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Early View

Original article

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Tøri Vigeland Lerum, Trond Mogens Aaløkken, Eivind Brønstad, Bernt Aarli, Eirik Ikdahl, Kristine Marie Aarberg Lund, Michael T. Durheim, Jezabel Rivero Rodriguez, Carin Meltzer, Kristian Tonby, Knut Stavem, Ole Henning Skjønsberg, Haseem Ashraf, Gunnar Einvik

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Dyspnoea, lung function and CT findings three months after hospital admission for COVID-19

Lerum Tøri Vigeland[1], Aaløkken Trond Mogens[2,3], Brønstad Eivind[4,5], Aarli Bernt[6,7], Ikdahl Eirik[8], Lund Kristine Marie Aarberg[9], Durheim Michael T.[3,10], Rodriguez Jezabel Rivero[2], Meltzer Carin[2], Tonby Kristian[3,11], Stavem Knut[3,8,12], Skjønsberg Ole Henning[1,3], Ashraf Haseem[3,13*], Einvik Gunnar[3,8*]

[1] Department of Pulmonary Medicine, Oslo University Hospital Ullevål, Oslo, Norway

[2] Department of Radiology and Nuclear Medicine, Oslo University Hospital Ullevål, Oslo, Norway

[3] Institute for Clinical Medicine, University of Oslo, Oslo, Norway

[4] Thoracic Department, St. Olavs Hospital, Trondheim, Norway

[5] Department of Circulation and Medical Imaging, Faculty of Medicine and Health Sciences NTNU, Trondheim, Norway

[6] Department of Thoracic Medicine, Haukeland University Hospital, Haukeland, Norway

[7] Department of Clinical Science, University of Bergen, Bergen, Norway

[8] Pulmonary Department, Akershus University Hospital, Lørenskog, Norway

[9] Department of Infectious Diseases, Østfold Hospital Trust Kalnes, Grålum, Norway

[10] Department of Respiratory Medicine, Oslo University Hospital Rikshospitalet, Oslo, Norway

[11] Department of Infectious Diseases, Oslo University Hospital Ullevål, Oslo, Norway

[12] Health Services Research Unit, Akershus University Hospital, Lørenskog, Norway

[13] Department of Diagnostic Imaging, Akershus University Hospital, Lørenskog, Norway

*shared last authors

Corresponding author

Gunnar Einvik, Pulmonary Department, Akershus University Hospital, 1470 Lørenskog, Norway. E-mail gunnar.einvik@medisin.uio.no, phone +4741104542.

Take-home message

Three months after discharge, one-fourth of COVID-19 survivors have reduced gas diffusion capacity and persistent parenchymal opacities. ICU treatment is associated with persistent parenchymal opacities, but not with dyspnoea or reduced diffusion capacity.

Summary

The long-term pulmonary outcomes of coronavirus disease 2019 (COVID-19) are unknown. We aimed to describe self-reported dyspnoea, quality of life, pulmonary function, and chest CT findings three months following hospital admission for COVID-19. We hypothesized outcomes to be inferior for patients admitted to intensive care units (ICU), compared with non-ICU patients.

Discharged COVID-19-patients from six Norwegian hospitals were consecutively enrolled in a prospective cohort study. The current report describes the first 103 participants, including 15 ICU patients. Modified Medical Research Council dyspnoea scale (mMRC), EuroQol Group's Questionnaire, spirometry, diffusion capacity (DL_{CO}), six-minute walk test, pulse oximetry, and low-dose CT scan were performed three months after discharge.

mMRC was >0 in 54% and >1 in 19% of the participants. The median (25^{th}-75^{th} percentile) forced vital capacity and forced expiratory volume in one second were 94% (76, 121) and 92% (84, 106) of predicted, respectively. DL_{CO} was below the lower limit of normal in 24%. Ground-glass opacities (GGO) with >10% distribution in ≥1 of 4 pulmonary zones were present in 25%, while 19% had parenchymal bands on chest CT. ICU survivors had similar dyspnoea scores and pulmonary function as non-ICU patients, but higher prevalence of GGO (adjusted odds ratio [95% confidence interval] 4.2 [1.1, 15.6]) and performance in lower usual activities.

Three months after admission for COVID-19, one fourth of the participants had chest CT opacities and reduced diffusion capacity. Admission to ICU was associated with pathological CT findings. This was not reflected in increased dyspnoea or impaired lung function.

Key words: COVID-19, lung function, interstitial lung disease, dyspnoea

Introduction

The lower airways and lungs are the primary targets for the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The majority of patients requiring hospital admission for coronavirus disease 2019 (COVID-19) have respiratory symptoms such as cough and dyspnoea, in addition to signs of impaired lung function with varying degrees of hypoxemia [1]. These symptoms are associated with widespread ground-glass opacities (GGO) on chest computed tomography (CT) scans and chest x-rays [2, 3]. Approximately 15-30 % percent of hospital admitted COVID-19 patients develop severe respiratory failure and acute respiratory distress syndrome (ARDS), which necessitate admission to intensive care units (ICU) and possibly mechanical ventilation [1, 4, 5]. According to the World Health Organization (WHO) the fatality rate from COVID-19 is 1–10 %, depending on age and underlying comorbidities [6].

As the COVID-19 pandemic represents a new disease, the long-term pulmonary outcomes in survivors of COVID-19 are unknown. Evidence from other coronavirus pneumonias, such as SARS and Middle East Respiratory Syndrome (MERS), suggests that impaired lung function and parenchymal opacities persist only in a minority of patients not having required mechanical ventilation [7]. In patients developing ARDS, however, as many as 11-45 % have impaired lung function and persistent infiltrates on x-ray after 10–12 months [8]. In order to identify and manage potential long-term sequelae of COVID-19, more research on the natural course of the disease is warranted [9]. Early reports of survivors following hospital admission for COVID-19 show reduced diffusion capacity, total lung capacity, exercise capacity, or abnormal chest CT scan in almost 50% after 1 month [10].

In the current study, we assessed patient-reported dyspnoea, lung function, quality of life (QoL), and parenchymal opacities in chest CT scans three months after hospital admission for COVID-19 in a prospective, consecutive Norwegian cohort of patients with or without ICU treatment.

Materials and methods

Design and participants

Patient-reported outcomes and lung function after hospital admission for COVID-19 (PROLUN) is a multicentre prospective cohort study performed in six major hospitals in Norway. The study was approved by the Regional Ethics Committee for South-Eastern Norway (no. 125384), by

data protection officers at each participating centre, and registered to ClinicalTrials.gov (NCT04535154).

Patients aged above 18 years who had been admitted for >8 hours with a discharge diagnosis (International Statistical Classification of Diseases and Related Health Problems 10) of U07.1 (COVID-19, virus identified), U07.2 (COVID-19, virus unidentified) or J12.x (viral pneumonia, in combination with positive SARS-CoV-2 identification in nasopharyngeal swab) were considered for eligibility. Exclusion criteria included living outside the hospitals' catchment areas, inability to provide informed consent, or participation in the WHO trial Solidarity.

Eligible patients were invited by mail about six weeks after hospital discharge. Informed consent was obtained by return of a written signed consent form or through a secure digital consent form (Services for Sensitive Data, TSD, University of Oslo). One telephone reminder was performed for non-respondents.

In accordance with the study protocol, an interim report of the first 100 participants was planned. This number was achieved on June 24, 2020. The current study thus comprises all participants who had attended the three-month follow-up visit by June 24, 2020 (n=103).

Data collection

Participants returned to the respective hospitals' outpatient clinics for a three-month follow-up visit. The median (25^{th}-75^{th} percentile) time between the hospital admission and the three-month visit was 83 (73-90) days, 82 days (73-90) in the non-ICU, and 85 days (81-90) in the ICU-group (p=0.090). The criteria for admission to ICU were similar across centres; inability to maintain a satisfactory pulse oximetric saturation (SpO_2) through O_2-supplementation by nasal cannula or non-rebreather mask. In addition, the participants were assessed by an anaesthesiologist before transfer to ICU.

Self-reported dyspnoea: the modified Medical Research Council dyspnea scale (mMRC), range 0-4, was used [11, 12]. This measure was not administered for the first 18 participants, or at St. Olav Hospital. However, for these participants we performed additional analyses with the last value carried forward from self-reported mMRC four to six weeks prior to the visit.

QoL: the EuroQol Group's EQ-5D-5L questionnaire [13] was used to measure health-related QoL. It contains five items scored on an ordinal scale from 1 (no problems) to 5 (unable/extreme problems). This questionnaire was administered by mail or web-link four to six weeks prior to the visit. Scores were available for 88 (89%) of the participants. EQ-5D index values were prepared using the crosswalk method with UK weights [14].

Pulmonary function tests: Spirometry was conducted to measure the forced vital capacity (FVC) and the forced expiratory volume in one second (FEV_1) (Jaeger, Höechberg, Germany and CareFusion, Yorba Linda, CA, USA). The ratio of FEV_1/FVC was calculated. Diffusion capacity of the lungs for carbon monoxide (DL_{CO}) and alveolar ventilation (VA) were measured, and DL_{CO}/VA (KCO) was calculated. All procedures were executed according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines [15, 16]. The Global Lung Function Initiative Network (GLI) reference values were used to calculate the percentage of predicted values, the lower limit of normal (LLN), and z-scores [17, 18]. A six-minute walk test (6MWT) was performed according to ATS/ERS, with baseline SpO_2 measured by pulse oximetry on index fingers [19].

Chest CT: low-dose, thin-section CT images were obtained in supine and prone position, during breath-holding and deep inspiration. The same CT protocol, adjusted for the different CT-scanners employed, was used for all examinations. The tube current settings were adjusted to each patient's weight, with low dose references at 120 kVp, high pitch, and shortest possible rotation time. For evaluation of lung parenchyma, we applied thin reconstructed slice thickness (0.9–1.25mm), with a high-spatial-frequency kernel, and a softer kernel with thicker (2–3 mm) slices for mediastinal evaluation. Two experienced thoracic radiologists independently reviewed all images, blinded to the participants' clinical history. The degree of consensus was high. The presence, extent, and distribution of interstitial findings were registered using nomenclature recommended by the Fleischner Society [20]. For the purpose of the current analysis, GGO, and parenchymal bands were assessed. Findings were registered in four separate apico-basal zones of the lungs using anatomic landmarks in the mediastinum [21].

Other clinical variables: baseline demographic characteristics (sex, age, height, weight, history of smoking), body mass index (BMI), comorbidities (diabetes or hypertension), and data

from the COVID-19 hospital admissions were obtained from the electronic patient records. Clinical variables indicating the severity of COVID-19 were: use of oxygen, admission to ICU, use of mechanical ventilation, the maximal level of C-reactive protein (CRP), and D-dimer.

All collected data was stored in TSD, designed for storing and post processing sensitive data in compliance with the Norwegian "Personal Data Act" and "Health Research Act".

Statistical analyses

For continuous data, median and 25^{th}–75^{th} percentiles were reported in descriptive statistics. Group comparison was performed with Mann-Whitney U-tests or chi-square tests, as appropriate. For lung function variables the predicted value was calculated, reporting LLN and z-score.

Descriptive analyses of the cohort were considered important for this interim report. We also tested the hypothesis that participants admitted to the ICU would have more dyspnoea, lower lung function, lower QoL, and more pathological CT findings, than participants not admitted to the ICU.

The main outcome measures were (1) mMRC ≥1, (2) DL_{CO}<LLN, (3) >10% GGO in at least one lung zone, and (4) the presence of parenchymal bands. Secondary outcomes were 6MWT-distance, SpO_2, EQ-5D-5L-scores and EQ-5D index. The association between COVID-19 severity indices and main outcomes were assessed by univariate logistic regression analyses. The association between ICU admission, predefined as the major indicator of COVID-19 severity, and the main outcomes were adjusted by multivariable analysis. Due to a limited number of participants, only a few independent variables were allowed: age and sex, except for DL_{CO}<LLN, in which current/previous smoking vs. never smoking was adjusted for. All statistical analyses were performed using Stata version 16.1 (StataCorp., College Station, TX, USA). A p-level <0.05 was considered statistically significant.

Results

Demographic and clinical characteristics from the hospital admission are shown in Table 1. Several indices of COVID-19 severity were higher in participants admitted to ICU than in the non-ICU participants; length of stay, oxygen therapy, the maximum levels of CRP and D-dimer,

and the prevalence of bilateral lung densities. However, the demographic variables (sex, age, body mass index, and smoking status) were comparable between the groups. Hypertension was less commonly observed in those admitted to ICU than in non-ICU participants. The median (25^{th} to 75^{th} percentile) time from symptom onset to admission were 7 (5-9) and 9 (6-11) days in ICU and non-ICU participants, respectively (p=0.125).

Table 1. Clinical characteristics during admission for COVID-19. Median (25-75^{th} percentile) unless specified otherwise.

	Total	**ICU admission**	**No ICU admission**	**p**
	n=103	n = 15	n = 88	
Demographic data				
Male sex, n (%)	54 (52)	11 (73)	43 (49)	0.098
Age (years)	59 (49, 72)	52 (50, 59)	61 (49, 74)	0.116
Body mass index (kg/m^2)	25.8 (23.8, 29.6)	24.9 (23.7, 29.3)	25.9 (23.8, 29.1)	0.885
Current smoker, n (%)	3 (3.4)	0 (0)	3 (4)	0.216
Previous smoker, n (%)	34 (39)	3 (21)	31 (42)	
Medical comorbidity				
History of hypertension, n (%)	35 (35)	1 (7)	34 (40)	0.017
History of diabetes, n (%)	8 (8)	0 (0)	8 (9)	0.599
COVID-19 hospital admission				
Length of stay (days)	6 (3, 11)	17 (12, 25)	5 (3, 9)	<0.001
Oxygen treatment, n (%)	67 (66)	15 (100)	52 (59)	0.003
ICU admission, n (%)	15 (15)	N/A	N/A	N/A
Invasive ventilation, n (%)	9 (9)	9 (60)	N/A	N/A
Bilateral densities chest x-ray, n (%)	48 (49)	14 (93)	34 (41)	<0.001
Max level of C-reactive protein (mg/L)	120 (48, 217)	246 (189, 290)	107 (34, 175)	<0.001
Max level of D-dimer (mg/L)	1.0 (0.4, 1.9)	3.5 (1.9, 4.5)	0.8 (0.4, 1.4)	<0.001
Lowest level of lymphocytes (10^9/L)	0.9 (0.6, 1.4)	0.8 (0.6, 1.0)	1.0 (0.6, 1.5)	0.129

ICU, intensive care unit

Table 2. Pulmonary outcomes three months after hospitalization. Median (25-75th percentile) unless specified otherwise.

	N	All	ICU admission (n=15)	No ICU admission (n=88)	p
Spirometry	103				
FVC, L		3.6 (2.1, 6.0)	3.8 (3.2, 5.1)	3.6 (3.0, 4.4)	0.392
FVC, % of predicted		94 (76, 121)	92 (81, 110)	95 (87, 108)	0.730
FVC, z-score		-0.39 (-0.81, 0.37)	-0.58 (-1.34, 0.19)	-0.33 (-0.80, 0.42)	0.457
FVC<LLN, n (%)		7 (7)	2 (13)	5 (6)	0.269
FEV_1, L		2.8 (2.2, 3.3)	2.9 (2.5, 3.9)	2.7 (2.2, 3.2)	0.119
FEV_1, % of predicted		92 (84, 106)	93 (82, 112)	92 (84, 106)	0.706
FEV_1, z-score		-0.51 (-1.11, 0.32)	-0.54 (-1.2, 0.67)	-0.50 (-1.11, 0.22)	0.973
FEV_1<LLN, n (%)		11 (11)	2 (13)	9 (10)	0.661
FEV_1/FVC, %		0.77 (0.73, 0.81)	0.79 (0.76, 0.85)	0.76 (0.72, 0.81)	0.049
Gas diffusion	102				
DL_{CO}, mmol/kPa/min		6.8 (5.7, 8.8)	7.9 (5.2, 9.4)	6.7 (5.7, 8.3)	0.794
DL_{CO}, % of predicted		83 (72, 92)	83 (66, 86)	83 (72, 94)	0.278
DL_{CO}, z-score		-0.86 (-1.52, -0.06)	-0.74 (-1.04, -0.60)	-0.88 (-1.54, 0.02)	0.279
DL_{CO} <LLN, n (%)		24 (24)	4 (29)	20 (23)	0.735
DL_{CO}/VA, mmol/kPa/min/L		1.39 (1.16, 1.54)	1.34 (1.18, 1.55)	1.39 (1.16 1.53)	0.876
DL_{CO}/VA, % of predicted		95 (83, 105)	95 (94, 97)	96 (95, 98)	0.899
DL_{CO}/VA, z-score		-0.28 (-1.13, 0.39)	-0.46 (-0.90, 0.09)	-0.17 (-1.17, 0.41)	0.915
Dyspnoea, oxygen saturation and exercise capacity					
Dyspnoea, mMRC >0, n (%)	69	37 (54)	5 (42)	32 (56)	0.526

Peripheral oxygen saturation at rest, %	74	96 (95-97)	95 (94, 97)	96 (95, 98)	0.283
6-minute walking distance, m	73	580 (500, 640)	615 (441, 705)	588 (500, 640)	0.540
Chest CT	100				
Ground-glass opacities >10% in at least one zone, n (%)		25 (25)	6 (43)	19 (22)	0.108
Parenchymal bands, n (%)		19 (19)	5 (36)	14 (16)	0.134

CT, computed tomography; DL_{CO}, diffusion capacity of carbon monoxide; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; ICU, intensive care unit; LLN, lower limits of normal; mMRC, modified Medical Research Council Dyspnea Scale; VA, alveolar ventilation capacity

Table 2 presents self-reported dyspnoea, pulmonary function tests, and results of chest CT scans in the whole group, as well as according to ICU admission subgroup during the hospital stay. Dyspnoea (mMRC score>0) was reported by 37 (54%) of the respondents, while 13 (19%) reported mMRC score >1 (n=69). The prevalence of dyspnoea three months after discharge was similar between ICU and non-ICU participants (Table 2). In sensitivity analyses including additional 23 participants with mMRC scores reported a few weeks earlier, the prevalence of mMRC score >0 and mMRC score >1 were 52 (56%) and 22 (24%), respectively (n=93). For all pulmonary function tests, the majority of participants had values within the limits of normal. Approximately 10% had FVC or FEV_1 below LLN, while 24% had significantly reduced DL_{CO}. Furthermore, patients admitted to ICU during hospital admission did not have reduced lung function, six-minute walking distance, or oxygen saturation compared to those not admitted to ICU (Table 2).

GGO were common; 24% of the participants had one or more lung zones with at least 10% presence of GGO. The presence of GGO was associated with age and CRP in univariable logistic regression analysis (p=0.009 and p=0.001, respectively) (Supplementary table 1). The crude prevalence of GGO was not significantly different between ICU and non-ICU participants, however, after adjustment for age and sex, the odds of having these pathological CT findings

were significantly higher in participants admitted to ICU, compared to those not admitted to ICU (Table 3). Parenchymal bands, indicating early progression to fibrosis, were found in one of five participants. With regard to parenchymal bands, an association with CRP and ventilator treatment was observed (p=0.018 and p=0.038, respectively) (Supplementary table 1). There was no difference between participants admitted to ICU and participants not admitted to ICU (Table 3).

Table 3. Association of dyspnea, gas diffusion capacity, ground-glass opacities, or parenchymal bands, with admission to the ICU. Multivariate logistic regression analysis.

	Odds ratio (95% CI)	P
Dyspnea (mMRC>0 vs. mMRC=0, n=69)*		
Male gender	0.39 (0.14-1.08)	0.069
Age per 10 year	0.81 (0.57-1.14)	0.231
ICU admission	0.67 (0.18-2.50)	0.553
Gas diffusion capacity (DL_{CO}<LLN vs. DL_{CO} ≥LLN, n=102)*		
History of smoking	1.56 (0.61-4.03)	0.356
ICU admission	1.54 (0.42-5.61)	0.517
GGO in chest CT (>10% GGO in ≥1 zone vs. none, n=101)*		
Male gender	1.25 (0.45-3.46)	0.662
Age per 10 year	1.81 (1.21-2.72)	0.004
ICU admission	4.22 (1.14-15.6)	0.031
Parenchymal bands in chest CT (yes vs. no, n=101*		
Male gender	1.35 (0.47-3.89)	0.584
Age per year	1.19 (0.81-1.74)	0.376
ICU admission	2.99 (0.83-10.8)	0.093

*Dependent variable.

CI, confidence interval; CT, computed tomography; DL_{CO}, diffusion capacity of carbon monoxide; GGO, ground-glass opacities; ICU, intensive care unit; LLN, lower limits of normal; mMRC, modified Medical Research Council dyspnea scale.

The scores on the five EQ-5D-5L items are shown in Figure 1. Participants admitted to ICU had a higher median score on usual activities than participants admitted to regular wards only, 4 (25-75th percentile 2-4) vs 2 (1-2), respectively (p=0.014)). The median EQ-5D index scores (SD) were 0.61 (0.23) and 0.72 (0.19) for ICU and non-ICU patients, respectively (p=0.087).

Discussion

In this three-month follow-up of a prospective cohort study of patients surviving hospital admission for COVID-19, approximately half of all participants had persistent dyspnoea on exertion, and one in four had reduced diffusion capacity for carbon monoxide. Persistent GGO on CT-scans were present in one fourth of the participants, while one in five had parenchymal bands. Participants admitted to ICU during hospital admission had higher prevalence of persistent CT abnormalities and reported more problems in usual activities, but similar lung function and self-reported dyspnoea to those not admitted to ICU.

The favourable spirometry outcomes observed in this cohort were accompanied by a low prevalence of reduced peripheral oxygen levels and reduced exercise capacity, as indicated by the 6MWT. In total, our results indicate that development of chronic respiratory failure after three months is not common in survivors of COVID-19 hospital admission, including survivors of ICU admission. The degree of self-reported dyspnoea three months after hospital admission was not associated with prior ICU stay, which we used as a marker of COVID-19 severity. Dyspnoea is subjective and may be influenced by a number of other variables. The proportion of participants in our study with reduced diffusion capacity after three months was comparable to studies of SARS and MERS, and to other early reports in COVID-19 survivors [7, 10, 22, 23].

Persistent opacities in at least 10% of one or more lung parenchyma zones, as assessed by CT, were present in approximately one in four participants after three months. Compared with reports after four weeks of follow-up in another cohort [10], this finding suggests that COVID-19 related GGO may resolve without development of persistent fibrosis. However, some of these CT findings may persist and gradually develop into fibrotic changes, as reflected by the finding of parenchymal bands in one fifth of our study population [24]. In a retrospective study of COVID-19 patients eight weeks after hospital discharge, approximately 25 % showed signs of early fibrosis [22]. This is consistent with findings in our cohort. We found that age was

associated with persistent GGO in our material, which is consistent with findings regarding community-acquired pneumonia [25]. In addition, explorative analyses find the inflammatory marker CRP to be associated with both persistent GGO and parenchymal bands. Interestingly, parenchymal bands were also associated with ventilator treatment. However, it is still unknown if the persistent pathological CT findings will progress to symptomatic pulmonary fibrosis over time or if various treatments for COVID-19 may influence the long-term outcome of parenchymal opacities.

We found CT abnormalities after three months to be more common in participants admitted to ICU. Yet, there were no differences in lung function or diffusion capacity, SpO2, or 6MWT distance between these participants and participants not admitted to ICU, in spite of ICU-patients having more bilateral lung opacities on chest x-ray and higher levels of markers of systemic inflammation during hospital admission. All patient-reported outcomes were also similar between groups, except that more participants admitted to ICU reported an impaired ability to perform usual activities. If replicated in additional studies, the association between ICU-admission, persistent pathological CT opacities, and lower performance of usual activities may indicate that patients admitted to ICU warrant closer clinical follow-up than other patients admitted to hospital for COVID-19.

A strength of the study is the multicentre prospective design, where all survivors from hospitals covering a catchment area of 1.8 million residents were assessed for eligibility. The age and prevalence of ICU admission were similar between our sample and metadata from the Norwegian COVID-19 statistics (https://www.fhi.no/sv/smittsomme-sykdommer/corona). Yet, we cannot exclude participation bias. Participation in the WHO Solidarity trial was an exclusion criterion, but the hospitals in the current study started inclusion in Solidarity only towards the end of the inclusion period of the current study. Overall, we believe the study cohort to be representative for survivors of COVID-19 hospital admission in Norway. Finally, due to the limited sample size, the current study was not powered to explore associations between possible pathophysiological mechanisms and persistent dyspnoea, reduced diffusion capacity, or parenchymal opacities.

Conclusion

In our Norwegian cohort, approximately half of all participants reported dyspnoea on exertion three months after hospital admission for COVID-19. The majority of participants had lung volumes within the reference limits, while one fourth had reduced diffusion capacity. CT scans showed that one in four had persistent ground-glass opacities, and one in five had parenchymal bands. ICU admission was associated with persistent CT-abnormalities and reduced ability to perform usual activities, but not with dyspnoea, impaired lung function or reduced functional capacity, three months after discharge from the hospital.

Declaration of interests

TVL, TMA, EB, BA, EI, KMA, JRR, CM, KT, KS, and OHS report no conflict of interests. MTD has received research grants and consulting fees from Boehringer Ingelheim, and consulting fees from Roche and AstraZeneca, all unrelated to the current study. GE has received research grants from AstraZeneca. HA and GE have received research grants from Boehringer Ingelheim to perform the current study.

Contribution by authors

GE conceived the study. The protocol was designed by TMA, EB, EI, MTD, KS, OHS, HA, and GE in collaboration. Patient inclusion and data collection were performed by TVL, EB, BA, KMAL, KT, KS, OHS, and GE. TMA, JRR, CM, and HA interpreted and analysed the CT-findings. Statistical analyses were done and analysed by TVL, KS, and GE. The first draft of the manuscript was written by TVL, OHS, KS, and GE. All authors contributed with considerable critical review of the manuscript and approval of the final version.

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Data sharing and supplementary material

The full protocol has been published on www.clinicaltrials.gov (NCT04535154). An anonymized data file will be shared through the website of the journal upon publication. The

statement of the authors to each item on the STROBE checklist is available as supplementary material.

Legend

Figure 1. Distribution of EQ-5D-5L dimension scores for ICU (n=13) and non-ICU patients (n=75).
1=No problems, 2=Slight problems, 3=Moderate problems, 4=Severe problems, 5=Unable/Extreme problems.

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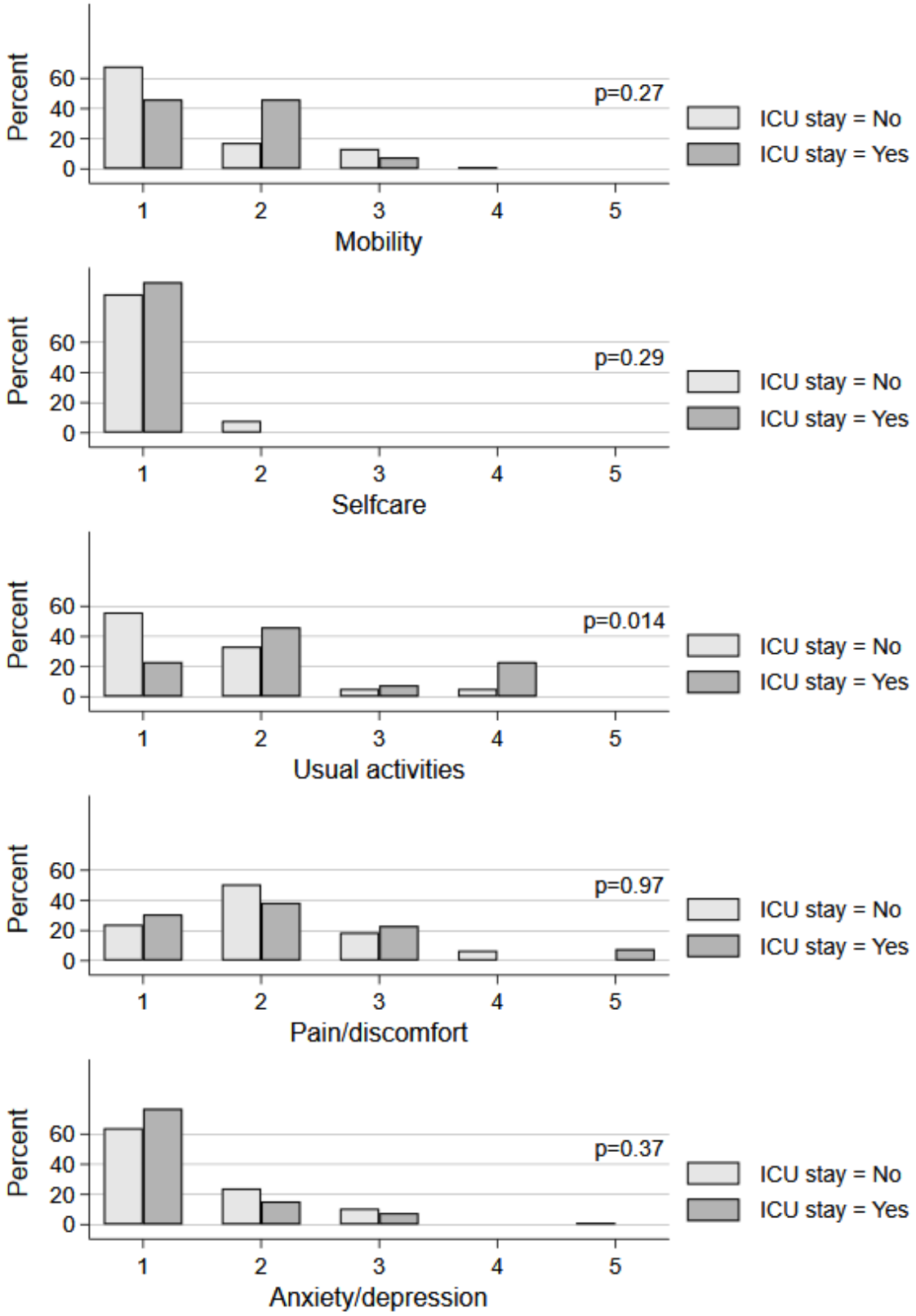
Supplementary Table 1. Univariate associations between main outcomes and age, gender and severity indices during COVID-19.

	OR (95% CI)	p
Dyspnea (mMRC>0 vs. mMRC=0, n=69)		
Male gender	0.41 (0.15-1.08)	0.071
Age per 10 year	0.87 (0.63-1.21)	0.410
ICU admission	0.55 (0.16-1.97)	0.355
Ventilator treatment	0.60 (0.12-2.89)	0.520
Length of stay	0.98 (0.94-1.02)	0.325
CRP max per 10mg/dL	0.99 (0.95-1.04)	0.689
D-dimer max	1.07 (0.86-1.32)	0.557
Gas diffusion capacity (DL_{CO} <LLN vs. DL_{CO} ≥LLN, n=102)		
History of smoking	1.47 (0.58-3.72)	0.411
ICU admission	1.36 (0.39-4.80)	0.633
Ventilator treatment	1.75 (0.40-7.62)	0.456
Length of stay	1.01 (0.98-1.04)	0.562
CRP max per 10g/L	1.04 (0.99-1.09)	0.099
D-dimer max	1.17 (0.92-1.49)	0.188
GGO in chest CT (>10% GGO in ≥1 zone vs. none, n=101)		
Male gender	1.05 (0.43-2.61)	0.908
Age per 10 year	1.60 (1.12-2.26)	0.009
ICU admission	2.64 (0.82-8.56)	0.105
Ventilator treatment	3.63 (0.83-15.9)	0.087
Length of stay	1.03 (0.99-1.08)	0.117
CRP max per 10mg/dL	1.09 (1.04-1.15)	0.001
D-dimer max	1.38 (0.97-1.97)	0.072
Parenchymal bands in chest CT (yes vs. no, n=101)		
Male gender	1.41 (0.52-3.87)	0.505

Age per 10 year	1.10 (0.78-1.56)	0.588
ICU admission	2.86 (0.83-9.81)	0.095
Ventilator treatment	4.87 (1.09-21.7)	0.038
Length of stay	1.03 (0.99-1.07)	0.129
CRP max per 10mg/dL	1.06 (1.01-1.12)	0.018
D-dimer max	1.29 (0.94-1.78)	0.120

OR, odds ratio; CI, confidential interval; mMRC, modified Medical Research Council dyspnoea scale; ICU, intensive care unit; CRP, C-reactive protein; DL_{CO}, diffusion capacity of the lungs for carbon monoxide; LLN, lower limit of normal; CT, computed tomography; GGO, ground glass opacities;


Percent
60
40
20
0
p=0.27
1
2
3
4
5
Mobility
ICU stay = No
ICU stay = Yes
Percent
60
40
20
0
p=0.29
1
2
3
4
5
Selfcare
ICU stay = No
ICU stay = Yes
Percent
60
40
20
0
p=0.014
1
2
3
4
5
Usual activities
ICU stay = No
ICU stay = Yes
Percent
60
40
20
0
p=0.97
1
2
3
4
5
Pain/discomfort
ICU stay = No
ICU stay = Yes
Percent
60
40
20
0
p=0.37
1
2
3
4
5
Anxiety/depression
ICU stay = No
ICU stay = Yes