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Experimental Gerontology 167 (2022) 111907

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Symptomatology and imaging findings in early post-Covid period: A comparative study in older vs younger patients

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ARTICLE INFO

Section Editor: Daniela Frasca

Keywords:
Covid-19
Follow-up
Recovery
Outpatient
Symptom
Imaging

ABSTRACT

Background: While there are substantial reports on the acute phase of Covid-19, the data on post-Covid phase are limited.
Aim: To report the data on older post-Covid patients comparatively with the young adults.
Study design: Retrospective, single-center study in post-Covid outpatient clinic. Clinical characteristics, laboratory examination, chest imagings were examined.
Results: 665 patients were included (median age, 46; 53 %, male; 10.5 %, aged ≥65). We assessed patients at 47th day (median) after recovery. 43.6 % were suffering from one or more ongoing symptomatology. The prevalence of symptoms or physical examination findings were not different between older and younger groups. Most prevalent ongoing symptom was dyspnea (14.3 % and 11.8 % older and younger group, respectively). Most common laboratory abnormality was high pro-BNP (12.2 %, in both age groups). Despite there was no differences regarding imaging findings at acute-phase, there were higher rates of control imaging abnormalities in older subgroup (35.7 % vs 19.4 %; $p = 0.006$). On admission 28.4 % younger patients had normal imaging, of whom 12.4 % developed some form of sequela; however, in older group, 40.0 % had normal imaging, of whom 25.0 % developed sequela.
Conclusion: Complaints related to Covid-19 persisted in about half of the patients at about 1.5 months after Covid. More than 1/3 older post-Covid patients displayed pulmonary sequela in the post-acute period which was more prevalent than those in younger adults. Hence, compared to the younger counterparts, the clinicians should be alert in follow-up of older adults for subsequent pulmonary sequela, even among those that had normal imaging finding on initial presentation.

1. Introduction

Covid-19 came front as an unprecedented health emergency affecting the world beginning from late 2019. It can follow an asymptomatic course, especially in those who are younger and have no accompanying co-morbidities. However, in older adults and those with comorbidities, it can follow a severe course requiring intensive care unit (ICU), and may be mortal. We reported the clinical characteristics of 362 hospitalized Covid-19 patients in our center at the beginning of pandemic previously (Medetalibeyoğlu et al., n.d.) outlining that older patients presented with less symptomatology but severer respiratory signs and laboratory abnormalities than younger group.

Covid-19 is a new disease with a variable systemic involvement. Our understanding of the disease stems from the follow-ups of the patients. While there are substantial reports on the acute phase of the infection, the data following the infection are very limited (Carfì et al., 2020; Moreno-Pérez et al., 2021; Tleyjeh et al., 2021; Groff et al., 2021; Sonnweber et al., 2022; Han et al., 2022). Covid-19 may have consequences that may continue to affect patients in the early post-infectious period and later in life (Bahat, 2020). The diseases related to the viruses

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https://doi.org/10.1016/j.exger.2022.111907
Received 28 June 2022; Received in revised form 26 July 2022; Accepted 27 July 2022
Available online 6 August 2022

from the same human coronavirus family, i.e. SARS-CoV and MERS have been shown to be associated with post-acute pulmonary problems (https://www.england.nhs.uk/coronavirus/publication/after-care-needs-of-inpatients-recovering-from-covid-19). Accordingly, in patients recovered from Covid-19, identification of respiratory problems including chronic cough and fibrotic lung disease, have been recommended (https://www.england.nhs.uk/coronavirus/publication/after-care-needs-of-inpatients-recovering-from-covid-19; Fraser, 2020) to provide data about the course in these patients.

Our center is the first that identified the first Covid-19 case in the metropolitan Istanbul city on March 11, 2020 in our country. Consequently, it served as a pandemic hospital being one of the very crowded centers during the early phase of the pandemic. Moreover, Istanbul has been the major source of the pandemic. The number of Covid-19 cases is highest in Istanbul, owing to be the largest city in the country inhabiting individuals more than many European countries. The population number is about 15 million and has many international links (http://tuik.gov.tr/UstMenu.do?metod=temelist). As a unique city, Istanbul reported about half of all cases in Turkiye (https://dosyamerkez.saglik.gov.tr/Eklenti/38284). We organized an outpatient follow-up clinic for Covid-19 patients with the involvement of multi-disciplines with a dedicated comprehensive geriatric assessment unit (Bahat et al., 2021). Here, we aimed to report the data on the follow-up course of older patients comparatively with younger ones.

2. Methods

2.1. Study design and population

We conducted a retrospective, single-center study to report the follow-up data of recovered Covid-19 patients between May 8 and June 21, 2020 in 6 weeks period. 665 patients were involved. We obtained written consent and the local ethical board approved the study (2020/1041). We accepted patients not only hospitalized in our center but also led from multiple pandemic hospitals in the course. The patients required to meet the following criteria for discontinuation of quarantine: no fever for three consecutive days, improvement in other symptoms, and at least two negative test results for the PCR-analysis. We recruited patients that were at >1 month period after discharge in inpatients, and after initial symptomatology in outpatients. Exclusion criteria were aged <18 and patients with ongoing fever.

2.2. Setting

We established an outpatient follow-up clinic for Covid-19 patients in Istanbul University, Istanbul Faculty of Medicine (Bahat et al., 2021). It is the first and only one in the city. It was established on April 28, 2020, with the aim of identify the problems that may develop in the short and long term in Covid-19 patients, thereby collecting data that may shed light on the future possible complications of Covid-19 infections. It is active and has been collecting data on the course of the post-acute phase dynamically. Patients were contacted to make an appointment. In this outpatient clinic, we planned to follow all patients every three months for one year.

2.3. Acquisition of data

We performed a multi-branched medical and social assessment. Five medical departments were involved in patient care; general internal medicine, infectious disease, pulmonary disease, public health, and geriatric medicine. We recorded the clinical characteristics, lifestyle factors, vaccination status, and physical examination findings (respiratory rate, peripheral oxygen saturation, heart rate and blood pressure) with a structured form within the electronic data-collecting system. In addition, the symptoms of the patients on admission that were hospitalized in our center were inquired. We performed a detailed laboratory assessment and a control chest imaging in the follow-up visit. The normal ranges of each parameter were assessed by the laboratory thresholds. We recommended chest X-ray for the patients who were considered having low-risk for pulmonary involvement. For those who had higher risk of pulmonary involvement and free of contraindications, we performed low dose computed-tomography (CT). Any fibrotic image was noted as a fibrotic sequela.

2.4. Statistical analysis

Continuous variables were evaluated with a Kolmogorov–Smirnov test to assess for normal distribution. Continuous variables were given as mean (standard deviation) or median (interquartile range) as appropriate and categorical variables as counts/percentages. Pearson's Chi-square test and Fisher's exact test were used as appropriate for categorical data. Two independent groups were compared with Mann–Whitney *U* test for nonparametric continuous variables. The severity of pneumonic involvement and control imaging abnormalities were compared with the Linear-by-Linear Association test. A Bonferroni correction was used for post-hoc chi-square statistics between current computerized tomography and age groups. We performed statistical analyses using SPSS 21.0 version. The alpha value was set to <0.05 to determine significance.

3. Results

3.1. Participants

Among 665 recruited patients, most (69.6 %) were from our center. We assessed patients at a median of 47 days (IQR: 37) after recovery. We outlined the characteristics of the population in Table 1.

Older adults (≥65 years) constituted 10.5 % (n = 70) of the participants. 346 (53 %) patients were males; 10 (1.5 %) had required ICU care. Almost half of the patients (43.6 %) were suffering from one or more ongoing symptomatology (except fever), the rates were similar between younger and older subgroups (42.5 % vs 42.9, p = 0.96). The medications used to manage acute infection were similar in both groups (p > 0.05).

3.2. Current symptomatology and physical examination findings (Table 1)

The prevalence of symptoms was not different between younger and older participants (p > 0.05, for all). The most prevalent ongoing symptom in both groups was dyspnea (14.3 % and 11.8 % in older and younger groups, respectively). Likewise, the physical examination findings were indifferent between the groups (p > 0.05).

We outlined the prevalence of symptomatology during the acute phase and this first follow-up visit in patients treated in the main study center (69.6 % of participants) (Fig. 1, younger subgroup; Fig. 2, older subgroup).

3.3. Laboratory examination (Table 1)

The most common ongoing laboratory abnormality was presence of high pro-BNP in both groups (12.2 % in both groups). There was no difference between younger and older groups in terms of CRP, high ferritin (>500 ng/ml), d-dimer (>1000 μg/l), 2.9 %; troponin-T (>14 pg/ml), 4.6 %; thrombocytopenia (<150,000/mm^3), lymphopenia (<1000/mm^3).

Serum glucose, creatinine, ALP levels were somewhat higher and prevalence of high LDH and median troponin-T and AST values were lower in older subgroup (p > 0.05).

Table 1
The characteristics of the post-acute Covid-19 patients in the follow-up.

	All (n = 665)	<65 (n = 595)	≥65 (n = 70)	p
Hospitalization center				
Istanbul Medical School	463 (69.6 %)	405 (68.1 %)	58 (82.9 %)	0.01[c,f]
Other multiple pandemic centers	202 (30.4 %)	190 (31.9 %)	12 (17.1 %)	
Body mass index	28.1 (8.3)	28.1 (8)	29.0 (9.2)	0.71[e]
Sex (male/female)				
Male	346 (52 %)	307 (51.6 %)	39 (55.7 %)	0.51[c]
Female	319 (48 %)	288 (48.4 %)	31 (44.3 %)	
Previous BCG vaccination	540 (81.2 %)	482 (81.6 %)	58 (82.9 %)	0.79[c]
Smoking (active) (n = 322)	27 (8.4 %)	26 (9.5 %)	1 (2 %)	0.09[d]
Personal protective equipment uses (+)	321 (48.3 %)	286 (57.3 %)	35 (60.3 %)	0.68[c]
Treatment setting				
Hospitalized	306 (46 %)	262 (44 %)	44 (62.9 %)	0.03[c,f]
Outpatient	359 (54 %)	333 (56 %)	26 (37.1 %)	
ICU follow-up	10 (1.5 %)	10 (1.7 %)	0 (0 %)	0.61[d]
Co-morbidities				
Hypertension	132 (19.8 %)	115 (19.3 %)	17 (24.3 %)	0.32[c]
Diabetes mellitus	82 (12.3 %)	71 (11.9 %)	11 (15.7 %)	0.36[c]
Chronic obstructive pulmonary disease/asthma	44 (6.7 %)	41 (6.9 %)	3 (4.3 %)	0.61[d]
Hypothyroidism	39 (5.9 %)	36 (6.1 %)	3 (4.3 %)	0.79[d]
Solid tumors	18 (2.7 %)	13 (2.2 %)	5 (7.1 %)	0.03[d,f]
Anxiety disorder	12 (1.8 %)	11 (1.8 %)	1 (1.4 %)	1[d]
Chronic renal failure	10 (1.5 %)	7 (1.2 %)	3 (4.3 %)	0.08[d]
Congestive heart failure	4 (0.6 %)	3 (0.5 %)	1 (1.4 %)	0.36[d]
Pregnancy	2 (0.3 %)	2 (0.3 %)	0 (0 %)	–
Prior treatments				
Hydroxychloroquine	648 (97.4 %)	580 (97.5 %)	68 (97.1 %)	0.69[d]
Azithromycin	427 (64.2 %)	388 (65.2 %)	39 (55.7 %)	0.12[c]
Oseltamivir	342 (51.4 %)	300 (50.4 %)	42 (60 %)	0.13[c]
Favipiravir	123 (18.5 %)	113 (19 %)	10 (14.3 %)	0.34[c]
Low molecular weight heparin	259 (38.9 %)	237 (39.8 %)	22 (31.4 %)	0.17[c]
Dipyridamole	169 (25.4 %)	156 (26.2 %)	13 (18.6 %)	0.17[c]
Aspirin	19 (2.9 %)	17 (2.9 %)	2 (2.9 %)	1[d]
Tocilizumab	37 (5.6 %)	35 (5.9 %)	2 (2.9 %)	0.41[d]
Anakinra	14 (2.1 %)	14 (2.4 %)	0 (%)	0.38[d]
Current symptoms				
Fatigue	93 (14 %)	85 (14.3 %)	8 (11.4 %)	0.51[c]
Dyspnea	80 (12 %)	70 (11.8 %)	10 (14.3 %)	0.54[c]
Dry cough	76 (11.4 %)	69 (11.6 %)	7 (10 %)	0.69[c]
Chest pain	40 (6 %)	36 (6.1 %)	4 (5.7 %)	0.91[c]
Diarrhea	22 (3.3 %)	18 (3 %)	4 (5.7 %)	0.28[d]
Loss of smell/taste			0 (0 %)	0.39[d]
	16 (2.4 %)	16 (2.7 %)		
Nausea	12 (1.8 %)	11 (1.8 %)	1 (1.4 %)	1[d]
Headache	7 (1.1 %)	7 (1.2 %)	0 (0 %)	1[d]
Forgetfulness	3 (0.5 %)	2 (0.3 %)	1 (1.4 %)	0.28[d]
Current physical examination				
Respiratory rate (/min)[b]	14 (2)	14 (2)	14 (2)	0.35[e]
Peripheric oxygen saturation (%)[b]	98 (2)	98 (2)	98 (1)	0.44[e]
Heart rate (/min)[b]	85 (18)	85 (18)	85,5 (23)	0.72[e]
Blood pressure (mm Hg)[b]	134/80 (28/19)	134/80 (28/19)	134/84 (25/18)	0.41/ 0.91[e]
Current laboratory characteristics				
CRP (mg/l)[b]	1 (3)	1,2 (3)	1 (2)	0.34[c]
CRP > 5 mg/l	100 (15.1 %)	94 (15.8 %)	6 (8.7 %)	0.12[c]
CRP > 40 mg/l	10 (1.5 %)	10 (1.7 %)	0 (0 %)	0.61[d]
Leukocytes < 4000	31 (4.7 %)	30 (5.1 %)	1 (1.4 %)	0.24[d]
Leukocytes > 10,000/mm^3	21 (3.2 %)	19 (3.2 %)	2 (2.9 %)	1[d]
Lymphocytes < 1000/mm^3	14 (2.1 %)	12 (2 %)	2 (2.9 %)	0.65[d]
Neutrophils > 7700/mm^3	9 (1.4 %)	7 (1.2 %)	2 (2.9 %)	0.24[d]
Hb (g/dl)[b]	13.5 (2)	13.5 (2.3)	13.1 (1.7)	0.99[e]
Thrombocytes < 150,000/mm^3	17 (2.6 %)	16 (2.7 %)	1 (1.4 %)	1[d]
Glucose (mg/dl)[b]	99 (22)	98 (20.5)	108 (32)	<0.001[e,f]
Creatinine (mg/dl)[b]	0.8 (0.3)	0.7 (0.3)	0.9 (0.3)	<0.001[e,f]
Creatinine > 1.2 mg/dl	29 (4.4 %)	17 (2.9 %)	12 (17.1 %)	<0.001[d,f]
Urate (mg/dl)[b]	5.1 (2)	5.1 (2)	5.2 (2)	0.26[e]
Na (mmol/l)[b]	141 (3)	141 (3)	141 (3)	0.88[e]
K (mmol/l)[b]	4.3 (0.5)	4.3 (0.5)	4.4 (0.7)	0.01[e]
Ca (mg/dl)[b]	9.5 (0.5)	9.5 (0.5)	9.6 (0.7)	0.31[e]
P (mg/dl)[b]	3.4 (0.8)	3.4 (0.8)	3.4 (0.7)	0.17[e]
ALP (U/l)[b]	66 (25)	65 (25)	71 (27)	0.002[e,f]
AST (U/l)[b]	18 (7)	18 (7)	17 (8)	0.047[e,f]
AST > 42 U/l[b]	15 (2.3 %)	14 (2.4 %)	1 (1.4 %)	1[d]
ALT[b]	19 (16)	19 (16)	21 (16)	0.71[e]
ALT > 45 U/l[b]	69 (10.4 %)	62 (10.4 %)	7 (10.1 %)	0.94[d]
GGT (u/l)[b]	18 (16)	18 (17)	19 (17)	0.12[e]
LDH (u/l)[b]	192 (43)	193 (43)	190 (39)	0.22[e]
LDH > 250 U/l[b]	49 (7.4 %)	48 (8.1 %)	1 (1.4 %)	0.046[c,f]
Albumin (g/dl)[b]	4.6 (0.4)	4.6 (0.4)	4.6 (0.3)	0.66[e]
Albumin < 3.5 g/dl	0 %	0 (0 %)	0 (0 %)	–
Triglycerides (mg/dl)[b]	123 (103)	123 (102)	115 (101)	0.64[e]
Total cholesterol (mg/dl)[b]	201 (56)	201 (54)	203 (65)	0.81[e]
LDL-cholesterol (mg/dl)[b]	123 (47)	123 (46)	128,5 (61)	0.67[e]
HDL-cholesterol (mg/dl)[b]	50 (20)	50 (21)	50 (14)	0.96[e]
Ferritin (ng/ml)[b]	62 (101)	63 (101)	56 (102)	0.70[e]
Ferritin > 500 ng/ml	10 (1.6 %)	9 (1.6 %)	1 (1.4 %)	1[d]
D-dimer > 1000 u/l	35 (5.3 %)	33 (5.5 %)	2 (2.9 %)	0.57[d]
Pro-BNP > 125 pg/ml	77 (12.2 %)	69 (12.2 %)	8 (12.3 %)	0.98[d]
Troponin-T (pg/ml)[b]	4 (4)	4 (4)	3.5 (2.9)	0.04[e,f]
Troponin-T > 14 pg/ml	48 (7.6 %)	45 (8 %)	3 (4.6 %)	0.46[d]
TSH (mIU/l)[b]	2 (1.6)	1.9 (1.6)	2 (1.7)	0.93[e]
Free-T4[b]	15 (3)	15 (3.4)	15 (2.1)	0.73[e]
Anti-TPO (+)	79 (14.1 %)	74 (14.7 %)	5 (8.8 %)	0.23[d]
Anti-TG	46 (8.2 %)	44 (8.7 %)	2 (3.5 %)	0.21[d]

(continued on next page)

Table 1 (*continued*)

	All (n = 665)	<65 (n = 595)	≥65 (n = 70)	p
Imaging findings				
Computerized tomography on admission				
Severe pneumonia	51 (7.7 %)	47 (4.9 %)	4 (5.7 %)	0.16[c]
Moderate pneumonia	180 (27.1 %)	162 (27.2 %)	18 (25.7 %)	
Mild pneumonia	233 (35 %)	215 (36.1 %)	18 (25.7 %)	
Normal	198 (29.8 %)	170 (28.6 %)	28 (40 %)	
Non-available	3 (0.5 %)	1 (0.2 %)	2 (2.9 %)	
Current computerized tomography				
Ground glass opacities	113 (17 %)	95 (16 %)	18 (25.7 %)	0.006[c,f,a]
Fibrosis	27 (4.1 %)	20 (3.4 %)	7 (10 %)	
Normal	522 (78.5 %)	477 (80.2 %)	45 (64.3 %)	
Non-available (pregnancy 1/3)	3 (0.4 %)	3 (0.5 %)	0 (0 %)	

[a] Post-hoc chi-square result showed a significant difference between "fibrosis" and "normal".
[b] Median (IQR).
[c] Pearson's chi square test.
[d] Fisher's exact test.
[e] Mann Whitney U test.
[f] Significant association.

3.4. Chest imaging

Control chest imaging was performed in 662 (99.5 %) patients. We performed a CT in 527 (79.2 %) patients and X-ray in 135 (20.3 %) patients. Imagings revealed 17 % ground-glass opacities, 4.1 % fibrosis while 78.5 % were normal.

There were no differences regarding imaging findings (i.e., severe to mild pneumonia or normal imaging) in between age groups during the acute-phase. However, there were significantly higher rates of imaging abnormality in older subgroup (i.e., ground glass opacities, 25.7 % vs 16.0 %; fibrosis, 10.0 % vs 3.4 %; p = 0.006). Post-hoc analysis revealed that the difference was significant for higher rates of fibrosis and lower rates of normal imaging findings in older group.

In younger group, there were 28.4 % (n = 169) patients who had normal imaging on admission. Among these patients (with normal imaging at initial presentation), there were ground glass opacities in 11.8 % and fibrosis in 0.6 %. In older group, 40 % (n = 28) patients had normal imaging on admission, of whom 21.4 % developed ground-glass opacities and 3.6 % developed fibrosis in follow-up (Table 2). There was a significant positive association between the severity of pneumonic involvement and control imaging abnormalities in younger group (p = 0.002). More severe, the initial presentation involvement, more prevalent, were the control abnormalities. In contrast, there was no association in older group (p = 0.076) (Table 2).

3.5. The association between symptoms and laboratory examination/ chest imaging (Table 3a, younger group; Table 3b, older group)

We examined whether the persistent symptoms, i.e., fatigue, dyspnea, and dry cough, were associated with abnormalities of the laboratory parameters, i.e., high CRP (>5 mg/l), pro-BNP (>125 pg/ml), troponin T (>14 pg/ml), D-dimer (>1000 μg/l), ferritin (>500 ng/ml), low lymphocytes (<1000/mm^3) or imaging findings in the control visit.

Lastly, we looked for the possible associations between the persistent symptoms, and laboratory parameters and post-acute pulmonary computerized tomography findings in both groups, separately.

In younger group, dyspnea was more common in those that have high CRP (p = 0.04) and d-dimer and fatigue were more common in those with ground-glass opacities and/or any pathology (ground-glass opacities or fibrosis) on imaging (p = 0.043, p = 0.012; respectively). In older group, the only symptom associated with an abnormal laboratory finding was the presence of persistent dry cough. Dry cough was more common in those that have high CRP (p = 0.01) and the association between dry cough and the presence of ground glass opacities was at borderline significance (p = 0.05).

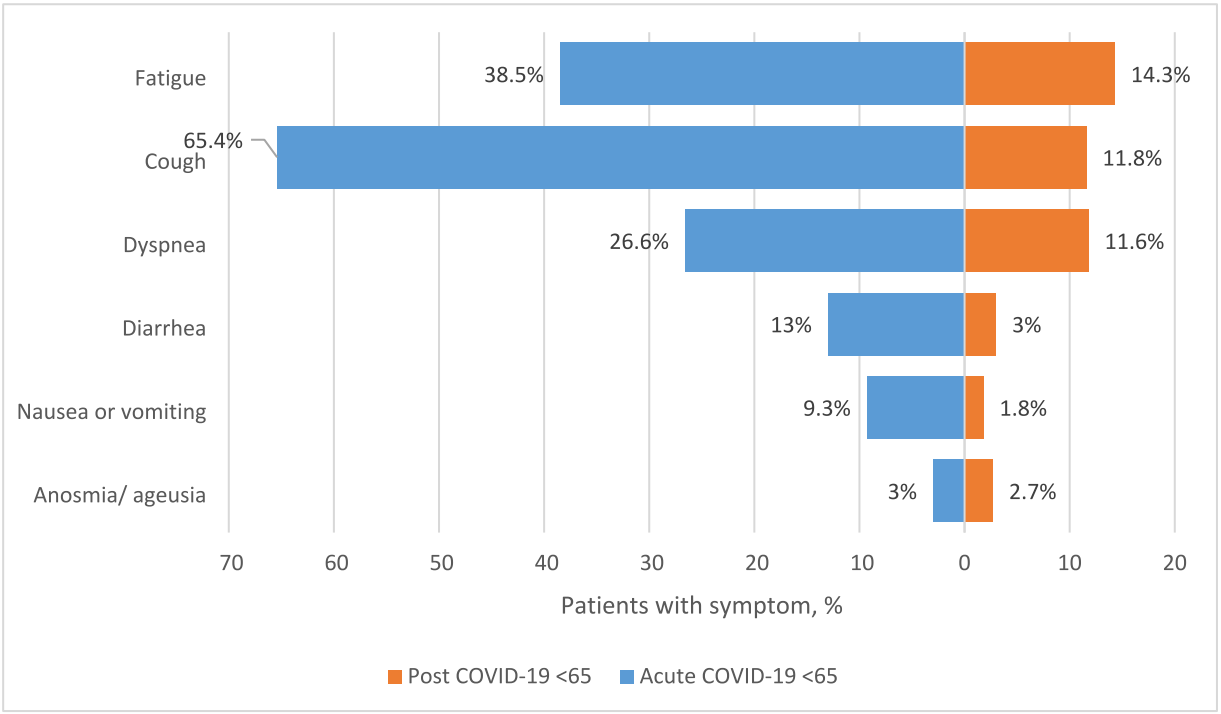

Fig. 1. Comparative symptoms between acute Covid-19 and post-acute Covid-19 in younger patients (aged <65).

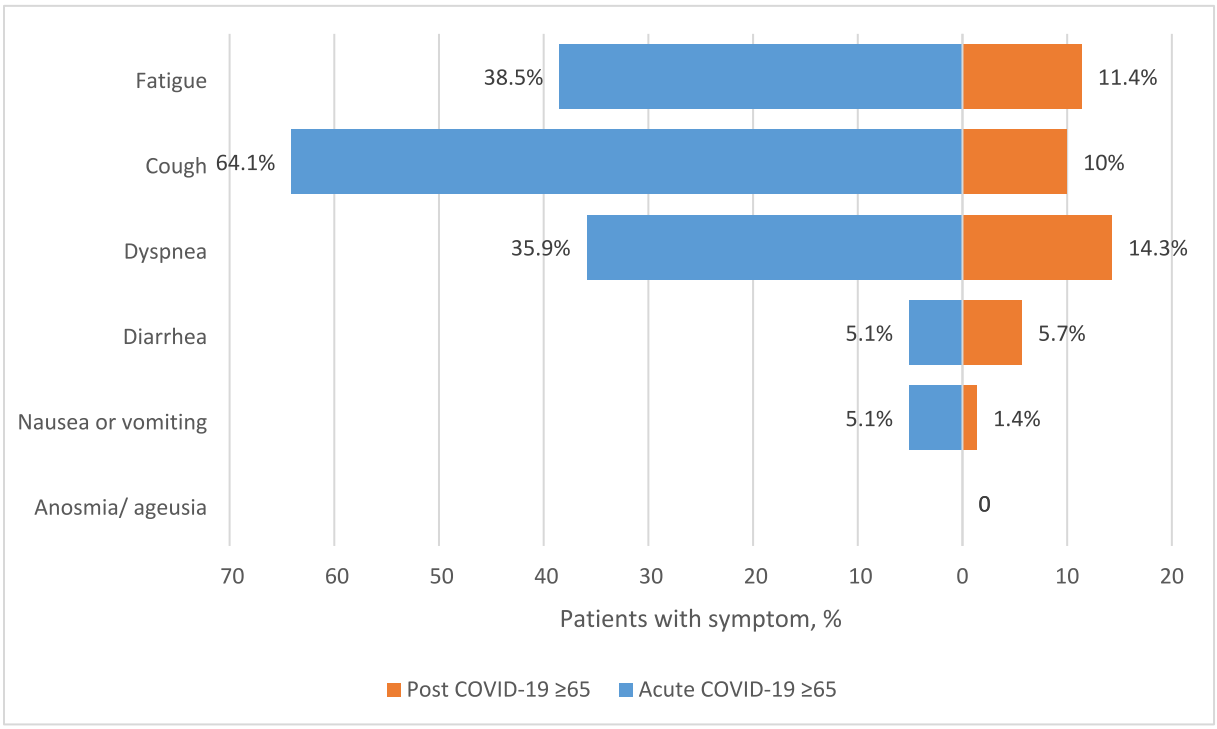

Fig. 2. Comparative symptoms between acute Covid-19 and post-acute Covid-19 in older patients (aged ≥65).

Table 2
Analyses on associations between the imaging findings on admission and current imaging (n = 659).

	Current imaging			
	Ground glass opacities	Fibrosis	Normal	p
<65 findings on admission				
Severe pneumonia (n = 47)	12 (12.6 %)	3 (15.0 %)	32 (6.7 %)	0.002[a,b]
Moderate pneumonia (n = 161)	31 (32.6 %)	8 (40 %)	122 (25.6 %)	
Mild pneumonia (n = 214)	32 (33.7 %)	8 (40 %)	174 (36.6 %)	
Normal (n = 169)	20 (21.1 %)	1 (5 %)	148 (31.1 %)	
≥65 findings on admission				
Severe pneumonia (n = 4)	3 (6.7 %)	0 (0 %)	1 (2.3 %)	0.076[a]
Moderate pneumonia (n = 18)	4 (22.2 %)	4 (57.1 %)	10 (23.3 %)	
Mild pneumonia (n = 18)	5 (27.8 %)	2 (28.6 %)	11 (25.6 %)	
Normal (n = 28)	6 (33.3 %)	1 (14.3 %)	21 (48.8 %)	

[a] Linear-by-Linear Association test.
[b] Significant association.

4. Discussion

The data on post-Covid phase are limited (Carfì et al., 2020; Moreno-Pérez et al., 2021; Tleyjeh et al., 2021; Groff et al., 2021; Sonnweber et al., 2022; Han et al., 2022) in the literature. Our study provided data on 665 post-Covid patients assessed at a median of about 1.5 months after recovery. Older adults comprised 10.5 % of the total study participants. This ratio is in line with the Turkiye's general demographic structure as the older adults constitute 9.7 % of the population according to Turkish Statistical Institute, last assessed on June, 2021 (*TÜİK Kurumsal*, 2022). A slight higher prevalence may be due to susceptibility of older people to Covid-19. These comparable figures suggest that our population represent the general population of Turkiye.

Almost half of the patients (43.6 %) were suffering from one or more ongoing symptomatology (dyspnea being the most frequent one) which were similar in older and younger groups. The rates of symptoms and physical examination findings were similar in age groups.

The detailed laboratory investigation showed that there were a few patients with laboratory abnormalities. High CRP (>5 mg/l) was present in 8.7 % of older adults, which can well be related to chronic diseases as atherosclerosis. Serum glucose, creatinine, ALP levels were somewhat higher in older group which may well be reflecting the age associated changes in glucose tolerance, renal functions and osteomalacia. Instead, the prevalence of high LDH and median troponin-T and AST values were lower in older subgroup. Together these results may be indicating higher cardiac myocardial involvement in younger patients than in older adults. Likewise, the most common ongoing laboratory abnormality was high pro-BNP as about 12 % in both age groups. This similar prevalence of high pro-BNP may be reflecting some baseline cardiac problems in older group and our documented prevalent involvement of cardiac tissue in younger group.

Control chest imaging was performed in 659 (99.1 %) patients, this was via CT imaging in ~80 % of them. About one in four Covid-19 patients displayed some imaging abnormalities in the early post-acute period. Remarkably, this rate was significantly higher in the older group as one out of three older post-Covid-19 patients displayed some form of pulmonary sequela in the post-acute period. Noteworthy, there were no differences regarding severity of pneumonia in between the age groups but imaging abnormalities were more common in older subgroup, displaying as mostly higher rates of fibrosis. This finding is important because it suggests that even though, they may suffer from similar pneumonic involvement, the sequela occurred more in older adults. Normal imaging on admission was more common in older group (40.0 % vs 28.6 %) which may be due to sluggish development of immune response in older adults resulting in delayed macroscopic/structural changes (Bajaj et al., 2021; Boe et al., 2017). We suggest that the higher rates of sequela may be related to the limited recovery potential

Table 3a
Associations between the persistent symptoms and laboratory parameters and post-acute pulmonary computerized tomography findings in patients aged <65 years (n = 595).

	Symptoms			p[a]	p[b]	p[c]
	Fatigue No vs yes	Dyspnea No vs yes	Dry cough No vs yes			
Laboratory parameters						
CRP > 5 (n = 94)	15.1 % vs 20 %	14.7 % vs 24.3 %	16 % vs 14.5 %	0.255[α]	0.04[α,*]	0.75[α]
Pro-BNP > 125 (n = 69)	12 % vs 13.3 %	11.2 % vs 19.4 %	12 % vs 14.1 %	0.75[α]	0.056[α]	0.63[α]
Tn-T > 14 (n = 45)	8.5 % vs 4.8 %	7.6 % vs 10.4 %	8.2 % vs 6.3 %	0.25[α]	0.42[α]	0.59[α]
D-dimer > 1000 (n = 33)	5.9 % vs 3.5 %	4.6 % vs 12.9 %	5.7 % vs 4.3 %	0.61[†]	0.01[†,*]	0.64[†]
Ferritin > 500 (n = 9)	1.9 % vs 0 %	1.4 % vs 3 %	1.8 % vs 0 %	0.36[†]	0.29[†]	0.61[†]
Lymphocytes < 1000 (n = 12)	2.4 % vs 0 %	1.9 % vs 2.9 %	2.1 % vs 1.4 %	0.23[†]	0.64[†]	1[†]
Imaging findings						
Ground glass opacities (n = 95)	14.8 % vs 23.5 %	15.7 % vs 18.8 %	15.3 % vs 21.7 %	0.043[α,*]	0.51[α]	0.17[α]
Fibrosis (n = 20)	3 % vs 5.9 %	3.6 % vs 1.4 %	3.1 % vs 5.8 %	0.19[α]	0.49[α]	0.28[α]
Any pathology[β] (n = 115)	17.8 % vs 29.4 %	19.3 % vs 20.3 %	18.4 % vs 27.5 %	0.012[α,*]	0.87[α]	0.071[α]

CRP, mg/l; pro-BNP, pg/ml; troponin-T, pg/ml; d-dimer, μg/l; ferritin (ng/ml); lymphocytes (/mm^3).
[β] Ground-glass opacities or fibrosis.
[α] Pearson's chi square test.
[†] Fisher's exact test.
[*] Significant association.
[a] p value for the association analyses between the individual laboratory parameters and fatigue.
[b] p value for the association analyses between the individual laboratory parameters and dyspnea.
[c] p value for the association analyses between the individual laboratory parameters and dry cough.

Table 3b
Associations between the persistent symptoms and laboratory parameters and post-acute pulmonary computerized tomography findings in patients aged ≥65 years (n = 70).

	Symptoms			p[a]	p[b]	p[c]
	Fatigue No vs yes	Dyspnea No vs yes	Dry cough No vs yes			
Laboratory parameters						
CRP > 5 (n = 6)	6.6 % vs 25 %	8.5 % vs 10 %	4.8 % vs 42.9 %	0.082[α]	0.87[α]	0.01[†,*]
Pro-BNP > 125 (n = 8)	12.1 % vs 14.3 %	12.7 % vs 10 %	13.8 % vs 0 %	0.86[α]	0.81[α]	0.58[†]
Tn-T > 14 (n = 3)	5.2 % vs 0 %	5.5 % vs 0 %	5.2 % vs 0 %	1[†]	1[†]	1[†]
D-dimer > 1000 (n = 2)	3.2 % vs 0 %	3.3 % vs 0 %	3.2 % vs 0 %	1[†]	1[†]	1[†]
Ferritin > 500 (n = 1)	1.7 % vs 0 %	1.8 % vs 0 %	1.7 % vs 0 %	1[†]	1[†]	1[†]
Lymphocytes < 1000 (n = 2)	1.6 % vs 12.5 %	3.4 % vs 0 %	3.2 % vs 0 %	0.085[α]	1[†]	1[†]
Imaging findings						
Ground glass opacities (n = 18)	26.7 % vs 25 %	27.6 % vs 20 %	23 % vs 57.1 %	0.92[α]	0.61[α]	0.05[α]
Fibrosis (n = 7)	10 % vs 12.5 %	8.6 % vs 20 %	11.5 % vs 0 %	0.83[α]	0.27[α]	1[†]
Any pathology[β] (n = 25)	36.7 % vs 37.5 %	36.2 % vs 40 %	34.4 % vs 57.1 %	0.96[α]	0.82[α]	0.41[†]

CRP, mg/l; pro-BNP, pg/ml; troponin-T, pg/ml; d-dimer, μg/l; ferritin (ng/ml); lymphocytes (/mm^3).
[β] Ground-glass opacities or fibrosis.
[α] Pearson's chi square test.
[†] Fisher's exact test.
[*] Significant association.
[a] p value for the association analyses between the individual laboratory parameters and fatigue.
[b] p value for the association analyses between the individual laboratory parameters and dyspnea.
[c] p value for the association analyses between the individual laboratory parameters and dry cough.

of older adults.

Another noteworthy finding is all Covid-19 patients had a high chance of developing sequela even if they had normal imaging findings when they were symptomatic and it was more prevalent in older adults (Table 2). Yet again, these findings should alert the clinicians for a need of closer follow-up in Covid patients, esp. in older group. The severity of pneumonic involvement and control imaging abnormalities were correlated in the younger group, which is a plausible association. On the contrary, there was no association between the severity of pneumonic involvement and control imaging in older group implying delayed immune-response and limited recovery potential in older adults.

We will present an overview for comparison of sequela associated with Covid-19 with those associated with recent previous pulmonary infection outbreaks related to other pathogens. Approximately 30 % of survivors of the global SARS outbreak caused by SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV) were reported to suffer from persistent physiological impairment and abnormal radiology (https://www.england.nhs.uk/coronavirus/publication/after-care-needs-of-inpatients-recovering-from-covid-19). In a study involving 110 confirmed SARS patients in the post-acute period, the participants were examined at the end of 3 and 6 months after symptom onset (Hui et al., 2005). At a later follow-up stage (i.e., 6 months), 30 % had abnormal chest radiographs, which is higher than our figures. Among them ~3.6–15.5 % had impaired lung volume, spirometry, or surface area for gas exchange measures, being mostly in forms of mild-modest deficits. The exercise capacity was assessed by the 6-meter walking distance which somewhat improved between 3 and 6 months, but the performance was still lower than normal same-aged controls. The problems were more prevalent in those with severe disease (Hui et al., 2005). Worth mentioning, the authors drew attention that the functional disability was out of proportion to the degree of functional lung impairment and suggested that it may be related to additional factors e.g. muscle deconditioning and steroid myopathy. Another study examined 36 patients with confirmed MERS-CoV that had follow-up chest radiographs after recovery from MERS-CoV at a median follow-up of 43 days. They revealed that follow-up chest radiographs were normal in only 64 %, again a figure worse than our study with SARS-coV2. The most common abnormalities were lung fibrosis in 33 %, ground-glass opacities in 5.5 %, and pleural thickening in 5.5 %, which

were, therefore, in forms of more severe involvements (Das et al., 2017).

Regarding serial CT follow-ups after SARS, Zhang et al. examined (Boe et al., 2017) the 15-year follow-up on the lung conditions of SARS patients using CT scans and pulmonary function tests. They involved 78 patients and noted that parenchymal abnormalities were present in 38 %. However, the percentage of pulmonary lesions on CT scans diminished after 1 year of follow-up and remained stable thereafter until 2018 which was the 15th year. They reported that SARS-mediated pulmonary interstitial damage and functional decline mostly recovered, with a greater extent of recovery within 2 years after rehabilitation. We need long-term data derived from Covid-19 survivors to comment on the comparison between SARS-CoV1 and SARS-coV2 infections in the long-term parenchymal lung damage. Yet, our findings suggest that the post-infectious pulmonary disruptions may be less prevalent and milder in Covid-19 patients than those in SARS-CoV1 and MERS infections.

All of the published studies so far show similar results for ongoing symptoms after the acute phase of Covid infection (Carfì et al., 2020; Moreno-Pérez et al., 2021; Tleyjeh et al., 2021; Groff et al., 2021; Sonnweber et al., 2022; Han et al., 2022). At the short term (1 month) and intermediate-term (2–3 months) follow ups, no major difference was observed regarding the prevalence of symptoms in these studies Rates of patients with at least 1 ongoing symptom ranged between 54 % (Groff et al., 2021) in short-term and 51 % (Moreno-Pérez et al., 2021) to 56,5 % (Tleyjeh et al., 2021) in intermediate-term, being 43,6 % in our research. Dyspnea and fatigue were the most common symptoms in line with the first presentation complaints (Moreno-Pérez et al., 2021; Tleyjeh et al., 2021). Rates of abnormal imaging findings were also similar in the published studies ranging between 18 % (Sonnweber et al., 2022) to 18,9 % (Moreno-Pérez et al., 2021), being 12,4 % in our younger subgroup and 25 % in our older subgroup. Imaging findings were not as common as ongoing symptomatology in these studies. In our study, there were no major differences between younger and older subgroups in terms of the rates of ongoing symptoms (fatigue 14,3 % in younger vs 11,4 % in elder), however, older subgroup had significantly more common control imaging findings (12,4 % in younger vs 25 % in elder). Even though symptomatology was consistent between studies, ongoing lab abnormalities varied as lymphopenia, high ferritin and D-dimer levels, being high Pro-BNP levels in our research (Moreno-Pérez et al., 2021). There was no major indicator for predicting high risk patients to have post-COVID symptoms (Moreno-Pérez et al., 2021; Tleyjeh et al., 2021). To our knowledge, none of these studies examined older vs younger patients comparatively. In this regard, our study comes front in geriatrics practice and may possess clinical implications for older adults' follow-up. An implication point for future practice is compared to younger equivalents, older adults had higher risk to develop pulmonary sequela, even though when they had normal imaging at initial presentation.

As we progress through the pandemic, naturally virus evolves, the most current variant being the Omicron. There are few studies comparing post-Covid symptoms of the Omicron variant to the earlier strains (Morioka et al., 2022; Jung et al., 2022; Magnusson et al., 2022). Whereas some comparative studies show that post-Covid symptoms are seen significantly lower in Omicron variant subgroup (Morioka et al., 2022), some suggest that post-Covid symptoms are similar to earlier strains other than pulmonary parenchymal sequela and shortness of breath caused by Omicron's affinity to upper respiratory tract instead of lower respiratory tract (Jung et al., 2022). There are also studies that show similar post-Covid symptom patterns after Omicron variant infections compared to the earlier strains (Magnusson et al., 2022). These various results suggest that post-Covid patient characteristics after Omicron variant are a field to be discovered and studied. In this regard, we further plan to collect more data from Omicron variant survivors for a future study, preferably with longer median follow-up duration.

4.1. Strengths and limitations

Our limitation are, we do not have information about the symptoms before the acute Covid-19 and did not assess the symptom severity of the particular symptoms. It is a single-center follow-up study, and we do not have a control group of patients that had been discharged from the hospital due to another respiratory infection. Some persistent symptoms as fatigue, dyspnea, and dry cough may also be noted after other respiratory illnesses. Although we aimed to report early post-Covid period characteristics of the patients in this research, the 47 days of median follow-up duration limits to judge long term post-Covid symptomatology. The 1-year follow-up data of our patient group have been compiled and we are working on the article to report the long-term data. Our strengths include the following points: All participants were PCR positive confirmed Covid-19 patients; we recorded the symptoms on admission recorded in the electronic patient files at the time of admission, therefore this approach is free from the risk of retrospective under-reporting of acute phase symptoms. We supplied a detailed laboratory and imaging re-examination with one of the highest participant number reported so far.

5. Conclusion

Our findings suggest that, complaints related to SARS-CoV2 infection persist in a significant proportion of the patients at post-Covid 1.5 months. In addition, the clinicians should be alert and more tentative in follow-up of older adults for subsequent pulmonary sequela, even though they have normal imaging finding on presentation.

Statements and declarations

We have read and approved the version to be submitted. All authors had access to all the study data, take responsibility for the accuracy of the analysis, and had authority over manuscript preparation and the decision to submit the manuscript for publication.

The authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

This manuscript, including related data and tables has not been previously published.

All data relevant to the study are included in the article.

The authors didn't receive any writing assistance.

Ethical approval and compliance with ethical standards

The study protocol was approved by the Istanbul University, Istanbul Medical School ethics committee (with the number of 2020/1041) and conducted according to the guidelines laid down in the Declaration of Helsinki.

Informed consent

All participants agreed to participate in the study and the guardian of each subject signed written informed consent form.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Gulistan Bahat: Concept and design, Preparation of the first draft, Stylistic/grammatical revisions of the manuscript and drafting
Alpay Medetalibeyoglu: Concept and design, Critical revision of the manuscript
Naci Senkal: Revisions to scientific content of manuscript
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Declaration of competing interest

All of authors have no conflicts of interest or financial or other contractual agreements that might cause conflicts of interest.

Data availability

Data will be made available on request.

Acknowledgements

The authors would like to thank Emine Bilge Caparali and Sena Bayrakdar for their contribution in editing of the manuscript.

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