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IONIZING RADIATION EXPOSURE IN PATIENTS WITH COVID-19: MORE THAN NEEDED

Isil Yurdaisik [1,*], Fuat Nurili[2], Suleyman Hilmi Aksoy[3], Ayse Gul Agirman[4] and Ahmet Aktan[5]
[1]Department of Radiology, Istinye University, Gaziosmanpasa Medical Park Hospital, 34250 Istanbul, Turkey
[2]Department of Radiology, Memorial Sloan Ketteting Cancer Center, Interventional Radiology, New York, NY 10065, USA
[3]Department of Radiology, Galata University, Hisar Intercontinental Hospital, 34768 Istanbul, Turkey
[4]Department of Radiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, 34668 Istanbul, Turkey
[5]Department of Radiology, Yalova Private Hospital, 77100 Yalova, Turkey

*Corresponding author: mdisilyurdaisik@gmail.com

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Objective: The aim of the study was to evaluate the ionizing radiation exposure in patients with Coronavirus disease 2019 (COVID-19). Materials and Methods: This was a retrospective study in which all patients presented with suggestive symptoms of COVID-19 were included. The study was carried out in a university-affiliated private hospital in Istanbul, Turkey. Biological radiation dose exposure (cumulative effective dose: CED) was evaluated in millisievert (mSv) units. Results: A total of 1410 patients were included in the study. Of all study subjects, 804 patients (57%) underwent only one chest computed tomography (CT) procedure. Six hundred and six patients (43%) had two or more chest CT procedures. Median CED was 6.02 (min–max:1.67–16.27) mSv. The number of patients who were exposed to $\leq$ 5 mSv were 149 (24.6%), whereas 457 patients (75.4%) were exposed to $>$5 mSv. Conclusion: The radiation exposure in COVID-19 patients seems unjustifiably high. Awareness should be increased as to the proper use of chest CT in COVID-19 as per to the society recommendations.

INTRODUCTION

After reporting of the first case in Wuhan province of China in December 2019, severe acute respiratory syndrome (SARS) coronavirus-2 (SARS-CoV-2) infection reached pandemic proportions in March 2020. The multisystem disease comprising cytokine storm and multiorgan dysfunction was named as Coronavirus disease 2019 (COVID-19) though the primary target of the virus is the lungs.

Rapid spread of the COVID-19 around the globe caught many nations off guard in terms of medical personnel, mechanical ventilator, personal protective equipment (PPE) and, hospital and intensive care unit beds. Add this to the scarcity of the primary diagnostic instrument, reverse transcriptase-polymerase chain reaction test (RT-PCR) for the identification of the virus; it is relatively straightforward to understand the gloomy situation at the outset of the pandemic in many countries.

In the early phases of the pandemic, particularly in resource-constrained countries, when the RT-PCR tests were limited and turnaround times were too long to make an effective patient triage in an already strained healthcare system, physicians heavily relied upon chest computed tomography (CT) for rapid diagnosis of COVID-19. It has been shown that chest CT was able to diagnose SARS-CoV-2 infection before the RT-PCR test become positive and herald recovery during the course of the disease before the RT-PCR test become negative[1]. The sensitivity of the chest CT in the diagnosis of COVID-19 was reported between 86 and 98%[2, 3].

Despite its high sensitivity and advantage of providing an early diagnosis, chest CT is not without its limitations. First, the specificity suffers from the fact that COVID-19 lung involvement does not have a pathognomonic radiologic finding, instead it shows usual signs of interstitial pneumonia and acute respiratory stress syndrome in most severe cases[4, 5]. Second, within the first 48 hours, chest CT results might be completely normal[6]. Third and perhaps the most overlooked, chest CT exposes the patient to ionizing radiation and, when used repeatedly, put the recovering patient at risk of future development of secondary malignancies[7].

Taken the abovementioned limitations and potential hazards into account, a number of societies published recommendations regarding the proper use of chest CT in the diagnosis and follow-up of COVID-19 patients[8–10].

To the best of our knowledge, there is only one multicenter study in the literature investigating the ionizing radiation exposure in patients diagnosed with COVID[11]. Hence, we aimed to evaluate the total dose of radiation exposure of COVID-19 patients during the initial stages of the outbreak in Turkey retrospectively. We believe that a better understanding of the current status with respect to radiation exposure will help increase awareness among health care providers as well as policy-makers.

MATERIALS AND METHODS

Design, setting and patients

This was a retrospective evaluation of radiation dose exposure through chest CT among patients who presented with symptoms suggestive of COVID-19 and/or had a suspicious contact with true COVID-19 patients in a university-affiliated private hospital in Istanbul, Turkey. We included all patients who presented to our private University-affiliated hospital and were deemed to have COVID-19 based on either RT-PCR or contact history and COVID-19 related symptoms or compatible chest CT results in March 2020. The University ethics committee approved the study protocol ((2017-KAEK-120)/2/2020.G-112).

As per the hospital guidelines, all patients who were evaluated with suspicion of having COVID-19 underwent low-dose chest CT irrespective of their RT-PCR test results. Indeed, many patients at that time were not tested with RT-PCR because of the insufficient number of test assays. During the course of the disease, all patients who showed signs of deterioration in clinical and/or laboratory findings underwent additional chest CT as well.

Age, gender, presenting symptoms, comorbid conditions, hospitalization status, length of hospital stay and survival status of the study patients were recorded from patient charts and hospital electronic database.

Chest CT protocol for COVID-19

To be able to evaluate the biologically harmful effects of the ionizing radiation, we quantified cumulative effective radiation dose (CED) arising from chest computed tomographic scans. We did not take into account other radiological procedures utilizing X-rays because few people underwent these procedures due to the difficulty in mobilization of the patients under extraordinary circumstances of the COVID-19 pandemic.

All chest CT scans were carried out with a low-dose protocol. In contrast to the method of standard procedure-specific radiation doses in previous studies, we measured and calculated true individual CED values in the current study[12–14]. The total ionizing radiation dose applied in the procedure was automatically calculated by the CT machine based on the body mass index of the patient. The doses were expressed as dose length product (DLP) in the picture archiving and communication system (PACS). We converted the measured dose of ionizing radiation in DLP units to an effective dose by multiplying it by 0.014. The CED was expressed in units of millisievert (mSv)[15].

Chest CT procedures were performed using a 128-slice multidetector CT scanner (Somatom Definition AS+ Erlangen, Germany). During each scan, the following standard parameters were used: slice thickness of 1.0 mm, reconstruction interval of 1.0–3.0 mm, tube voltage of 120 kV and automatic exposure controlled standard tube flow. The patients were imaged on the axial plane, in the supine position, and during end-inspiration.

Every necessary measure was taken to prevent the spread of the disease via the imaging procedure. All patients who would undergo chest CT imaging were instructed to wear a face mask throughout the procedure. Disposable bed sheets were used during each examination. The room and used equipment were thoroughly disinfected after each scan. Radiology staff wore a face mask, disposable gloves, gown and safety goggles during the patient admission and image acquisition.

Statistical analysis

The Kolmogorov–Smirnov test and QQ plots were used to check the normality assumptions of the data. All numeric variables distributed non-normally. Age was presented as mean ± standard deviation, whereas other numeric variables were given as median (interquartile range). We used the Mann–Whitney U test for comparison of numeric variables between the two groups. Categorical variables were presented as numbers and percentages. Chi-square was used for comparison of the categorical variables.

All statistical analyses were performed with SPSS 24 (SPSS Inc., Chicago, IL, USA) statistical software package. A p-value < 0.05 was accepted as statistically significant.

RESULTS

General characteristics of the patients

A total of 1410 patients (60.6% female) were included in the study. The mean age was 55.0 ± 16.2 years (min–max: 18–91 years). Of all included patients, only 154 (10.9%) were tested with RT-PCR. The positivity rate of the RT-PCR test was 41.6%.

All patients had at least one symptom and/or history of contact with a COVID-19 positive individual. The most common symptom was cough, which was present in 409 patients (29%). Sore throat and fever were present in 400 (28.4%) and 334 (23.7%) patients, respectively.

The most common comorbid condition among the patients was diabetes mellitus (20.9%), followed by hypertension (10.4%). Only 147 patients (10.4%)

Table 1. Clinicodemographic characteristics, clinical and chest CT features of the entire study cohort

	Patients ($n = 1410$)
Age (years) (median [IQR])	55.0 ± 16.2
Sex *n* (%)	
Female	854 (60.6%)
Male	556 (39.4%)
Frequency of PCR positivity *n* (%) ($n = 154$)	64 (41.6%)
Clinical symptoms *n* (%)	
Sore throat	400 (28.4%)
Fatigue	265 (18.8%)
Myalgia	197 (14.0%)
Anosmia and dysgeusia	73 (5.2%)
Cough	409 (29.0%)
Fever	334 (23.7%)
Comorbidities *n* (%)	
Coronary artery disease	139 (9.9%)
Hypertension	147 (10.4%)
Diabetes mellitus	295 (20.9%)
Chronic obstructive pulmonary disease	134 (9.5%)
Chest CT features (median [IQR])	
Number of chest CTs	1 (1–2)
Cumulative effective dose ($n = 606$)[a] (mSv)	6.02 (5.03–7.61)
Clinical outcomes	
Follow-up place (*n* (%))	
Home	1263 (89.6%)
Hospital	147 (10.4%)
Length of stay in hospital (days)[b] ($n = 51$) (median [IQR])	10 (4–22)
Deceased (*n* (%))	31 (2.2%)

[a]Patients who had two or more chest CT scans.
[b]Length of hospital stay data were available for 51 patients.

were admitted to the hospital for treatment, whereas the rest of the patients were followed up on an outpatient basis. The median length of stay in hospital was 10 days. During the study period, 31 patients (2.2%) died. Table 1 shows the general characteristics and chest CT features of the whole study population.

Chest CT and CED

All study participants underwent at least one chest CT procedure. Of all study subjects, 804 patients (57%) underwent only one chest CT procedure. Six hundred and six patients (43%) had two or more chest CT procedures. Number of patients who had one chest CT was 804 (57.0%), two chest CTs 448 (31.8%), three chest CTs 98 (7.0%), four chest CTs 37 (2.6%), five chest CTs 14 (1.0%), six chest CTs 6 (0.4%) and seven chest CTs was 3 (0.2%; Figure 1).

We calculated total radiation dose only for patients who underwent two or more chest CT procedures ($n = 606$). Because none of the patients who had only one chest CT received a total radiation dose no >5 mSv, which did not exceed the annual allowed radiation dose limit. Hence, the median cumulative effective dose was 6.02 (min–max: 1.67–16.27) mSv (Table 1). The number of patients who were exposed to ≤5 mSv were 149 (24.6%), whereas 457 patients (75.4%) were exposed to >5 mSv. There was no age difference between the patients who received >5 and <5 mSv CED ($p = 0.732$). When we compared the median CEDs between the geriatric group (>65 years) and young and middle-aged patients, there was no difference between the two groups (median CEDs 6.20 (5.03–8.04) and 5.87 (5.01–6.83), respectively, $p = 0.101$). The median CEDs in patients who underwent 2, 3, 4, 5, 6 and 7 chest CT scans are shown in Figure 2.

We compared the clinical characteristics of patients with one chest CT and patients who underwent two or more chest CT procedures. The mean ages were similar in both groups. There was no difference in terms of distribution of the COVID-19 related symptoms between the two groups. On the other hand, all comorbid conditions were more frequent in patients with two or more chest CTs. None of the patients who had only one chest CT was hospitalized, 24.3% of the patients with two or more chest

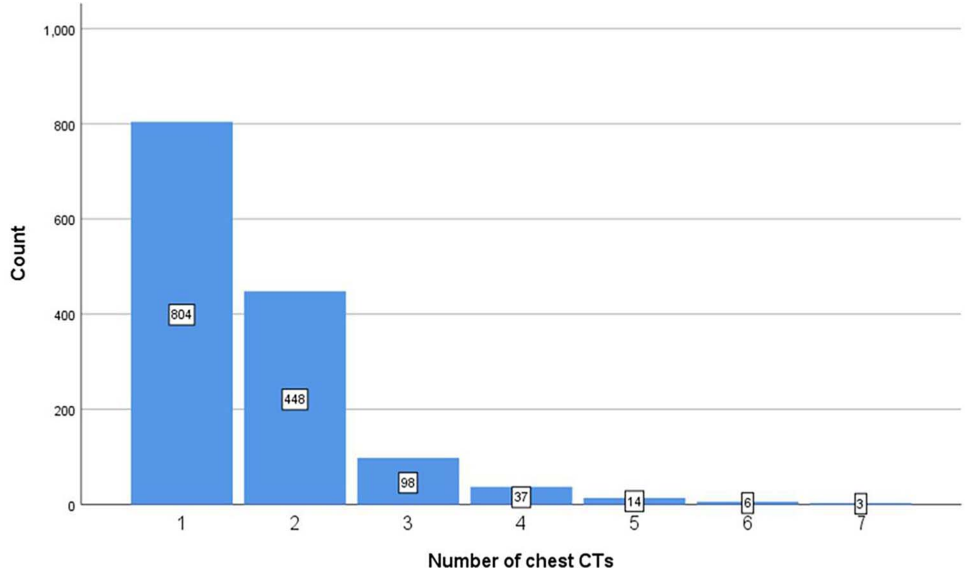

Figure 1: Bar chart showing the distribution of number of chest CTs in the whole study patients.

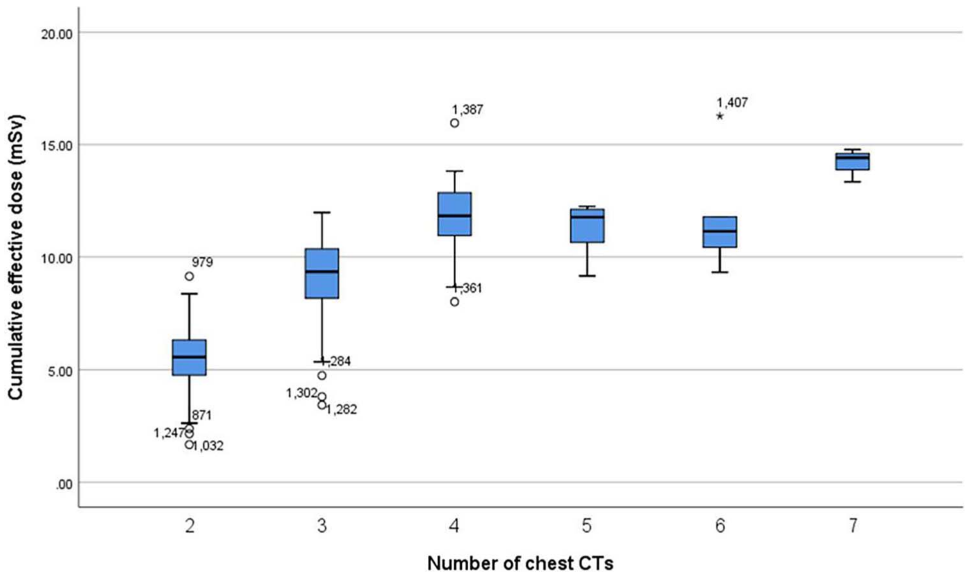

Figure 2: Box plot showing the distribution of mean CEDs according to the number of CTs.

CTs were hospitalized ($p < 0.001$). Mortality rates were comparable between the two groups (Table 2).

In comparison of the deceased and survivor patients, the latter group consisted of significantly more females. Cough, anosmia, and dysgeusia and sore throat were significantly more frequent among the deceased compared to the survivors. Apart from hypertension, comorbid conditions were also significantly more common among the deceased. Predictably, length of hospital stay was significantly longer in the deceased compared to the survivors (Table 3).

DISCUSSION

The salient findings of the present study were as follows: (1) All patients with a COVID-19 contact

Table 2. Comparison of clinicodemographic characteristics and clinical and chest CT features of patients with one and ≥2 chest CTs

	Group		
	Patients with 1 chest CT ($n = 804$)	Patients with ≥ 2 chest CT ($n = 606$)	p-value
Age (year) (median [IQR])	56 (46–63)	55 (42–72)	0.268
Sex *n* (%)			
Female	498 (61.9%)	356 (58.7%)	0227
Male	306 (38.1%)	250 (41.3%)	
Frequency of PCR positivity *n* (%) ($n = 154$)	8 (21.6%)	56 (47.9%)	**0.007**
Clinical symptoms *n* (%)			
Sore throat	237 (29.5%)	163 (26.9%)	0.310
Fatigue	151 (18.8%)	114 (18.8%)	1.000
Myalgia	112 (13.9%)	85 (14.0%)	1.000
Anosmia and dysgeusia	48 (6.0%)	25 (4.1%)	0.145
Cough	224 (27.9%)	185 (30.5%)	0.286
Fever	190 (23.6%)	144 (23.8%)	1.000
Comorbidities *n* (%)			
Coronary artery disease	26 (3.2%)	113 (18.6%)	<**0.001**
Hypertension	33 (4.1%)	114 (18.8%)	<**0.001**
Diabetes mellitus	105 (13.1%)	190 (31.4%)	<**0.001**
Chronic obstructive pulmonary disease	12 (1.5%)	122 (20.1%)	<**0.001**
Chest CT features (median [IQR])			
Number of chest CTs	1	2 (2–3)	
Cumulative effective dose ($n = 606$)[b] (mSv)	–	6.02 (5.03–7.61)	
Clinical outcomes			
Follow-up place (*n* (%))			
Home	804 (100%)	459 (75.7%)	<**0.001**
Hospital	0	147 (24.3%)	
Length of stay in hospital[a] (days) ($n = 51$) (median [IQR])	–	10 (4–22)	
Deceased (n (%))	17 (2.1%)	14 (2.3%)	0.855

[a]Patients who had two or more chest CT scans.
[b]Length of hospital stay data were available for 51 patients.
$p < 0.001$ statistically strong significance

history and/or COVID-19 related symptoms underwent low-dose chest CT irrespective of their RT-PCR test results. (2) Six hundred and six patients (43%) had two or more chest CT procedures. Three patients had seven chest CT scans each. (3) Median CED for patients with two or more chest CTs was 6.02 (min–max: 1.67–16.27) mSv. (4) The number of patients who were exposed to >5 mSv CED was 457 (75.4%).

The gold standard diagnostic test in SARS-CoV-2 infection is a demonstration of the viral nucleic acid with RT-PCR. However, at the initial stages of the pandemic, PCR test assays were limited in many developing countries as well as developed ones. Moreover, turnaround times for PCR testing were very long (2–3 days in Turkey in March 2020), which makes timely triage impossible. Fortunately, chest CT came to the rescue with its high sensitivity and now near-universal presence in developing and developed countries.

At the very outset of the outbreak, chest CT was used extensively for diagnostic purposes in China[(16)]. And the situation was repeated in many other countries at the beginning of their share of the pandemic. Several studies showed high sensitivity of chest CT in patients with suspected COVID-19. In a very recent Cochrane systematic review, Salameh *et al.* included 78 studies comprising 8105 patients who underwent chest CT[(17)]. The authors concluded that chest CT was sensitive but not specific in the diagnosis of COVID-19. Poor study qualities and poor sensitivity of the reference test (PCR) were blamed for the observed low specificity. However, more recent studies also point to the ability of chest CT in differentiating COVID-19 from other viral infections. Teles *et al.* reported a high specificity and positive predictive value for standardized chest CT classification[(18)]. Conduction of randomized controlled studies seems imperative to settle the issue.

Aside from the specificity problem of chest CT in COVID-19, cumulative radiation exposure is another consideration. The multicenter study conducted by Homayounieh *et al.* evaluated CT application

Table 3. Comparison of clinicodemographic characteristics and clinical and chest CT features of deceased and survivor patients

	Group		
	Deceased ($n = 31$)	Survivors ($n = 1379$)	p-value
Age (year) (median [IQR])			
Sex *n* (%)			
Female	8 (25.8%)	846 (61.3%)	**<0.001**
Male	23 (74.2%)	533 (38.7%)	
Frequency of PCR positivity n (%) ($n = 154$)	5 (83.3%)	59 (39.9%)	0.082
Clinical symptoms *n* (%)			
Sore throat	16 (51.6%)	384 (27.8%)	**0.005**
Fatigue	10 (32.3%)	255 (18.5%)	0.062
Myalgia	7 (22.6%)	10 (13.8%)	0.185
Anosmia and dysgeusia	6 (19.4%)	67 (4.9%)	**0.004**
Cough	15 (48.4%)	394 (28.6%)	**0.019**
Fever	12 (38.7%)	322 (23.4%)	0.055
Comorbidities *n* (%)			
Coronary artery disease	9 (29%)	130 (9.4%)	**0.002**
Hypertension	3 (9.7%)	144 (10.4%)	1.000
Diabetes mellitus	16 (51.6%)	279 (20.2%)	**<0.001**
Chronic obstructive pulmonary disease	9 (29.0%)	125 (9.1%)	**0.002**
Chest CT features (median [IQR])			
Number of chest CTs	1 (1–2))	1 (1–2)	0.390
Number of patients with ≥2 chest CTs (*n* (%))	14 (45.2%)	592 (42.9%)	0.855
Median cumulative effective dose ($n = 606$)[a] (mSv)	7.41 (5.67–11.94)	5.99 (5.02–7.57)	**0.029**
Clinical outcomes			
Follow-up place (*n* (%))			
Home	24 (77.4%)	1239 (89.8%)	**0.036**
Hospital	7 (22.6%)	140 (10.2%)	
Length of Stay in hospital (days)[b]	18 (18–29)	8 (4–22)	0.053

[a]Patients who had two or more chest CT scans.
[b]Length of hospital stay data were available for 51 patients.
$p < 0.05$ statistically significance
$p < 0.001$ statistically strong significance

practises in patients with COVID-19 from 28 different countries. The authors reported that there was considerable variation in CT protocols and radiation doses from country to the country and even in different centers in the same country. In 20% of the study centers chest CT examinations were performed multiple times in the same patients[11]. Rawashdeh and Saade reported their concern regarding the detrimental health effects of ionizing radiation in COVID-19 patients[19]. Actually, several studies investigated the place of low- and ultralow-dose chest CT in the diagnosis of COVID-19 as a method of reducing radiation exposure. In a recent study, Steuwe *et al.* reported that the diagnostic performance of chest CT with a mean effective dose of 1.3 ± 0.4 mSv was sufficient without missing any COVID-19 diagnosis[20]. In a comparison study, Shiri *et al.*[21] found that ultralow-dose chest CT images were devoid of critical imaging information that would unfavorably affect diagnostic accuracy. However, when the ultralow-dose CT images could be rendered full-dose with artificial intelligence, the image quality was on par with normal full-dose chest CT. This approach was helpful in reducing radiation exposure. A number of studies also lent support to the role of low-dose CT in diagnosis of COVID-19[22–24].

The radiation dose reduction benefit gained by low-dose chest CT is offset by the repeat of chest CT several times in the same patient. The reasons for repeat CTs vary but generally include a change in the clinical situation of the patient and before discharge to ascertain the resolution of previous pathologic imaging findings. In some studies, it is apparent that many patients underwent repeated chest CT scans, in some cases up to eight CT for a single patient[25]. In some retrospective studies, patients underwent a mean number of four chest CT scans with 5-day intervals[26, 27]. Our results were also in agreement with these studies in that many patients underwent multiple chest CTs during hospitalization or outpatient follow-up. The peak number of chest CT scans was 7 for a single patient in our study.

To limit the unrestricted use and attendant untoward radiation exposure, several radiological societies published recommendations as to the role of chest CT in the diagnosis and follow-up of COVID-19. The American College of Radiology first declared that chest CT should not be used to screen for or as a first-line test to diagnose COVID-19. However, in an update, the ACR justified the use of chest CT as an interim measure until more widespread COVID-19 testing is available with warnings regarding the sensitivity and specificity of chest CT[8]. Then, the Fleischner society published their recommendations regarding the place of chest CT in COVID[28]. The international consensus statement recommended against routine use of chest CT as a COVID-19 screening test in asymptomatic patients. Imaging was not recommended for patients with mild symptoms unless these patients were at risk for disease progression. The major disease progression risks were defined as age >65 years and presence of medical comorbidities. The society justified the use of chest CT in suspected COVID-19 patients with moderate to severe symptoms irrespective of their PCR test results. They also recommended chest CT in recovered patients who develop functional impairment of hypoxia. However, the latter recommendation might increase the already high chest CT numbers further. Because some studies reported fibrotic changes in the lungs after resolution of the infection[29]. However, it is not clear whether chest CT provides findings strong enough to change the management of the patient beyond lung function tests. In Turkey, the Scientific Advisory Committee on COVID-19 chaired by Ministry of Health recommended chest CT in patients with negative initial PCR tests to expedite the triage process. The committee advised against the routine use of chest CT in the evaluation of treatment response[9].

International Commission on Radiological Protection (ICRP) recommends that the acceptable, effective radiation dose should not exceed 5 mSv for community members in 1 year[30, 31]. However, it should be remembered that these limits are generally arbitrary and the relation of ionizing radiation with cancer risk is continuous[32]. Thus, the lower the radiation dose gained from radiological imaging procedures, the better it is for the patient's future health (ALARA: As Low As Reasonably Achievable). In the present study 43% of the patients had two or more CT scans during the 1-month study period. It should be kept in mind that; hospitalization of some patients might have continued beyond our study period and these patients might have undergone additional chest CT scans which would surely increase the mean CED. Some patients underwent a total of 6 ($n = 6$) or 7 ($n = 3$) CT scans that can hardly be justified on the ground of clinical needs of the patients. The median CED of the patients with multiple chest CTs (6.02 mSv) was over annually allowed CED limit of 5 mSv. Moreover, three quarters of the patients were exposed to CED >5 mSv. Since many of these patients will have some long-term pulmonary complications due to COVID-19 lung disease, these patients certainly will be followed and more chest CTs might be ordered adding to the already high CEDs.

We think that the chest CT pattern observed in this study may still be at work in some parts of our country as well as many other countries. Median CEDs were comparable in elderly patients and young and middle-aged patients. However, all comorbidities were more common in patients who had multiple chest CT scans despite no apparent difference between the symptom patterns. Thus, it might be one reason for more doctor orders of chest CTs for patients with chronic medical conditions. Surely, the major drives for performing multiple chest CT studies were limited number, low sensitivity and long turnaround times of RT-PCR tests.

Some limitations of the present work deserve mention: first, we did not evaluate radiological procedures with X-rays other than chest CT although these were limited in number and cumulative radiation dose. Second, this was a single-center retrospective study focused a time period early on the pandemic. Thus, our results cannot be generalized to other countries and possibly the current situation in our country. Because elapsed time from the beginning of the pandemic healed many material and service restrictions, more PCR tests were provided for hospitals all around the world and in Turkey. In addition, a number of bodies published recommendations as to the role of chest CT in the diagnosis and follow-up of COVID-19 patients. We think that a more rational approach might be underway in Turkey and in other developing and developed countries right now. However, particularly for resource-constrained countries, we think that our results will increase the awareness of the caring physicians in terms of the detrimental health outcomes of ionizing radiation. Considering the young age of many patients who underwent repeated CT procedures for COVID-19, the emergence of late effects of increased radiation exposure is more likely in these patients compared with older COVID-19 patients.

One of the strengths of the present study was that a single CT machine was used with a standardized technique. This avoided high variance from distinct procedures as commonly reported in previous radiation exposure studies in different patient populations. Besides, our patient number is over 1500 and, as such, better reflects the situation of radiation exposure. To the best of our knowledge, this is the first single-center report of cumulative radiation dose exposure in COVID-19 patients.

In conclusion, we think similar approaches to ours are at play in many countries around the world due to various reasons despite recommendations of proper use of chest CT from radiological societies. Almost half of our study population of COVID-19 patients had >two chest CTs during the study period. The majority (75%) of patients who had two or more chest CT scans were exposed to >5 mSv CED. Of course, saving lives in urgent care settings are of paramount importance. However, we should not put these patients at risk of future malignancies because of high radiation exposure in a short time period. More rational use of chest CT scans should be a part of COVID-19 patient care. More supplies of RT-PCR tests with high sensitivity and very short turnaround times, along with better physician awareness of the health risks of radiation exposure will certainly curb the unjustifiable enthusiasm of ordering multiple chest CTs in COVID-19 care.

CONFLICT OF INTEREST

The authors declare no conflict of interest to disclose.

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