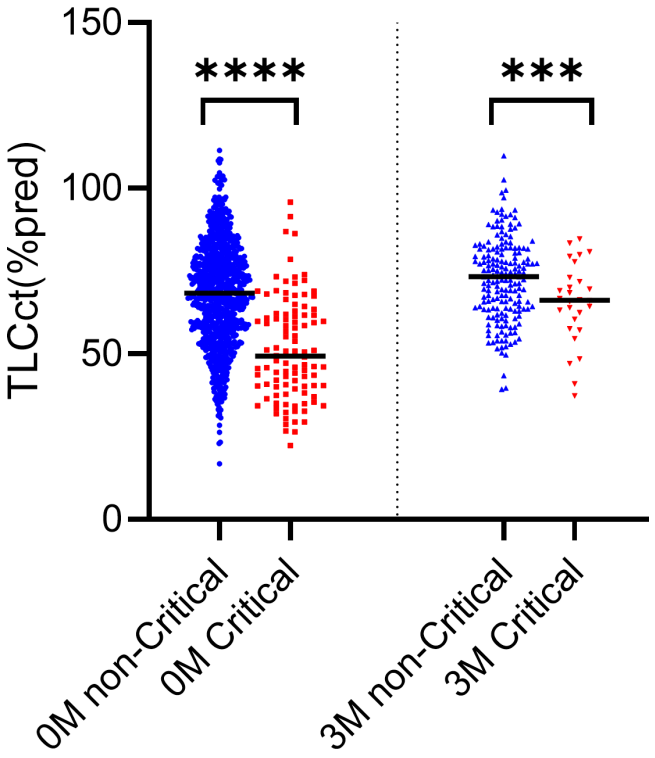

Figure 4 Comparison of TLC_{ct} (%pred) at 3 months. Longitudinal changes in TLC_{ct} (%pred) stratified by patients with and without critical outcomes. ***p<0.001, ****p<0.0001. TLCct (%pred), total lung capacity on CT (%predicted).

qualitative assessment, suggesting that diminished lung volume itself may correlate with the severity of the illness. Qualitative evaluation of lung shadows by radiologists using chest CT can predict infection severity in the early stages of an outbreak.[32] However, variability in evaluations among radiologists is problematic.[33] An advantage of automated lung volume measurement is its robust quantitative evaluation compared with qualitative evaluation by a radiologist. The strength of this study is that we demonstrated an association between CT-derived lung volume and outcomes in a large sample size and a multicentre long-term patient cohort. A previous report[17] examined the association between lung volume and disease severity in COVID-19 but found no association with outcomes. This discrepancy may be partly attributed to substantial differences in sample sizes between the two studies. The large number of patients in this study also allowed for multivariate analysis, thereby demonstrating that CT-derived lung volume predicted the outcomes after adjusting for known risk factors. In routine clinical practice, it is difficult to perform CT imaging under the same conditions, particularly during pandemics. Although this study included multiple CT scanner models and imaging conditions, the results were clinically meaningful for predicting disease severity. SARS-CoV-2 has caused multiple epidemics worldwide.[31] The clinical characteristics of patients vary across different periods owing to various factors, including advances in therapeutic agents, vaccines and viral variants. This study is the first to demonstrate the utility of CT-derived lung volume measurements for predicting severe disease, regardless of epidemic waves. These findings have significant clinical implications for future pandemics.

Owing to concerns regarding transmission, COVID-19 complicates the assessment of pulmonary function in the acute phase.[34] Previous reports showed that CT-derived lung volume strongly correlated with the pulmonary function test results.[8 9] Therefore, CT-derived lung volume could serve as a surrogate marker for the physiological assessment of COVID-19 in the acute phase. In this study, patients with decreased lung volume exhibited a higher incidence of multiorgan complications. Severe COVID-19 is associated with various posthospitalisation complications and poor outcomes.[35] Our study demonstrated that lung volume measurements can predict these complications and enable early intervention.

The decreased lung volume in COVID-19 may be caused by several factors: (1) virus-induced damage to the type II alveolar epithelium, resulting in a reduction in surfactants that maintain alveolar expansion; (2) increased vascular permeability triggered by inflammatory cytokines, leading to alveolar collapse due to effusion and (3) inflammatory microvascular thrombi inducing capillary vasospasm in the alveolar space, resulting in augmented dead-space ventilation and subsequent alveolar collapse.[16] In this study, the low TLC_{ct} (%pred) group exhibited elevated levels of markers suggestive of alveolar epithelial damage (LDH and KL-6), other inflammatory markers (CRP and procalcitonin) and coagulation system markers (D-dimer), which aligns with the proposed mechanism. Additionally, we revealed that the low TLC_{ct} (%pred) group exhibited clinical characteristics such as male sex, high BMI, hypertension and chronic kidney disease. These results are consistent with previous reports showing that these factors predict COVID-19 severity.[36–39]

COVID-19 is widely known to cause sequelae after the acute phase and is termed long COVID.[40] Chest CT is a useful tool for evaluating structural sequelae of the lungs, and a qualitative evaluation by a radiologist revealed that 84% of patients exhibited residual lung shadows at 3 months.[23] Additionally, these residual lesions correlate with pulmonary sequelae, worse pulmonary function and decreased exercise tolerability.[23 41] This study revealed that the lung volumes of almost all patients recovered gradually from 0 to 3 months but were still lower in critical cases at 3 months. These results are consistent with a previous report showing that qualitative lung shadows improve over time[21] and that severely ill patients are more likely to have residual qualitative lung shadows.[22] Consequently, clinicians should be aware of a residual reduction in lung volume, especially in critically ill patients.

Our study has several limitations. First, the number of CT follow-up cases after 3 months was small owing to dropouts. In this study, we performed CT analyses after a 3-month interval based on the findings of a previous study, which showed that a 3-month period was optimal for evaluating residual shadows.[42] Another study found that residual shadows at 3 months were correlated with physiological sequelae and dyspnoea.[22–24] Notably, mild cases frequently interrupt hospital visits, resulting in potential bias. Second, the lung volume measurements were affected by the extent of inspiration. Total lung capacity is affected by sex and body size, and to redress these influences, the predicted TLC_{ct}% was calculated based on the predicted values. Nevertheless, in instances characterised by deficient inspiration attributable to hypoxia or other physiological symptoms, the total lung capacity may be underestimated, particularly in severe cases. Although the usefulness of respiratory-synchronised CT has been reported,[43] we were unable to study it because COVID-19 is an emergency disease and many patients are admitted to the emergency department for CT during emergency admission. Third, lung volume measurements were affected by pre-existing lung diseases. Although reduced lung volume has been reported in pulmonary diseases such as ILD, COPD and asthma, the present study collected patient history only through interviews, the and we did not make a diagnosis based on imaging or pulmonary function test results of potential background diseases. Consequently, the impact of these background conditions could not be entirely ruled out and might have influenced the results.

In conclusion, low CT-derived lung volume at admission is associated with poor clinical outcomes and posthospitalisation complications in COVID-19 patients. CT-derived lung volumes recovered gradually over 3

months but were still lower in critical cases at 3 months. Future studies are warranted to investigate these effects in patients with decreased lung volume over time.

Author affiliations
[1]ivision of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Tokyo, Japan
[2]Department of Respiratory Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan
[3]Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Tokyo, Japan
[4]Department of Respiratory Medicine, National Hospital Organization Tokyo Medical Centre, Tokyo, Japan
[5]Department of Internal Medicine, Saitama Medical Center, Tokyo, Japan
[6]Division of Respiratory Medicine, Juntendo University School of Medicine Graduate School of Medicine, Bunkyo-ku, Japan
[7]Department of Pulmonary Medicine, Saitama City Hospital, Saitama, Japan
[8]Keio University Department of Radiology, Shinjuku-ku, Tokyo, Japan
[9]Respiratory Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan
[10]Department of Statistical Genetics, Osaka University Graduate School of Medicine, Suita, Japan
[11]Department of Genome Informatics, The University of Tokyo Graduate School of Medicine Faculty of Medicine, Bunkyo-ku, Japan
[12]Department of Pharmacovigilance, Tokyo Medical and Dental University, Tokyo, Japan
[13]Faculty of Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan
[14]Center for Infectious Diseases and Infection Control, Keio University, School of Medicine, Tokyo, Japan
[15]Medical Research Institute, Tokyo Medical and Dental University, Tokyo, Japan
[16]The University of Tokyo, Bunkyo-ku, Japan
[17]Tokyo Medical and Dental University, Bunkyo-ku, Japan
[18]Department of Pathology and Tumor Biology, Kyoto University Graduate School of Medicine Faculty of Medicine, Kyoto, Japan
[19]Department of Medicine, Regenerative Medicine Karolinska Institute, Stockholm, Sweden
[20]Division of Gastroenterology and Hepatology Department of Internal Medicine, Keio University School of Medicine, Shinjuku-ku, Japan

Contributors Guarantor: SC. Conceptualisation: SOtake, YS, SC, NT, TM and YY. Data curation: SOtake, YS, SC, HN, TS, SA, KN, HTanaka, TF, MW and HTerai. Formal analysis: SOtake, YS, SC, NT, TM and TA. Methodology: SOtake, YS, SC, NT, YS, TM, TA, HN and YY. Project administration: SC and NT. Resource: SOtake, SC, HN, TS, SA, KN, HTanaka, TF, MW, HTerai, MS, SU, YK, NH, SS, SY, HTateno and KF. Software: YS, NT, TM and YY. Supervision: SC, NT, HN, YY, MJ, TH, YO, RK, MI, NH, AK, SI, SM, SOgawa, TK and KF. Visualisation: HTateno, TM, SC, NT and TA. Writing–original draft: HTerai, TM, SC, NT, YS and YY. Writing–review and editing: TA, HN, HTanaka, MS, SU, YK, NH, SS, SY, HTateno, MJ, TH, YO, RK, MI, NH, AK, SI, SM, SOgawa, TK and KF. All the authors have read and approved the final manuscript.

Funding This study was supported by the Japan Agency for Medical Research and Development (AMED) (grant numbers JP20nk0101612, JP20fk0108415, JP21jk0210034, JP21km0405211, JP21km0405217, JP21wm0325031, JP21fk0108563, JP21fk0108573, JP20fk0108452, JP21fk0108553, JP21fk0108431, JP22fk0108510, JP22fk0108513, JP22wm0325031, JP22fk0108573, JP23tm0524008), Japan Science and Technology Agency (JST) CREST (grant number JPMJCR20H2], Japan Science and Technology Agency (JST) PRESTO [grant number JPMJPR21R7], and the Ministry of Health, Labour and Welfare (grant number 20CA2054).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the ethics committee of the Keio University School of Medicine (20200061) and related research institutions. All the participants provided informed consent. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The datasets used and/or analysed in the current study are available from the corresponding author on reasonable request.

ORCID iDs
Shotaro Chubachi http://orcid.org/0000-0002-5046-3762
Naoya Tanabe http://orcid.org/0000-0002-7481-0212
Norihiro Harada http://orcid.org/0000-0002-0962-5731

REFERENCES

1 Zheng C, Shao W, Chen X, *et al*. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. *Int J Infect Dis* 2022;114:252–60.
2 Beigel JH, Tomashek KM, Dodd LE, *et al*. Remdesivir for the treatment of covid-19 — final report. *N Engl J Med* 2020;383:1813–26.
3 El Sahly HM, Baden LR, Essink B, *et al*. Efficacy of the mRNA-1273 SARS-Cov-2 vaccine at completion of blinded phase. *N Engl J Med* 2021;385:1774–85.
4 Tanaka H, Lee H, Morita A, *et al*. Clinical characteristics of patients with Coronavirus disease (COVID-19): preliminary baseline report of Japan COVID-19 task force, a nationwide consortium to investigate host Genetics of COVID-19. *Int J Infect Dis* 2021;113:74–81.
5 Fernandes Q, Inchakalody VP, Merhi M, *et al*. Emerging COVID-19 variants and their impact on SARS-Cov-2 diagnosis, Therapeutics and vaccines. *Ann Med* 2022;54:524–40.
6 Zhang K, Liu X, Shen J, *et al*. Clinically applicable AI system for accurate diagnosis, quantitative measurements, and prognosis of COVID-19 pneumonia using computed tomography. *Cell* 2020;181:1423–33.
7 Francone M, Iafrate F, Masci GM, *et al*. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *Eur Radiol* 2020;30:6808–17.
8 Chubachi S, Okamori S, Yamada Y, *et al*. Differences in lung and lobe volumes between supine and upright computed tomography in patients with idiopathic lung fibrosis. *Sci Rep* 2022;12:19408.
9 Bakker JT, Klooster K, Vliegenthart R, *et al*. Measuring pulmonary function in COPD using quantitative chest computed tomography analysis. *Eur Respir Rev* 2021;30:210031.
10 Delgado BJ, Bajaj T. Physiology, Lung Capacity. Treasure Island, FL: StatPearls Publishing LLC, 2024.
11 Tantucci C, Bottone D, Borghesi A, *et al*. Methods for measuring lung volumes: is there a better one *Respiration* 2016;91:273–80.
12 Robbie H, Wells AU, Fang C, *et al*. Serial decline in lung volume parameters on computed tomography (CT) predicts outcome in idiopathic pulmonary fibrosis (IPF). *Eur Radiol* 2022;32:2650–60.
13 Si-Mohamed SA, Nasser M, Colevray M, *et al*. Automatic quantitative computed tomography measurement of longitudinal lung volume loss in interstitial lung diseases. *Eur Radiol* 2022;32:4292–303.
14 Batah SS, Fabro AT. Pulmonary pathology of ARDS in COVID-19: A pathological review for Clinicians. *Respir Med* 2021;176:S0954-6111(20)30379-6.
15 Ojo AS, Balogun SA, Williams OT, *et al*. Pulmonary fibrosis in COVID-19 survivors: predictive factors and risk reduction strategies. *Pulm Med* 2020;2020:6175964.
16 Savaş R, Öz Özcan A. Evaluation of lung volume loss with 3d CT Volumetry in COVID-19 patients. *Diagn Interv Radiol* 2021;27:155–6.
17 Ippolito D, Ragusi M, Gandola D, *et al*. Computed tomography semi-automated lung volume Quantification in SARS-Cov-2-related pneumonia. *Eur Radiol* 2021;31:2726–36.

18 Timaran-Montenegro DE, Torres-Ramírez CA, Morales-Jaramillo LM, *et al*. Computed tomography-based lung residual volume and mortality of patients with Coronavirus Disease-19 (COVID-19). *J Thorac Imaging* 2021;36:65–72.
19 Chen Q, Chen L, Liu S, *et al*. n.d. Three-dimensional CT for Quantification of longitudinal lung and pneumonia variations in COVID-19 patients. *Front Med*8:643917.
20 Desai AD, Lavelle M, Boursiquot BC, *et al*. Long-term complications of COVID-19. *Am J Physiol Cell Physiol* 2022;322:C1–11.
21 Bocchino M, Lieto R, Romano F, *et al*. Chest CT-based assessment of 1-year outcomes after moderate COVID-19 pneumonia. *Radiology* 2022;305:479–85.
22 Wu X, Liu X, Zhou Y, *et al*. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related Hospitalisation: a prospective study. *Lancet Respir Med* 2021;9:747–54.
23 González J, Benítez ID, Carmona P, *et al*. Pulmonary function and Radiologic features in survivors of critical COVID-19: A 3-month prospective cohort. *Chest* 2021;160:187–98.
24 Balbi M, Conti C, Imeri G, *et al*. Post-discharge chest CT findings and pulmonary function tests in severe COVID-19 patients. *Eur J Radiol* 2021;138:S0720-048X(21)00156-X.
25 Tanaka H, Maetani T, Chubachi S, *et al*. Clinical utilization of artificial intelligence-based COVID-19 pneumonia Quantification using chest computed tomography - a multicenter retrospective cohort study in Japan. *Respir Res* 2023;24:241.
26 Quanjer PH, Tammeling GJ, Cotes JE, *et al*. Lung volumes and forced ventilatory flows. report working party standardization of lung function tests, European Community for steel and coal, official statement of the European respiratory society. *Eur Respir J* 1993;16:5–40.
27 Docherty AB, Harrison EM, Green CA, *et al*. Features of 20 133 UK patients in hospital with COVID-19 using the ISARIC WHO clinical Characterisation protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.
28 Deng G, Yin M, Chen X, *et al*. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care* 2020;24:179.
29 Harrison SL, Buckley BJR, Rivera-Caravaca JM, *et al*. Cardiovascular risk factors, cardiovascular disease, and COVID-19: an umbrella review of systematic reviews. *Eur Heart J Qual Care Clin Outcomes* 2021;7:330–9.
30 Fukushima T, Chubachi S, Namkoong H, *et al*. U-shaped association between abnormal serum uric acid levels and COVID-19 severity: reports from the Japan COVID-19 task force. *Int J Infect Dis* 2022;122:747–54.
31 Lee H, Chubachi S, Namkoong H, *et al*. Characteristics of hospitalized patients with COVID-19 during the first to fifth waves of infection: a report from the Japan COVID-19 task force. *BMC Infect Dis* 2022;22:935.
32 Elmokadem AH, Mounir AM, Ramadan ZA, *et al*. Comparison of chest CT severity scoring systems for COVID-19. *Eur Radiol* 2022;32:3501–12.
33 Bai HX, Hsieh B, Xiong Z, *et al*. Performance of Radiologists in differentiating COVID-19 from non-COVID-19 viral pneumonia at chest CT. *Radiology* 2020;296:E46–54.
34 Kouri A, Gupta S, Yadollahi A, *et al*. Addressing reduced laboratory-based pulmonary function testing during a pandemic. *Chest* 2020;158:2502–10.
35 Figliozzi S, Masci PG, Ahmadi N, *et al*. Predictors of adverse prognosis in COVID-19: A systematic review and meta-analysis. *Eur J Clin Invest* 2020;50:e13362.
36 Bienvenu LA, Noonan J, Wang X, *et al*. Higher mortality of COVID-19 in males: sex differences in immune response and cardiovascular Comorbidities. *Cardiovasc Res* 2020;116:2197–206.
37 Lee H, Chubachi S, Namkoong H, *et al*. Effects of mild obesity on outcomes in Japanese patients with COVID-19: a nationwide consortium to investigate COVID-19 host Genetics. *Nutr Diabetes* 2022;12:38.
38 Mahamat-Saleh Y, Fiolet T, Rebeaud ME, *et al*. Diabetes, hypertension, body mass index, smoking and COVID-19-related mortality: a systematic review and meta-analysis of observational studies. *BMJ Open* 2021;11:e052777.
39 Chung EYM, Palmer SC, Natale P, *et al*. Incidence and outcomes of COVID-19 in people with CKD: A systematic review and meta-analysis. *Am J Kidney Dis* 2021;78:804–15.
40 Akbarialiabad H, Taghrir MH, Abdollahi A, *et al*. Long COVID, a comprehensive systematic Scoping review. *Infection* 2021;49:1163–86.
41 Camiciottoli G, Bartolucci M, Maluccio NM, *et al*. Spirometrically Gated high-resolution CT findings in COPD: lung Attenuation vs lung function and Dyspnea severity. *Chest* 2006;129:558–64.
42 Zhao Y, Wang D, Mei N, *et al*. n.d. Longitudinal radiological findings in patients with COVID-19 with different Severities: from onset to long-term follow-up after discharge. *Front Med*8:8.
43 Rodríguez-Romero R, Castro-Tejero P. The influence of respiratory motion on CT image volume definition. *Med Phys* 2014;41:041701.