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Catching the First Wave in the Pandemic: A Retrospective Evaluation of Chest CT Images for COVID-19

Pandemide İlk Dalgayı Yakalamak: COVID-19 için Göğüs BT Görüntülerinin Retrospektif Değerlendirilmesi

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Abstract

Pandemics generally begin in small areas and subsequently spread widely. In order to detect an outbreak in its early stage, observation of the data for small regions is important. The aim of this study to investigate the presence of COVID-19-like pneumonia findings in computed tomography (CT) taken before the COVID-19 pandemic in Turkey. The chest CTs performed in our hospital between December 1, 2019 and March 10, 2020 (study group) and those performed between December 1, 2018 and March 10, 2019 (control group) were retrospectively analyzed. A total of 1,432 chest CT images in the study group and 1,443 chest CT images in the control group were evaluated for COVID-19. The lesion characteristics on CT, length of hospital stay (LOS), and mortality rate were investigated. Typical lung involvement defined for COVID-19 was present in 1.39% (n=20/1,432) of CTs in the study group and 0.49% (n=7/1,443) in the control group (p=0.011). Seventy-five percent (n=15/20) of the study group were male, and the mean age of the patients was 51.8 (±17.1) years. All the patients in the study group had at least one of the symptoms of COVID-19, such as fever, cough, and respiratory distress. Ninety percent (n=18/20) of the patients in the study group had ground-glass opacities that showed a predominantly peripheral distribution. Five of these had accompanying consolidation and one had a reverse halo sign. According to clinical records, in-hospital mortality developed in seven of 20 patients (35%), the LOS was 5.5±6.2 days, and the median time from the symptom onset to admission was 4 (range: 1-12) days. Our study reveals that the onset of COVID-19 or a similar disease is more likely to occur earlier than first reported in the country.

Keywords: COVID-19, Early detection, Computed tomography, Epidemiology, Pandemic.

Özet

Pandemiler genellikle küçük alanlarda başlar ve daha sonra geniş bir alana yayılırlar. Bir salgını erken aşamada tespit etmek için küçük bölgelerdeki verilerin gözlemlenmesi önemlidir. Bu çalışmanın amacı Türkiye'de COVID-19 pandemisinden önce çekilen bilgisayarlı tomografi (BT) görüntülerinde COVID-19 benzeri pnömoni bulgularının varlığını araştırmaktır. Hastanemizde 1 Aralık 2019-10 Mart 2020 (çalışma grubu) ve 1

Aralık 2018-10 Mart 2019 (kontrol grubu) tarihleri arasında yapılan göğüs BT'leri geriye dönük olarak incelendi. Çalışma grubundaki toplam 1432 göğüs BT görüntüsü ve kontrol grubundaki 1443 göğüs BT görüntüsü COVID-19 için değerlendirildi. BT'de lezyon özellikleri, hastanede yatış süresi (HYS) ve mortalite oranı araştırıldı. COVID-19 için tanımlanan tipik akciğer tutulumu, çalışma grubundaki BT'lerin %1.39'unda (n=20/1432) ve kontrol grubunun %0.49'unda (n=7/1443) mevcuttu (p=0.011). Çalışma grubunun yüzde yetmiş beşi (n=15/20) erkek olup, hastaların yaş ortalaması 51.8’dir (±17,1). Çalışma grubundaki tüm hastalarda ateş, öksürük ve solunum sıkıntısı gibi COVID-19 semptomlarından en az biri vardı. Çalışma grubundaki hastaların yüzde doksanı (n=18/20) ağırlıklı olarak periferik dağılım gösteren buzlu cam opasitelerine sahipti. Bunlardan beşinde bu bulgulara konsolidasyon eşlik ederken ve birinde ters hale işareti vardı. Klinik kayıtlara göre 20 hastanın yedisinde (%35) hastane içi mortalite gelişti, HYS 5.5±6.2 gün ve semptom başlangıcından başvuruya kadar geçen medyan süre 4 (aralık: 1-12) gündü. Çalışmamız, COVID-19 veya benzeri bir hastalığın başlangıcının ülkemizde ilk bildirilenden daha erken ortaya çıkma olasılığının yüksek olduğunu ortaya koymaktadır.

Anahtar Kelimeler: COVID-19, Erken teşhis, Bilgisayarlı tomografi, Epidemiyoloji, Pandemi.

Introduction

In December 2019, a pneumonia case cluster of undetermined origin emerged in Wuhan, China, and this new situation began to be monitored by the World Health Organization (WHO) [1]. The cause of the infections that evolved into an epidemic was confirmed as the 2019 novel coronavirus (2019-nCov) on January 7, 2020, when Chinese scientists isolated the virus [2]. Later, on the basis of the similarity of its genomic structure to the virus causing severe acute respiratory syndrome (SARS-CoV), this virus was named SARS-CoV-2 by the international virus taxonomy committee [3]. The disease caused by the virus was defined as the coronavirus disease 2019 (COVID-19) [1]. WHO declared the disease a pandemic and a global public health emergency on March 11, 2020, considering that it could easily spread from person to person via respiratory droplets [4]. On March 10, 2020, a Turkish citizen who was identified to be infected while traveling from Turkey to Europe was announced as the first SARS-CoV-2 case in the country [5,6]. The first death in Turkey was reported on March 15, 2020, and the spread of the disease throughout the country was confirmed on April 1, 2020 [6]. On April 18, 2020, Turkey was the country with the highest number of laboratory-confirmed cases in the Middle East by surpassing Iran, and on April 20, 2020, the total number of cases surpassed China [7,8]. A precise characterization of the initial epidemic spread and transmission dynamics is more than expected in consideration of the need to improve statistical and epidemiological models. However, verifying this information can be difficult. Currently, the reverse transcriptase polymerase chain reaction (RT-PCR) test, which is used to detect COVID-19 from nasopharyngeal swabs, is the gold standard diagnostic test; however, RT-PCR cannot detect a previous infection [9]. Serological tests do not provide information on the precise time of infection, and the low sensitivity of serological tests and the rapid disappearance of antibodies against viral antigens in symptomatic and asymptomatic patients decrease the value of retrospective serological examinations [9,10]. However, whether the thoracic computed tomography (CT) findings of the pre-pandemic period reveal if the disease was present before the first confirmed case in a country is a topic worth investigating. For COVID-19 cases, most of which present with pneumonia, chest CT has high clinical sensitivity in the diagnosis and follow-up of the disease [11,12]. Chest CT can show characteristic findings including ground-glass areas with or without signs of reticulation, called the crazy paving pattern, consolidative pulmonary opacities in advanced stages, and the reverse halo sign [1,11]. In addition, the often peripheral predominant distribution of lesions has been described as a typical finding in the literature [13]. Viral pneumonias such as influenza and organized pneumonia causing acute lung injury (e.g., due to drug toxicity or secondary to connective tissue diseases or idiopathic organizing pneumonia) can be considered in the differential diagnosis of these findings [4,14].

In this study, the presence of typical radiological findings of the COVID-19 pneumonia was retrospectively investigated in the chest CTs performed between December 1, 2019 and March 10, 2020 in one of the largest referral hospital, located in the Southeast of Turkey, which is also in close commercial and touristic relationships with Iran, a country where the first case of COVID-19 had been reported earlier than Turkey. In addition, the CT images from one year earlier were screened, and the frequency of viral pneumonia between the two periods was investigated.

Material and Method

Study population

Local ethics committee approval was received for this single-center study (date: 21.12.2020, session: 22). Informed consent was waived given the retrospective nature and characteristics of the study. For this study, chest CTs performed in our hospital between December 1, 2019 and March 10, 2020 (study group) and those performed between December 1, 2018 and March 10, 2019 (control group) were retrospectively analyzed. CT images obtained for non-infection indications (trauma and oncology) were excluded from the study. A total of 1,432 chest CT images in the study group and 1,443 in the control group were evaluated with reference to the consensus guide of the Radiological Society of North America (RSNA) experts for COVID-19 [15]. The demographic characteristics of the patients, clinical and laboratory findings, characteristics of the lesions on CT, length of hospital stay, time from symptom onset to admission (days), comorbidities (chronic obstructive pulmonary disease, ischemic heart disease, diabetes, or hypertension) and mortality were obtained from the medical records.

CT protocol and evaluation

All chest CT examinations were performed using two 16 multi-slice CT scanners (Toshiba Aquilion, Toshiba Corporation, Medical Systems and Somatom Definition, Siemens Healthineers). CT images were obtained with the patient in the supine position at end-inspirium. The scanning ranged from the bilateral apex to base. The main scanning parameters were as follow: tube voltage, 110-130 kV; tube current-time product, 50-350 mAs; pitch, 1.25; matrix, 512 × 512; slice thickness, 10 mm; and reconstructed slice thickness, 0.625-1.250 mm. All CT images were obtained from the picture archiving and communication system (PACS) and reviewed by two different radiologists, M.T and E.K. (with eight and nine years of experience in chest imaging, respectively). The radiologists were blinded to the clinical and laboratory data. The chest CT images were evaluated based on consensus regarding the presence, distribution, and characteristics of the lesions. Patients with imaging findings identified and typical for COVID-19 pneumonia were recorded. The CT images were analyzed according to the typical appearance of COVID-19 pneumonia and commonly reported imaging features. These findings included peripheral and bilaterally distributed ground-glass opacities (GGO) with or without consolidation, visible intralobular lines (crazy-paving pattern), and the reverse halo sign.

Statistical analyses

All analyses were performed using SPSS software v. 22.0 (IBM SPSS Statistics Version 22.0. Armonk, NY: IBM Corp.). The variables were divided into two groups as categorical and continuous. Categorical variables were expressed as numbers and percentages and compared with the $\chi 2$ test. Continuous variables were expressed as mean ± standard deviation. The statistical significance level was accepted as $p < 0.05$.

Results

In the study group, 1.39% (n = 20/1432) of the chest CT examination performed between December 1, 2019 and March 10, 2020 had typical lung involvement defined for COVID-19, which was then classified as non-specific interstitial pneumonia. The control group was defined based on 1,443 chest CT scans performed between December 1, 2018 and March 10, 2019. The CT findings compatible with COVID-19 were detected in only seven of the control images (0.49%), and the frequency of these findings significantly differed from the study group (p = 0.011). The demographic data of both groups were similar, with 75% of the study group (n = 15) consisting of male and the mean age of the patients being 51.8 ± 17.1 (range: 24-85) years (p = 0.121 and p = 0.162, respectively) (Table 1). All the patients in the study group had at least one of the symptoms of COVID-19, such as fever, cough, and respiratory distress. Sputum culture was performed in 12 (60%) of 20 patients, and all were found to be negative. When the chest CTs in the study group were examined, 90% of the patients (n = 18/20) had GGOs that infiltrated the parenchyma of both lungs and showed a predominantly peripheral distribution. Five of these had an accompanying consolidation and one had the reverse halo sign (Figures 1, 2 and 3).

Table 1. Demographic, clinical and laboratory data of the patients in the study and control groups.

	Study group (n = 20)	Control group (n = 7)	P value
Male gender, n (%)	15 (75)	3 (42.9)	0.121
Age (years)	51.8 ± 17.1	61.3 ± 11.8	0.162
Lymphopenia frequency, n (%)	11 (55)	6 (85.7)	0.148
White blood cell count (10^3 cells/µL)	9.2 ± 6.8	12.3 ± 5.4	0.255
Lymphocyte count (10^3 cells/µL)	1.49 ± 0.89	1.55 ± 0.93	1.000
Neutrophil count (10^3 cells/µL)	7.1 ± 6.1	9.8 ± 4.9	0.149
Platelet count (10^3 cells/µL)	210.1 ± 79.8	242.9 ± 82.4	0.400
C-reactive protein (mg/L)	133.1 ± 87.1	78.9 ± 60.2	0.255
Mortality rate, n (%)	7 (35)	2 (28.6)	0.571

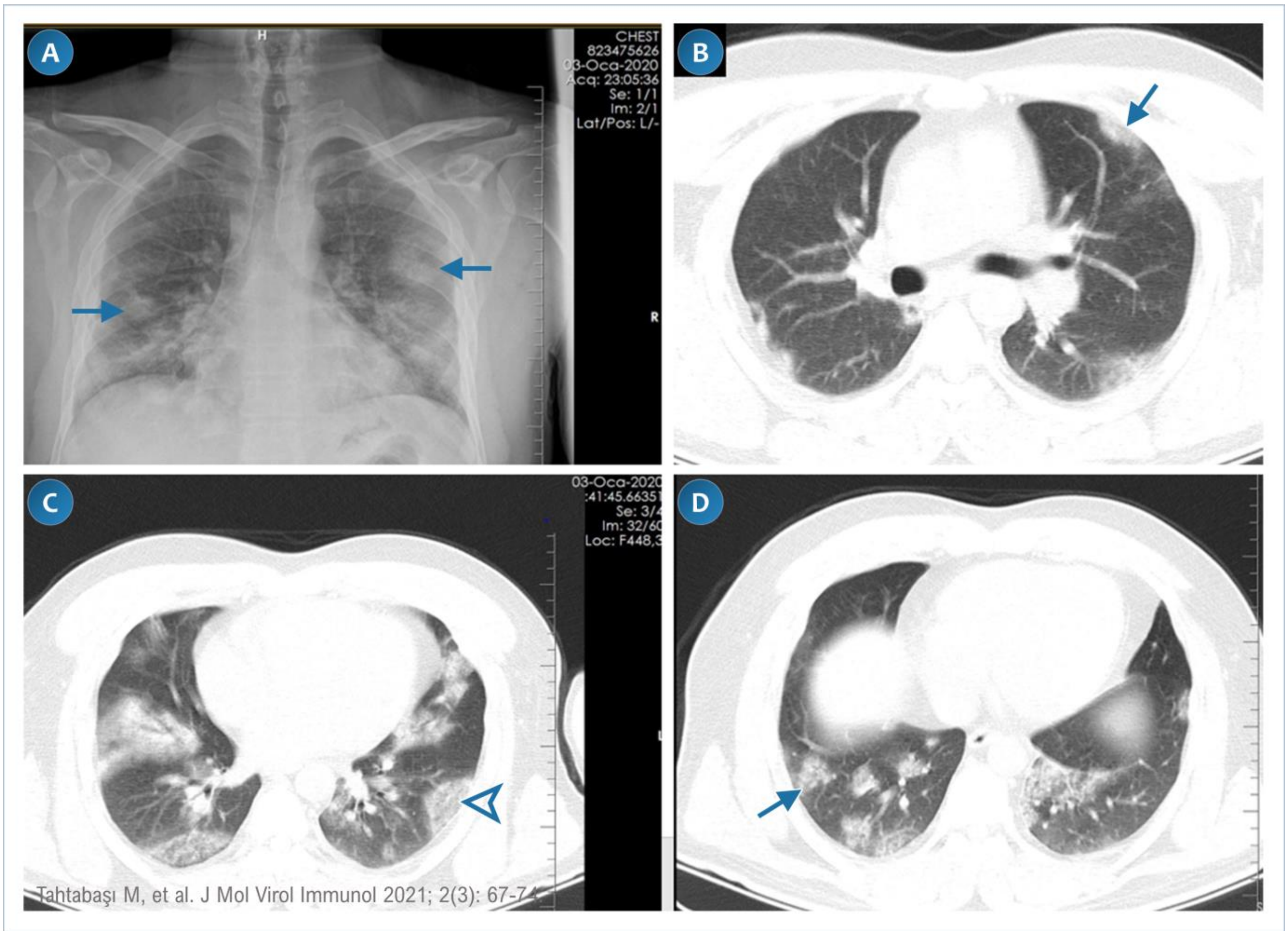

Figure 1: Chest X-ray and CT images of a 33-year-old male patient taken in January 2020. X-ray image (**A**) shows peripherally distributed opacities. CT images in the lung window (**B**,**C**,**D**) shows peripherally distributed ground glass opacities, and the reverse halo sign (arrowhead) with consolidated periphery and ground glass opacities in the center.

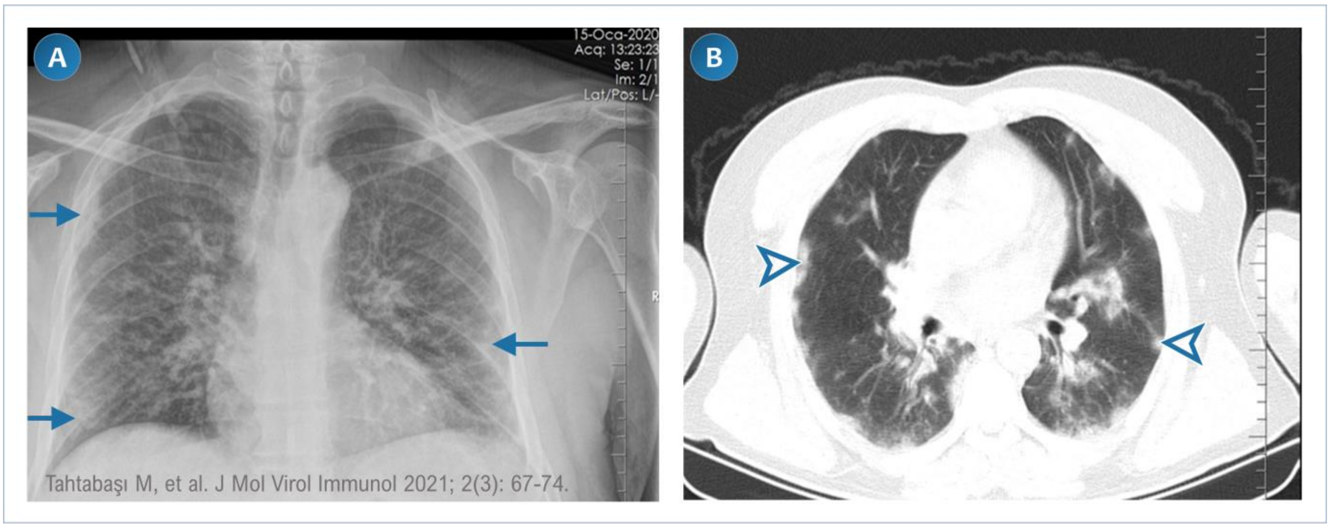

Figure 2: Chest X-ray and CT images of the lung window of a 50-year-old male patient taken in January 2020. X-ray (**A**) and CT (**B**) images show peripherally distributed ground glass opacities.

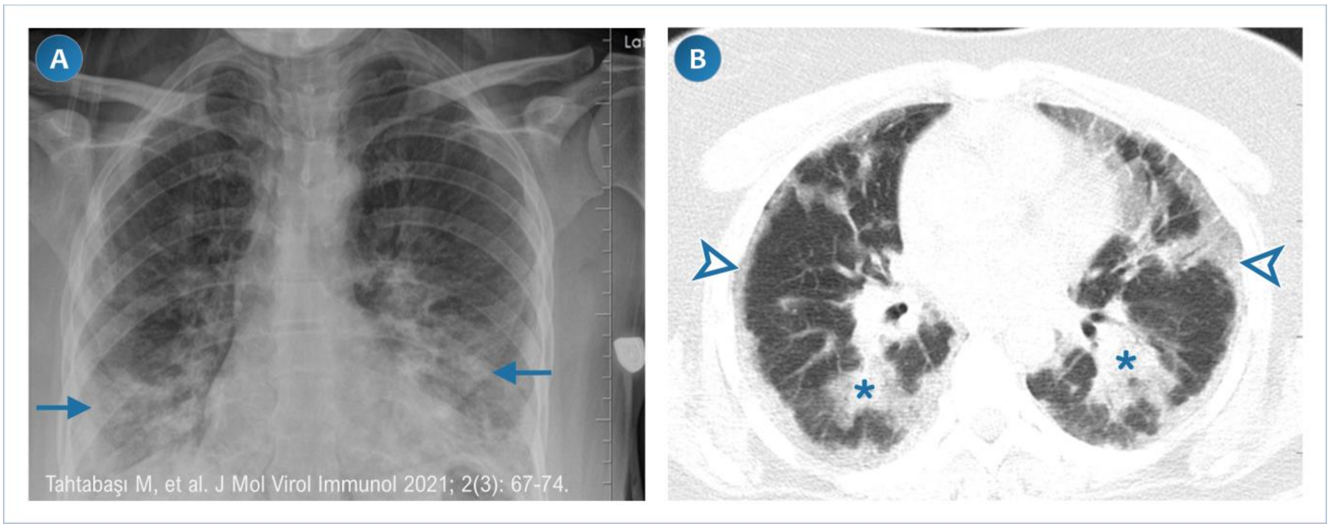

Figure 3: Chest X-ray and CT images in the lung window of a 39-year-old female patient taken in January 2020. (**A**) X-ray images show symmetrical opacities (arrows) in the lower zones of the lung. (**B**) CT images show ground glass opacities (arrowheads) located in the peripheral and subpleural parts of the lung and patchy consolidations (asterisk) in the lower lobes.

In addition, 10% (n = 2) of the patients had CT findings compatible with acute respiratory distress syndrome (ARDS). Twenty percent of the patients (n = 4) had comorbidities: chronic obstructive pulmonary disease (COPD) was present in three and COPD, ischemic heart disease, and hypertension in one patient. According to clinical records, in-hospital mortality developed in seven (35%) of 20 patients, of whom three had comorbid diseases. The mean hospitalization time of the cases in the study group was 5.5 ± 6.2 (range 1-25) days, and the median time from symptom onset to admission was 4 (range: 1-12) days. The laboratory findings of the patients in the study group revealed high C-reactive protein (CRP) in all patients and lymphopenia in 11 patients (55%). Table 1 shows the clinical and laboratory data of the study and control groups.

Discussion

In the last week of February 2020, COVID-19 cases began to be reported from European countries such as Italy, Germany, France and Spain and quickly spread to all European countries [16]. In an epidemiological study in Italy [17], it was reported that COVID-19 cases had emerged in the country long before the first cases were reported, and these patients had been diagnosed with other viral pneumonias such as influenza and adenovirus. Similarly, bilateral GGOs with a predominantly peripheral distribution were detected in the CTs of the patients included in our study, and it was determined that these findings, which were also found in patients with COVID-19, had been reported as atypical pneumonia. Although CT is not a specific method to distinguish COVID-19 from other viral pneumonias, the development of mortality in 35% of the cases in our study and the rapid course of clinical progression raise strong suspicion that these patients may be associated with the COVID-19 pandemic. This hypothesis is further supported by the high rate of viral pneumonia in the CT images screened in our study group compared to the previous year (control group) ($p = 0.011$). Elevated CRP associated with the severity of the immune response, other laboratory findings, and males being more affected also indicate that these infections may have been associated with COVID-19 [18]. In this context, according to the data of our study, it can be predicted that the onset of the pandemic in Turkey may have been before the date when the first case was reported. This information may be an important basis for planning early and rapid responses to similar outbreaks that may occur in future. We consider that an effective early warning system can be established for similar outbreaks by establishing an infrastructure to support syndromic surveillance systems used in the monitoring of influenza and influenza-like illness (ILI) and severe acute respiratory disease (SARI) with newly developed software programs (artificial intelligence-based) to monitor unexpected changes in CT data or by integrating recorded CT data into surveillance programs using other new technologies [19]. Many studies on this subject suggest that artificial intelligence-based diagnostic tools are very accurate in detecting the presence of SARS-CoV-2 using radiological imaging data and can be used as decision support tools [20].

One of the most frequently defined abnormal findings in the CT scans of patients with COVID-19 is GGOs. In addition, consolidation, lower lobe involvement and predominantly peripheral distribution are among the frequently described findings [4]. In light of these imaging findings, some authors suggest that every suspected patient should undergo chest CT, suggesting that RT-PCR may provide false negative results at the first stage of the disease [21]. However, these imaging findings are not specific to COVID-19 since they can also be seen in other viral pneumonias, such as influenza, adenovirus, and non-infectious diseases [22]. In recent studies, in COVID-19 pneumonia, a mixed pattern of predominantly bilateral GGOs, followed by GGOs and consolidation have been observed. Similarly, this involvement is dominant in non-COVID-19 viral pneumonias. However, compared with other viral pneumonias, COVID-19 demonstrates higher prevalence of peripheral distribution and involvement of the upper and middle lobes [23]. The lesions on CT being distributed peripherally in the current study can be interpreted in favor of COVID-19 pneumonia [13]. In addition, other findings such as ARDS or respiratory failure, shock, and multi-organ dysfunction may occur in the most severe form of COVID-19, the type defined as clinically critical disease [24]. In the current study, imaging findings compatible with ARDS were found in two patients.

On the other hand, the use of chest CT as a primary tool for screening patients suspected to have COVID-19 poses significant problems [25]. This approach will result in an increased number of CT examinations, even in clinically stable patients, which will not only increase costs and exposure to the harmful effects of ionizing radiation but also lead to reduced access to imaging units since the entire room needs to be thoroughly sterilized after each suspected case of COVID-19 [23,25]. Furthermore, CT units can function as a source of COVID-19 transmission. Therefore, the American College of Radiology (ACR) warrants caution in adopting CT as a standard approach in suspected COVID-19 cases, especially in the early stages of the disease considering that it may deter the patient from viral testing, quarantine, and appropriate treatment [26]. In this context, unnecessary imaging should be reduced by establishing a common decision mechanism and close communication between radiologists and clinicians to determine CT indications. Although CT is not always diagnostic due to the similar radiological findings of COVID-19 and other viral pneumonias, radiologists' expertise and experience in relation to minor details may play a role in the early diagnosis of new viral outbreaks. A meta-analysis study shows that the incubation period from the onset of symptoms and the first clinical visit of COVID-19 is longer in COVID-19 (4.92 days) compared to other acute respiratory viral infections, such as influenza A (1.43-1.64 days), parainfluenza (2.6 days), respiratory syncytial virus (4.4 days), and rhinovirus (1.4 days) [27]. In addition, the median incubation time for SARS was estimated at 4.0 days in 2009 [28]. The longer incubation period of COVID-19 is seen as one of the main factors that can help explain the rapid spread of previous coronavirus infections, namely SARS-CoV and Middle East respiratory syndrome-coronavirus [18]. In the current study, the time from the first onset of symptoms to clinical presentation (median value: 4 days) was found to be higher among the patients with COVID-19 compared to than that of non-COVID-19 viral pneumonias. Even this information is sufficient to warrant clinicians to be alert to the possibility of an unusually different viral agent. The most important limitations of this study are the retrospective design and the small number of patients. In addition, due to the lack of a RT-PCR test for patients with viral pneumonia, we were not able to differentiate between COVID-19 and other viral pneumonia. Nevertheless, we consider that the current study will help raise awareness for the early detection of possible future pandemics, such as COVID-19.

Conclusion

Our study shows that COVID-19 or a similar pandemic is more likely to occur earlier than the first reported case in a country. Given the complexity of determining the onset, emergence and acceleration phase of a pandemic, such situations require a multifaceted and rapidly adapting public health response, including time to develop agent-specific vaccines. It is considered that radiological imaging methods, especially artificial intelligence-based models, will play an important role in detecting possible epidemics at an early stage since it seems difficult for clinicians who first encounter patients to detect the onset of the pandemic observationally.

Ethics committee approval: Ethics Committee approval for the study was obtained from the local ethic committee (date: 21.12.2020, session: 22)

Informed consent: Informed consent was waived given the retrospective nature and characteristics of the study.

Conflict of interest: The authors have no conflicts of interest to declare.

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